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Research Article

BJMP 2015;8(4):a835

Comparing the use of traditional sites and alternative sites puncture for determination of blood glucose by glucometer

Crisafulli Cristiano, Massimo Catanuso, Carmelo Di Gregorio, Adriana Di Gregorio, Gaetano Profeta and Antonino Di Guardo

Abstract

Self-monitoring of blood glucose (SMBG) is important in evaluating the efficacy of prescribed anti-hyperglycaemic therapies and can help the patient better understand the importance of achieving glycaemic control. Pain related to puncture of the fingertip, needed for determination of blood glucose, can notably reduce compliance of patients using self-monitoring devices. The use of glycated haemoglobin, while providing a measure of glycaemic control over the past 2-3 months, is an average of pre- and post-prandial glycaemia and does not take into account glycaemic variability, which is an important cardiovascular risk factor that can be assessed by SMBG. The search for sites as an alternative to the fingertip that are associated with less pain and good reproducibility and accuracy of blood glucose measurements is an area of growing interest. The present study enrolled 5 general practitioners and 70 patients with diabetes and without diabetes-related or neurological/vascular complications that could alter pain perception. Traditional and periungual puncture sites were assessed. In contrast to the fingertip, no pain was perceived at the alternative site, while there was no significant difference in the values of blood glucose obtained using traditional and alternative sites.

Abbreviations: SMBG - Auto Monitoring Glycaemic, HbA1c - Haemoglobin glycated, VAS - Visual Analogue Scale

The increasing collaboration between diabetologists and general practitioners (GPs) (e.g. the IGEA project) has resulted in the GP taking a more relevant role in management of patients with diabetes. Just as measurement of arterial blood pressure has become an important tool in follow-up of patients with hypertension by the GP, SMBG has become a valuable tool to evaluate glycaemic control. In particular, self-monitoring of both blood pressure and glycaemia are important to assess the efficacy of prescribed therapies, and can help the patient to better understand the importance of control of blood pressure and blood glucose.

Several instruments for measurement of blood pressure have been validated by important medical societies involved in hypertension, and much effort has been given to compliance and patient comfort. However, less attention has been dedicated to glucometers. In particular, little consideration has been given to patient compliance, and SMBG is often perceived as an agonising experience. Moreover, hourly pre-visit glucose curves for glycaemic control, even if important, do not have the same value as a standard control over 2 to 3 months between visits. In addition, after an initial period of "enthusiasm" the fear and hassle of pricking oneself and the unpleasant feeling of pain often cause the patient to abandon SMBG.

A literature search on PubMed using the term “self-measurement of blood glucose (SMBG) and pain” retrieved only two publications, demonstrating a general lack of interest of the medical community. However, SMBG can be of important diagnostic-therapeutic value. Pain related to skin pricks on the fingertip, needed for determination of glucometric blood glucose, can significantly reduce compliance to SMBG, thus depriving the physician of a useful tool for monitoring the efficacy of anti-hyperglycaemic therapy and glycaemic control. Moreover, HbA_{1c} has clear limitations, even if it provides a good idea of glycaemic control over the past 2-3 months, as it is a mean value of pre- and post-prandial blood glucose. It does not, therefore, measure glycaemic variability, which is an important cardiovascular risk factor. Thus, more research is needed into puncture sites as an alternative to the fingertip that are associated with less pain, which could favour greater use of SMBG.

Another problem of significant importance concerns the reproducibility and accuracy of blood glucose measurements. In the traditional method, blood samples for self-monitoring are taken from the fingertip of any finger using a lancing device with a semi-rigid prick (Figs. 1 and 2). The large blood vessels in the derma of the fingertip (Fig. 3) are lanced, and a drop of blood is obtained for the glucometer. All lances are optimised to prick the skin at a depth greater than 0.5 mm with a variability of ± 0.2 mm (Fig. 4).

Unfortunately, by pricking the fingertip at this depth, numerous tactile corpuscles in the dermis are also touched, causing the unpleasant sensation of pain. In a recent study by

Koschinsky[1] on around 1000 patients with type 1 (T1D) and type 2 diabetes (T2D), about one-half (51%) referred that they normally pricked themselves on the side of the fingertip because it is less painful.

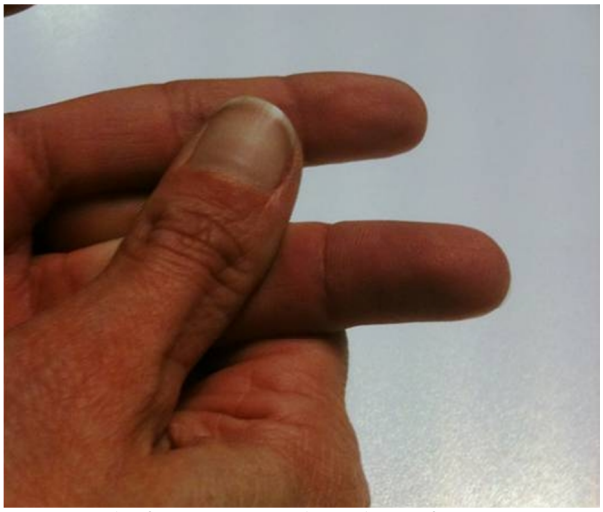

Figure 1. The fingertip as a traditional site of puncture using a lancet.

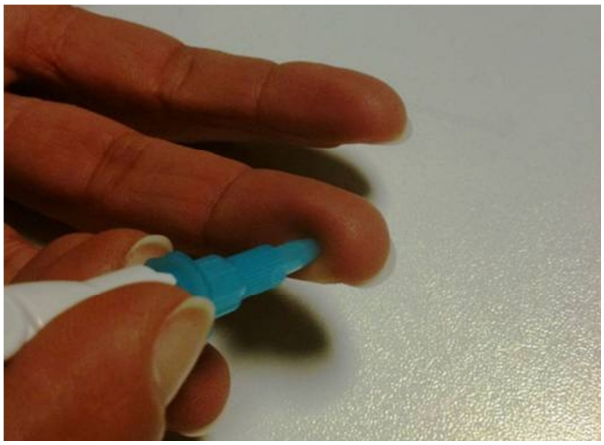

Figure 2. Traditional method for self-monitoring of blood glucose.

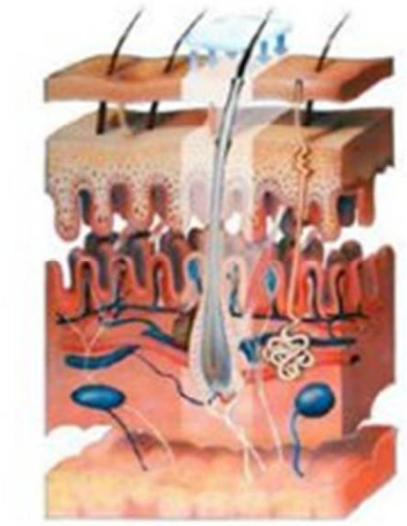

Figure 3. Vascularisation of derma.

However, almost one-third (31%) used the centre of the fingertip, which is the site associated with the most pain. Other sites of puncture on the fingers are used much less frequently (5%), while 12% used other places on the body. It is also interesting to see how many times patients reused the lancet: 10% once, 19% for 2-4 times, 22% for 5-7 times, 25% for 8-10 times and 21% for more than 11 times. Pricking oneself [2] several times daily for years is not only troublesome for patients, but also leads to the formation of scars and callouses, and reduces fingertip perception and tactile sensitivity. Notwithstanding, alternative sites of puncture such as the arm, forearm and abdomen have not been evaluated in a systemic manner.

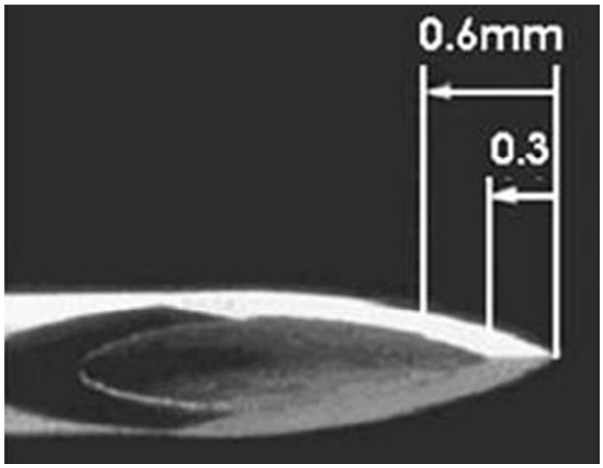

Figure 4. Traditional lancet.

Other sites of puncture on the fingers are used much less frequently (5%), while 12% used other places on the body. It is also interesting to see how many times patients reused the lancet: 10% once, 19% for 2-4 times, 22% for 5-7 times, 25% for 8-10 times and 21% for more than 11 times. Pricking oneself [2] several times daily for years is not only troublesome for patients, but also leads to the formation of scars and callouses, and reduces fingertip perception and tactile sensitivity. Notwithstanding, alternative sites of puncture such as the arm, forearm and abdomen have not been evaluated in a systemic manner.

The objective of the present study is to compare alternative sites of puncture using a new semi-rigid lancet and determine if blood glucose values are similar to those obtained using traditional methods. A new puncture site was chosen, namely the area proximal to the nail bed of each finger. The sensation associated with puncture (with or without pain) was used to compare the two groups. Pain was assessed with a visual analogue scale (VAS). Blood glucose was measured in the morning after 12 hours of fasting.

Materials and methods

The present study enrolled 5 general practitioners and 70 patients with diabetes and without diabetes-related (micro-albuminuria, retinopathy, arterial disease of the lower limbs) complications. In addition, patients with diabetic neuropathy or neurological/vascular complications that could alter pain perception were excluded. The study population was composed of 20 women and 50 men with a mean age of 47.8 ± 15.3 years

and a mean duration of diabetes of 11.4 ± 10.3 years; 34.3% had T1D and 65.7% had T2D. The study was carried out according to the standards of Good Clinical Practice and the Declaration of Helsinki. All patients provided signed informed consent for participation.

Semi-rigid lancets were provided by Terumo Corporation (Tokyo, Japan) and consisted in a 23-gauge needle that was remodelled to permit less painful puncture than a traditional lancet (Fig. 5). Punctures (nominal penetration from 0.2 to 0.6 mm) were made at a depth variation of ± 0.13 mm. In addition, a novel puncture site was used, namely the area proximal to the nail bed of each finger (Figs. 6-8). In this area of the finger, blood flow is abundant and it is easy to obtain a blood sample. Moreover, the area has fewer tactile and pain receptors than the fingertip, and thus when lanced less pain is produced.

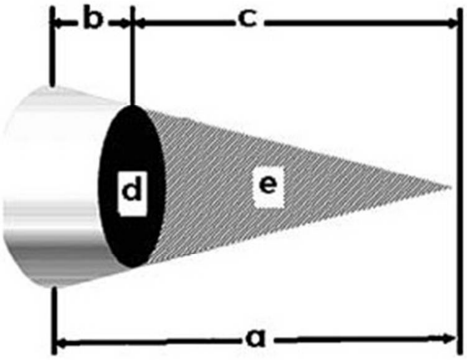

Figure 5. New lancet

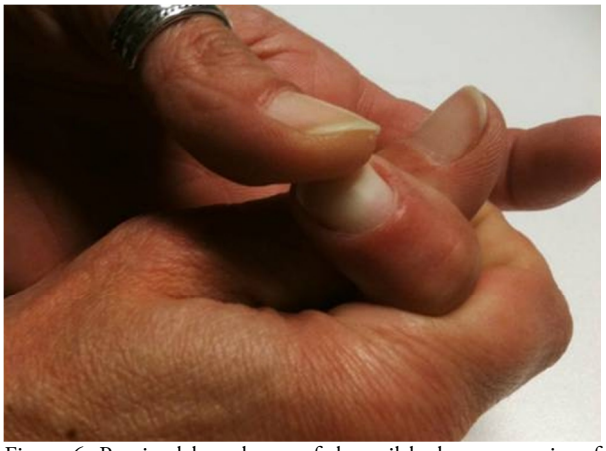

Figure 6. Proximal lateral area of the nail bed as a new site of puncture.

Six fingers were used in a random fashion to evaluate puncture of the anterior part of the finger, the periungual zone and the lateral area of the fingertip (depth 0.2-0.6 mm), and compared to fingertip puncture at a depth of 0.6 mm. The sensation provoked by puncture (with or without pain) was used to compare groups. Pain was evaluated using a VAS ranging from 'no pain' to 'worst pain imaginable'. The VAS is a unidimensional tool that quantifies the subjective sensation such as pain felt by the patient and considers physical, psychological and spiritual variables without distinguishing the impact of the different components.

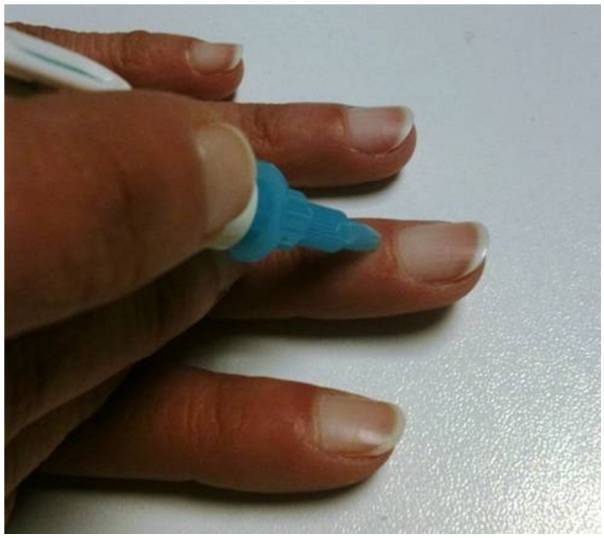

Figure 7. Method of lancing.

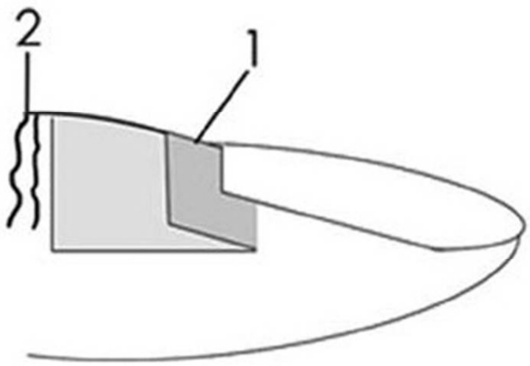

Figure 8. Site of lancing

Blood glucose was measured in the morning after 12 hours of fasting. The Fine Touch glucometer used was provided by Terumo Corporation (Tokyo, Japan). Statistical analysis was carried out using Fisher's two-sided test. Differences in blood glucose with the two methods were analysed using Wilcoxon matched pairs signed ranks test. A P value <0.05 was considered statistically significant.

Results

Pain was not perceived in 90% and 94.28% of subjects punctured in the lateral area of the fingertip at a depth of 0.2 and 0.3 mm, respectively. At a depth of 0.4 mm, 67.14% of subjects did not perceive pain, while at 0.5 mm and 0.6 mm, 47.14% and 17.14% of subjects did not feel pain, respectively. There was no significant difference in pain considering punctures at 0.2 or 0.3 mm, while significant differences were seen between 0.2 and 0.4 mm ($p < 0.05$), 0.5 mm ($p < 0.001$) and 0.6 mm ($p < 0.001$). All subjects who performed puncture in the central zone of the fingertip referred a painful sensation.

Using a periungual puncture site, pain was not referred by any subject, although a bothersome sensation was noted by some. The same results were obtained for all fingers used. Blood

glucose levels obtained using traditional and alternative puncture sites were highly similar with no significant differences between groups (134.18 mg/dl ± 5.15 vs. 135.18 mg/dl ± 5.71 mg/dl; p = 0.5957).

Discussion

The present study evaluated the use of alternative puncture sites that are associated with less pain. These encouraging results undoubtedly warrant further investigation in a larger cohort, but nonetheless suggest that compliance with SMBG can be optimised. The use of the area close to the nail bed allowed high quality blood samples to be obtained for measurement of blood glucose, with an accuracy that was the same as that seen using the fingertip. The design of the lancet used herein was also associated with a lower perception of pain, which is composed of a hypodermic needle in a rigid casing that prevents accidental needle sticks both before and after use. Thanks to the needle point that was made using a triple-bevel cut, epidermal penetration is less traumatic and as a consequence less painful. This further favours rapid recovery of tactile function of patients with T2D. This allows the use of a larger transversal section using a puncture with less depth, and less involvement of nerves present in skin. In addition, the characteristics of the novel lancing device (Fine Touch, Terumo Corporation, Tokyo, Japan) allows adjusting the depth of puncture to the characteristics of each patient (e.g. in children, adolescents and adults).

The depth of penetration of the lancet can be varied from 0.3 to 1.8 mm with a self-incorporated selector; the maximum deviation of the lancing device in terms of depth is approximately 0.1 mm. Due to the possibility to select a minimal depth of only 0.3 mm, it can be used at alternative sites that allow a reduction in the frequency of samples taken from the fingertip. In theory, compared to traditional lancets, this would allow less perception of pain even at traditional sites as well as at periungual zones, and it was our intention to compare the different types of lancets to reinforce this idea. No puncture-related complications were reported, and another fundamental aspect that is not reported in other studies comparing traditional and alternative puncture sites is that no differences in blood glucose were observed.

In conclusion, it is our belief that a new type of finger lancet that decreases or eliminates pain associated with lancing merits additional consideration. Further studies are warranted on larger patient cohorts to confirm the present results. If validated, this would enable patients with diabetes - especially those who need to take several daily blood glucose samples - to perform SMBG with greater peace of mind and less distress.

Competing Interests
None declared

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Research Article

BJMP 2015;8(4):a833

Socio-demographic correlates of substance use disorder patients seeking de-addiction services in Kashmir India -A cross sectional study

Nazima Bashir, Ajaz Ahmad Sheikh, Sufoora Bilques and Muhammad Mudasir Firdosi

Abstract

Background: Kashmir valley is thought to be one of the hardest hit places with drug use and the scenario worsened by the prevailing turmoil. The present study was undertaken to find the epidemiological profile and pattern of drug use in patients seeking treatment at De-addiction Centres in Srinagar India.

Methods: The present cross sectional study, was conducted at two Drug De-addiction and treatment Centers in Srinagar. Total of 125 Substance Use Disorder Patients were interviewed by using pretested semi-structured proforma, emphasizing on socio-demographic profile and reasons for starting use of substance.

Results: Majority (50.4%) of patients belonged to young and productive age group. Most of the patients started taking substances in the age group of 10-19 years and more so in case of nicotine (76.8%), volatile substances (76.9%) and cannabis (70.5%). Besides nicotine (89.6%), the most common substances used were cannabis (48.8%), codeine (48%), propoxyphene (37.6%), alcohol (36.8%) and benzodiazepines (36%). Peer pressure was the most common (72.8%) reason for starting the use of substance.

Conclusion: There is need for further studies to find the community prevalence of drug use. The service provision is very limited restricted to the capital city and none in the rural areas. There is a worrying trend of early age of initiation with adverse consequences including dropping out of school. The control of prescription drug use is another major issue which needs to be addressed. It is also worrying that female drug users are not able to seek help due to lack of appropriate facilities.

Keywords: Addiction, drug abuse, treatment, Kashmir, conflict

Introduction

Drug abuse is a universal phenomenon and people have always sought mood or perception altering substances. Similarly the attitude of people towards addiction varies depending upon various factors and can come across as prohibition and condemnation to tolerance and treatment[1]. The United Nations Narcotics Bureau describes drug abuse as the worse epidemic in the global history [2].India like rest of the world has huge drug problem. Located between two prominent drug producing hubs in the world, i.e. Golden Triangle (Burma, Laos and Thailand) and Golden Crescent (Iran, Afghanistan and Pakistan), India acts as a natural transit zone and thus faces a major problem of drug trafficking. Similarly the geographic location of Jammu and Kashmir is such that the transit of drugs is easily possible across the state. In addition the prevailing turmoil is claimed to have worsened the drug abuse problem alongside an unusual increase in other psychiatric disorders in Kashmir [3].

There are not many studies about drug use from Kashmir and hardly any about the actual community prevalence. In addition, it is difficult to conduct a study in a community affected by drug abuse due to stigma associated with drug addiction. Furthermore people hesitate to volunteer information due to laws prohibiting sale and purchase of such substances and risk of being criminally charged. In view of this difficulty the present study was conducted on the treatment seeking patients at the Drug De-addiction Centers. The present study was aimed at highlighting the epidemiological profile and pattern of drug use in Kashmir Valley.

Material and Methods

This cross-sectional study was undertaken at two Drug De-addiction Treatment Centers (Government Psychiatric Disease Hospital and Police Hospital, Srinagar). Government Psychiatric Disease Hospital is the only psychiatric hospital in the Kashmir valley that also provides treatment for substance use disorder patients. The De-addiction center at the Police Hospital is run by Police Department in the capital city Srinagar. Both these centres have a huge catchment area comprising all districts of the valley, due to lack of such services outside the capital city, thus reflecting the community scenario to a greater extent.

Table 1: Socio-demographic profile

		N	%
Age (years)	10 to 19	20	16.0
	20 to 29	63	50.4
	30 to 39	27	21.6
	40 to 49	12	9.6
	≥ 50	3	2.4
Gender	Male	125	100.0
Religion	Islam	120	96.0
	Sikh	3	2.4
	Hindu	2	1.6
Residence	Urban	56	44.8
	Rural	69	55.2
Marital Status	Unmarried	92	73.6
	Currently Married	27	21.6
	Separated/Divorced	6	4.8
Education	Illiterate	5	4.0
	</= high school	71	56.8
	> high school	49	39.2
Occupation	Unemployed	21	16.8
	Student	25	20.0
	Government Job	16	12.8
	Self employed	63	50.4
Type of family	Joint	36	28.8
	Nuclear	89	71.2
Socio-economic status	Class I	67	53.6
	Class II	36	28.8
	Class III	18	14.4
	Class IV	3	2.4
	Class V	1	0.8

The study was conducted for a period of one year from July 2010 to June 2011. Substance Use Disorder Patients were diagnosed as per the Diagnostic and Statistical Manual-IV (DSM IV 2004) criteria [4]. Following informed consent, a total of 125 patients were included in the study. In case of minors (<18 years of age), the consent was obtained from the guardian. Information was collected regarding the age, sex, residence, religion, marital status, educational status, history of school dropout, occupation and type of family, reasons for starting the substance of abuse, type of the substance abused, and age of initiation. The socio-economic status of the patients was evaluated by using the modified Prasad's scale for the year 2010, based on per capita income per month [5].

Results

A total of 125 Substance Use Disorder patients were studied and all were males. The majority of the patients (50.4%) were in the age group of 20-29 years and most (73.6%) were unmarried. Most of the patients were Muslims (96%). There was nearly an equal urban to rural ratio. Most of the patients had completed their educationup to high school level or higher. There was a high rate of school dropouts (41.7%) and among those, substance use being common reason (46%) for school dropout. 71.2% belonged to nuclear families. Most of the patients (53.6%) belonged to socio-economic class I as per Prasad's scale [Table 1]. Majority of the patients started taking substances in the age group of 10-19 years [Table 2]. Besides nicotine (89.6%), the most common substances used were cannabis (48.8%), codeine (48%), propoxyphene (37.6%), alcohol (36.8%) and benzodiazepines (36%) [Table3].

Table 2: Age at onset of initiation of Substance use by the patients seeking treatment for Substance Use disorder

Substance	< 10 years		10 to 19 years		> 19 years	
	N	%	N	%	n	%
Nicotine	11	9.8	86	76.8	15	13.4
Volatile Solvents	0	0	10	76.9	3	23.1
Cannabis	0	0	43	70.5	18	29.5
Codeine	0	0	33	55	27	45
Propoxyphene	0	0	24	51.1	23	48.9
Benzodiazepines	0	0	20	44.4	25	55.6
Alcohol	0	0	19	41.3	27	58.7

Table 3: Type of substance used by the patients seeking treatment for Substance Use disorder*

Substance	N	%
Nicotine	112	89.6
Cannabis	61	48.8
Codeine	60	48.0
Propoxyphene	47	37.6
Alcohol	46	36.8
Benzodiazepines	45	36.0
Volatile substances/inhalant**	13	10.4
Others***	23	18.4

*multiple responses

**petrol, correction fluid, paint thinners, nail polish remover,

hair sprays, dry cleaning fluids, adhesives, varnishes and deodorants
***cocaine, heroin, raw opium, guthka, lysergic acid diethylamide, dexamethasone, psilocybin, methylene di-oxy methamphetamine, snake bite

Table 4: Reason for starting the Substances among the patients seeking treatment for Substance Use disorder*

Reason	N	%
Peer Pressure	91	72.8
Relief from psychological stress**	49	39.2
Curiosity/Experimenting	27	21.6
Fun/Pleasure Seeking	13	10.4
Prescription medicine abuse***	12	9.6
Others****	6	4.8

*multiple responses
** (family tragedy like death or disease in the family; history of arrests, torture in jail or death and disability in the family due to the prevailing turmoil; conflicts within family; loss of job or job dissatisfaction.
***deliberate use of prescription medications for recreational purposes in order to achieve intoxicating or euphoric psychoactive effects, irrespective of prescription status
****Family history, routine work or boredom, availability.

Peer pressure was the most common (72.8%) reason for starting the use of substance [Table 4]. Majority of the patients started using substances in the age group of 10 to 19 years with 76.8% nicotine users, 76.9% volatile substances and 70.5% cannabis users among this group. The age of onset was higher (>19 years) in case of benzodiazepines and alcohol.

Discussion:

Kashmir Valley has a population of over 6 million with around 70% people living in rural areas.[6]

There is almost no data available on the community prevalence of drug use in the valley. Population is predominantly Muslim with strong taboo on use of alcohol and other drugs. Interestingly, none of the patients in our sample are female which could be due to stigma associated with drug use and hence reluctance to seek treatment. The police drug addiction centre is locally in the police lines with heavy security which requires frisking, which may also prevent people, especially women, from seeking help. This does not mean females do not use drugs as evident from clinical practice and previous studies [7]. The sample is mostly comprised of a young age group of 20-29 years (50.4%) followed by 30-39 years (21.6%). Similar findings have been shown by the previous study conducted by Kadri et al.[8] Another study on college going male students showed a prevalence of 37.5 %[9], suggesting young age at initiation and high prevalence in students. The results also show high school dropout rate due to drug use which could be due to the associated problems with drug use and negative impact on the overall quality of life and future prospects.

There is a minor rural predominance in the sample. This is consistent with findings of Drug Abuse Monitoring System India and other studies [10-12], which reveal a nearly equal rural urban ratio with slight rural predominance. This could be due to the stigma associated with these centres and reluctance from local population to seek help due to fear of being identified and shamed.

73.6% of the patients were unmarried with 4.8% separated or divorced. Similar results have been shown by Hasin DS et al [13] and Martins SS et al[14]. The reason for predominant unmarried sample in our study could be due the higher number of younger age patients as compared to the current marriageable age.

The majority of the patients in our study were using cannabis, medicinal opioids (codeine and Propoxyphene), benzodiazepines and alcohol. One of the major reasons for high rate of opioids and benzodiazepines abuse in present study can be explained by over the counter sale of these drugs without the prescription from the doctor. This is a worrying trend as there is no proper drug control and it is easy to access any medication. Although there are only a few outlets selling alcohol in the whole of Kashmir, it is surprising how alcohol use is so common. It is speculated that current political turmoil may be responsible and people buy alcohol legally or illegally from army depots.

Most of the substance users had started taking drugs at the age of 10 to 19 years and more so in the case of nicotine, volatile substances and cannabis. Similar results have been found in the earlier studies. [15] Nicotine was typically the first substance of abuse. Tobacco is often considered as a gateway to other drugs [16].

The overall prevalence of volatile substance abuse in this study was 10.4% but significantly higher in the adolescent age group (53.8%). About three fourths of the patients had started using volatile solvents in the age group of 10-19 years. Inhalant use has been identified as most prevalent form of substance abuse among adolescents by different studies [17-18]. The observation in present study could be explained by the easy accessibility, cheap price, faster onset of action, and a regular "high" with volatile substances like glues, paint thinners, nail polish removers, dry cleaning fluids, correction fluids, petrol, adhesives, varnishes, deodorants and hair sprays.

Peer pressure is the most common cause of initiation of drug use only to be followed by self-medication for psychological stress. Previous studies have shown similar results in relation to peer pressure and also the ongoing conflict situation to be responsible for increased drug use in the valley [19-20].

Conclusion:

There is a need for further studies to find the community prevalence of drug use. The service provision is very limited, restricted to the capital city and with none in the rural areas. There is a worrying trend of early age of initiation with adverse consequences including dropping out of school. The control of prescription drug use is another major issue which needs to be addressed. It is also worrying that female drug users are not able to seek help due to lack of appropriate facilities.

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Competing Interests

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Review Article

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Bednar tumour: an infrequent diagnosis

Manveen Kaur,Varsha Dalal and Anju Bansal

Abstract

Bednar tumour is a pigmented variant of dermatofibrosarcoma protuberans (DFSP), constituting 1 to 5% of all DFSPs, which in turn, represent 0.1% of skin malignancies. It is histopathologically characterised by scattered melanosome-containing dendritic cells within an otherwise typical DFSP. Bednar tumour poses a clinical diagnostic challenge and requires histopathological and immunohistochemical examination to arrive at the correct diagnosis. We report a case of Bednar tumour occurring on the shoulder of a 29-year-old male.

Keywords: Bednar, DFSP, pigmented tumour

Introduction

Bednar tumour, first described by Bednar in 1957, is a pigmented variant of dermatofibrosarcoma protuberans (DFSP).It is a rare entity, constituting1 to 5% of all DFSPs, which in turn, represent 0.1% of skin malignancies. It differs from DFSP by the presence of dendritic cells containing melanin, interspersed between the fusiform cells characteristic of DFSP. The most frequent location is in the trunk followed by upper and lower extremities and the head and neck region. We report a case of Bednar tumour occurring on the shoulder of a 29-year-old male.

Case report

A 29 year old male patient presented with a slow-growing swelling on his left shoulder for the past two years. Physical examination revealed a large, nodular, subcutaneous mass measuring 8x7 cm in left suprascapular region. Clinical impression was of soft tissue tumour and total resection with 3-cm margins was performed. Grossly, tumour measured 9x4.5 cm, with grey white to grey black cut surface (Figure 1a, 1b). Microscopy showed spindled cells arranged in a tight storiform pattern admixed with scattered heavily pigmented cells (Figure 2). On immunohistochemistry, tumour cells were positive for vimentin and CD34 (Figure 3a, 3b) and negative for S100, SMA and desmin. Pigmented cells were found positive for S100 and HMB 45 (Figure 4a, 4b) and negative for other markers. Thus, a final diagnosis of Bednar tumour was rendered.

Discussion

Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive soft tissue neoplasm with intermediate malignant potential, regarded as a low grade sarcoma by the WHO classification of tumours of the skin.[1,2,3]

It was first described by Darier and Ferrand as a distinct cutaneous disease entity called progressive and recurring dermatofibroma in 1924. The term dermatofibrosarcoma protuberans was officially coined in 1925 by Hoffman.[4]

Histopathologically, DFSP is characterised by irregular, short, intersecting fascicles of tumour cells arranged in a characteristic storiform pattern. Cells have spindle-shaped nuclei which are embedded fairly uniformly in a collagenous stroma. There are several histological variants of DFSP. These include Bednar tumour, fibrosarcomatous, fibrosarcomatous with myoid/myofibroblastic change, myxoid, granular cell, palisaded, giant cell fibroblastoma, combined and indeterminate.[5]

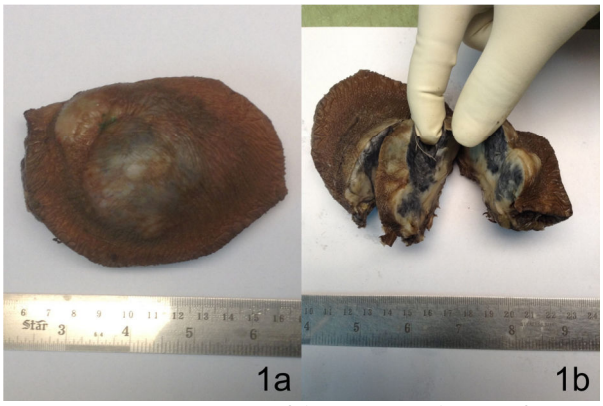

Figure 1 - Gross appearance of the tumour with cut surface grey white to grey black

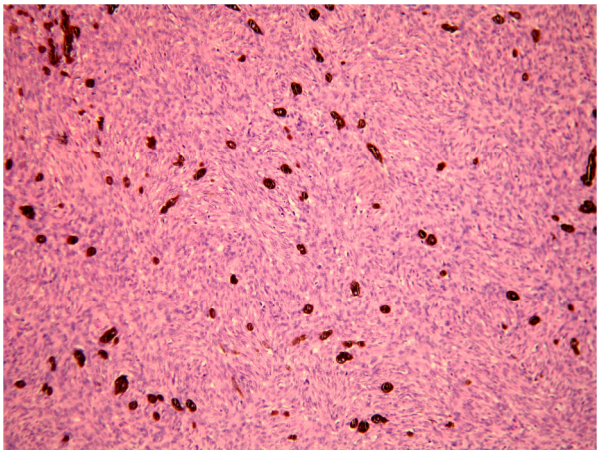

Figure 2 - Spindle cells in storiform pattern admixed with scattered heavily pigmented cells

Pigmented DFSP (Bednar tumour), first designated as storiform neurofibroma by Bednar, is a clinically and morphologicallydistinct variant of DFSP, constituting 5%-10% of all cases of DFSP.[1,5] Clinical presentation is in the form of erythematous blue or brown coloured plaque lesions, with a smooth or irregular surface, often adhering to the deep tissue. The tumour may be exophytic, nodular or multilobulated and is generally firm in consistency.[2] The lesions present as a slow growth, over a period of months or years. They have been described in all ethnic groups, with preponderance in blacks. They occur in third and fourth decades of life, however they may also occur in infancy and show a slight male predominance.[1,5]

The histogenesis of Bednar tumour is controversial. Some authors regard these tumours as being of neuroectodermal origin because of the presence of dendritic melanocytes and cells suggestive of Schwannian differentiation; while others believe attribute the origin to various kinds of local traumas, such as previous burns, vaccination scars, insect bites or vaccination such as BCG.[3,6]

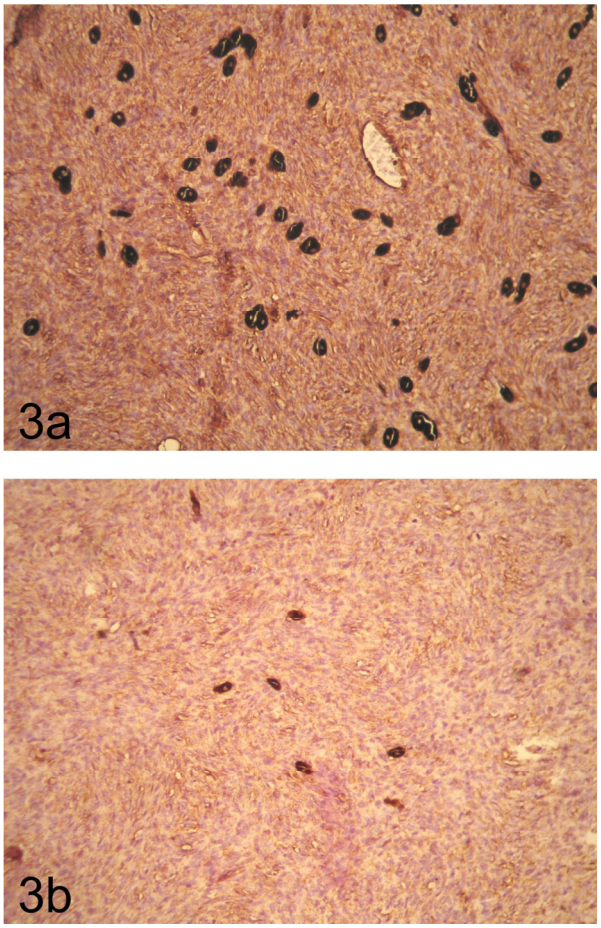

Figure 3 - Tumour cells were positive for vimentin (3a) and CD34 (3b)

Histopathologically, Bednar tumour is characterised by scattered melanosome-containing dendritic cells within an otherwise typical DFSP. The number of melanin-containing cells varies from case to case. Abundant pigmented dendritic cells can cause black discoloration of the tumor, whereas scant pigmented cells can be only identified microscopically.[3,5]They grow invasively into the dermis and may reach the subcutaneous strata, fascia and musculature, in a manner similar to that of dermatofibrosarcoma protuberans. Occasionally, Bednar tumour may undergo fibrosarcomatous transformation with rare examples of pulmonary metastasis.[5] Wang et al have reported a case of Bednar tumour with prominent meningothelial- like whorls.[7]

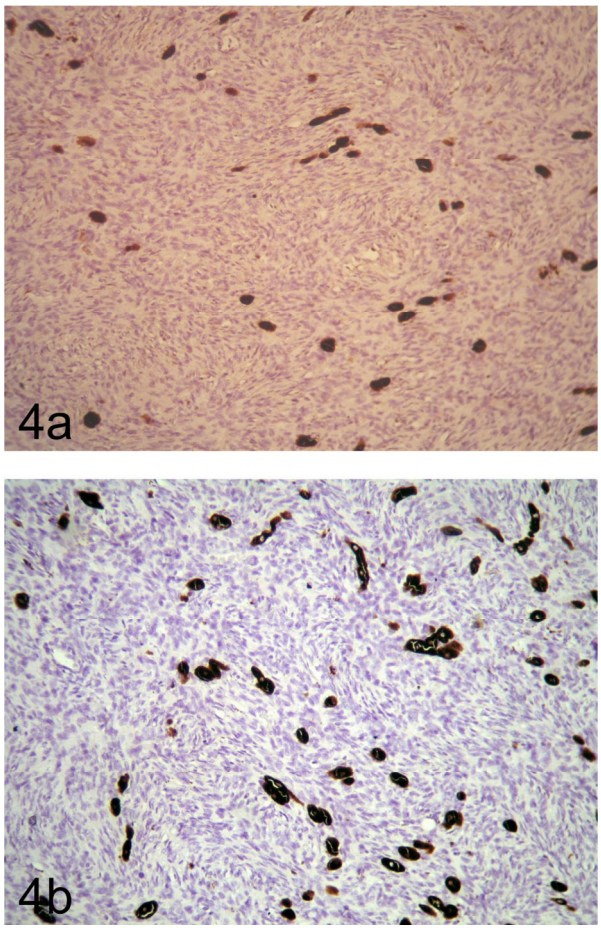

Figure 4 - Pigmented cells showed positivity for S100 (4a) and HMB 45 (4b)

Immunohistochemically, most of the tumour cells stain positively with CD 34 and vimentin, and are negative for neuron-specific enolase, HMB-45 and protein S-100. However, cells containing melanin are positive for the usual melanocytic markers such as S-100 protein.[5] On electron microscopy, three populations of cells have been identified, most of the cells being represented by fibroblasts. The second population exhibits fine elongations, enclosed in basal membrane while the third population consists of dendritic cells containing melanosomes and premelanosomes.[3,5]

The differential diagnoses include pigmented (melanotic) neurofibroma, psammomatous melanotic schwannoma, and desmoplastic (neurotrophic) melanoma. Pigmented neurofibroma can be differentiated from Bednar tumour by more extensive storiform growth and strong positivity for CD34 in latter. Psammamatous melanotic schwannoma is circumscribed, heavily pigmented with psammoma bodies,

tumour cells being S- 100 positive and CD34 negative. Desmoplastic melanoma shows junctional activity and neurotropism.

Treatment consists of complete excision of the tumour with maximum preservation of normal tissue to maintain function and for optimal cosmesis. Moh's Micrographic Surgery (MMS) or staged wide excision "Slow Moh's "(with formal histopathological sectioning and delayed reconstruction for complete circumferential peripheral and deep margin assessment) has become the standard surgical treatment for DFSP.[6,8]

Bednar tumour presents a diagnostic challenge to the clinician because of resemblance to other commonly occurring pigmented lesions. Histopathological and immune-histochemical examination are necessary to arrive at the correct diagnosis.

Competing Interests
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Review Article

The Autoimmune and Infectious Etiological Factors of a Subset of Schizophrenia

James Paul Pandarakalam

Abstract

Despite progress in neurotransmitter identifications and the emergence of novel antipsychotics, the treatment of schizophrenia remains frustrating. There is now a flurry of research trying to figure out the aetiology of schizophrenia and potential etiological models other than neurotransmitter dysfunction deserve consideration. Recent years have witnessed a revival of interest in the viral and immunity based etiological models of schizophrenia. . A subset of schizophrenia may have a pure biological aetiology. There are several commonalities between schizophrenia and autoimmune disorders. Coexistence of established autoimmune disorders along with schizophrenia is suggestive that the latter could also have an autoimmune component. Antipsychotics may be working on the principle of immune modulatory and neuro- modulatory mechanisms. The well recognized 1% global consistency of the incidence of schizophrenia indicates that the aetiology of schizophrenia involve an evolutionary genetic vulnerability and universally present environmental factors. There may be a genetic predisposition to the hypothetical "schizovirus" determining the development of schizophrenia in certain individuals. Certain people are genetically vulnerable to microbial infections in the sense that they have a highly sensitive surveillance system to the microbial infection and respond to the microbial adversary in an exaggerated way. Such a vulnerability and anomalous reaction to infection could result in the schizophrenia psycho-pathogenesis.

Keywords: schizophrenia, autoimmune disorders, schizovirus, genetic vulnerability

Introduction

A clearer understanding of the aetio-pathogenesis of schizophrenia would ultimately lead to effective treatment strategies and provide the impetus for elucidation. The autoimmune hypothesis promulgates that it is the auto-antibodies that are responsible for schizophrenia and, according to the viral hypothesis, it may be the body's abnormal response to a slow viral infection or the undefeated viral antigens causing the schizophrenia pathology. The autoimmune and viral hypotheses are interlinked, as autoimmune disorders can be triggered by microbial infection. Viral aetiology is less convincing than the autoimmune model, but from a treatment perspective, the former is more promising than the latter. To gain a detailed understanding of aetiological models of a subset of schizophrenia, herein the author has reported on a review of the literature relating to the immunity- and viral-based aetiological models of schizophrenia. Genetic vulnerability has been highlighted in the schizophrenia literature alongside environmental factors. The veracity and contestability of the immunity- and viral-based aetiological hypothesis of schizophrenia merits further investigation.

Schizophrenic Syndromes

A prerequisite for incorporating autoimmune and viral aetiology into a scientific discussion would be acceptance of the heterogeneous hypothesis of schizophrenias; they may be a cluster of entities with different aetiologies and the end-stage of different disease processes.[1] Autoimmune or viral aetiology may account for one subgroup.

Schizophrenia has diverse signs and symptoms, and a long history of controversy. Nosologists designate it as polythetic, whereas most other mental illnesses are monothetic, seemingly affecting only one brain system.[2] In the second half of the twentieth century, the psychosocial model gave way to evidence that it is a brain disorder. Schizophrenia has a long history of controversies and there has been much contention over the aetiology, psychopathology, nomenclature, and diagnostic criteria. Schizophrenia is currently seen as a neurodevelopmental encephalopathy, in which the cognitive deficits are produced due to the errors during the normal development of the brain[3] or a neuro-degenerative disorder and the cognitive deficits are derived from a degenerative process that goes on unalterably. Modern neuroimaging techniques and an intensification of studies of necropsy tissue have been responsible for this shift. Researchers seem to agree that a neurodevelopmental or degenerative assault precedes the symptoms by several decades.

The aetiology of the cognitive deficits is unidentified and several potential factors, genetic and epigenetic, are envisaged. Environmental factors—including infectious agents and disturbance in utero through malnutrition—account for a few cases. Autoimmunity and viral theories would fit in with the neuro-developmental and neurodegenerative hypotheses. Proponents of viral aetiology view viruses as acting alongside

susceptible genes to initiate a trajectory that manifests as psychotic symptoms.

Lessons from Autoimmunity

Disorders of an autoimmune nature are known to occur with increasing frequency in patients with another autoimmune disease. This is somewhat like the coexistence of multiple psychosomatic disorders in a person; as per Halliday's psychosomatic formula, association of other psychosomatic afflictions justifies the diagnosis of a new psychosomatic condition. [4] It is well recognised that the central nervous system (CNS) may be directly affected by autoimmune processes, as in the case of multiple sclerosis (MS) and autoimmune limbic encephalitis. A physical autoimmune disease, such as systemic lupus erythematosus (SLE) and antiphospholipid syndrome are also associated with psychiatric morbidity. Paediatric autoimmune neuropsychiatry disorder is a post-infection (group A Beta-haemolytic streptococcal infection) autoimmune disorder characterised by abrupt onset of obsessive compulsive disorder (OCD) and Tourette's syndrome, brought about by molecular mimicry. [5] Nicholson et al observed that 20% of OCD patients were positive for anti-basal antibodies, considered to be part of a post-streptococcal autoimmune reaction. [6]

Autoimmunity is a misdirected response occurring when the immune system attacks the body; it is the loss of tolerance to self-antigens. Immunological tolerance to one's own tissue is probably normally acquired during foetal life, helping to prevent the occurrence of the autoimmune process (see Table1). Some clones of cells that can produce auto-antibodies (forbidden clones) are thought to be produced throughout life, and are suppressed by large amounts of self-antigens or antigen-specific T cells. Auto-antibodies are produced for a wide variety of antigens; some are organ-specific and others are non-organ-specific. Some microorganisms or drugs may trigger changes in individuals who are genetically vulnerable to autoimmunity.

A human disease may be considered of autoimmune origin on the basis of knowledge from molecular biology and hybridoma technology, [7] along with the Witebsky postulations. It is established by the presence of auto-antibodies and T cells that react with host antigens. Approximately 25% of patients with an autoimmune disease (AD) tend to build up additional auto-antibodies. Strausburg et al (1996) explained several hypotheses for the virally-triggered autoimmune mechanism (see Table 2). [8] Allergy is the consequence of a strong response to a harmless substance, but ADs are caused when the destructive potential of the immune system is misdirected to oneself. ADs share common effect or mechanisms with hypersensitivity reactions and can be classified into three main types corresponding to the type ii, type iii, and type IV categories of hypersensitivity reactions (see Table 3)

Table 1- Mechanisms preventing and causing autoimmunity

Tolerance to self molecules a. Clonal deletion-removing any lymphocytes that might react to self molecules b. Clonal anergy-decreasing the responsiveness of lymphocytes that recognise self-molecules. c. Receptor editing-rearrangement of B-cell receptors. d. Reduction or inhibition of molecules or antigens that may cause self recognition. Failure of self tolerance a. Release of isolated auto antigens-tissue trauma or infection may cause breakdown of anatomic barriers and may expose the hidden antigens for recognition of T cells that were not deleted during development. b. Structural alterations in self peptides- Once structurally altered by a trigger such as infection , the self-peptides become more antigenic and are subsequently recognised by the undetected T-cells evoking immune response. c. Molecular mimicry-based on a structural similarity between a pathogen or metabolite and self structures, evoking an immune response against the foreign particles but also an autoimmune response against the self molecules they resemble. d. Polyclonal activation-Infectious agents activate our immune system, B cells and T cells are stimulated resulting in abnormal production of immunoglobulin specific for self molecules. e. Genetic predisposition

Table 2 - Virally triggered autoimmune mechanisms

a. Molecular mimicry -a protein or polysaccharide on the virus may be structurally homologous to a host molecule and the immune system being unable to differentiate between the two, may then cross react with host cells and tissues expressing this molecule. b. The virus may cause release into the circulation of auto antigens that are normally hidden from the immune system. c. The virus might pick up host proteins from the cell membranes that become immunogenetic since they are present on the virus particle. d. The virus in the process of replication may structurally change the host proteins that in turn become recognized as foreign to the immune system.

Table 3 - Classification of Autoimmune disorders

Type i-no autoimmune diseases are caused by lgE, the source of type i hypersensitivity reactions. Type ii-caused by antibodies directed against components of cell surfaces or the extracellular matrix Type iii-caused by soluble immune complexes deposited in tissues Type iv- caused by effector T cells.

Shared Aetiology

ADs are characterised by shared threads in terms of their propensity to co-exist in a patient or direct relatives. Two major autoimmune clusters have been recognised via, thyrogastric—mostly organ-specific—diseases and lupus-associated—mainly multi systems—diseases. [9] Some ADs are distributed within either cluster and there are also overlaps within each cluster. These patterns of concurrence depend predominantly on genetic determinants.

Poly-autoimmunity is the term proposed for the association of multiple autoimmune disorders in a single patient and such co-occurrences indicate a common origin of the disease. [10] Adriana et al, by grouping diverse ADs in the same patient, demonstrated that they are true associations as part of autoimmune tautology rather than chance findings.

Co-Occurrence of ADs

Theories for autoimmune aspects of schizophrenia raise the concept of early infection by microorganisms with antigens so analogous to CNS tissue that resulting antibodies act against the brain. Some data suggest that an autoimmune process precedes schizophrenia, non-affective psychosis, and bipolar disorder, [11] but do not establish whether this is affected by viral attack, as viral footprints may be hard to detect, especially in the target organ, once the autoimmune process has begun. Psychosis is reported in 25% of SLE cases.

A Danish study revealed that schizophrenia is associated with a large range of ADs. [12] The researchers found that a history of any AD in the patient is allied with a 45% increase in the incidence of schizophrenia. Specifically, nine ADs have a higher prevalence rate among patients and 12 ADs have a higher prevalence rate among their parents than among comparison groups. In comparison with the control group, Thyrotoxicosis, Celiac disease, Acquired haemolytic anaemia, interstitial cystitis, and Sjogren's syndrome had a higher prevalence rate among schizophrenia sufferers and their family members.

Three of the Ads—namely, celiac disease, thyrotoxicosis, and acquired haemolytic anaemia—have been previously associated with schizophrenia. Celiac disease involves an immune reaction to wheat gluten. This could be due to increased permeability of the intestine, raising the level of antigen exposure, resulting in increased risk of an autoimmune response to brain components or it may be that gluten proteins are broken down into psychoactive peptides. Eaton et al opined that the association of schizophrenia and ADs could be due to common genetic causes, perhaps related to the HLA or other genes, and some cases of schizophrenia may be consequential to the production of autoantibodies that disrupt the brain function.

Researchers for a Taiwan study identified a greater variety of ADs in schizophrenic patients than anticipated and recommended further research. [13] Chen *et al.* found that 15 ADs are significantly associated with the schizophrenia group. Their studies also confirmed an earlier observation of a negative relationship between schizophrenia and rheumatoid arthritis (RA). It has been observed in a small sample study that mothers of schizophrenia patients have a lower risk for RA.[14]

Rheumatoid Connection

The negative correlation between schizophrenia and RA is puzzling. [15] Such dissociation was interpreted as the effect of antipsychotic medication. Similarly, the metabolic changes associated with one disease may inhibit another.[16] Genes predisposing a person to have one disorder may have a protective influence against another and, in that way, the negative rheumatoid connection with schizophrenia is consistent with an autoimmune model.

RA has a genetic predisposition partly mediated by major histocompatibility complex (MHC) alleles and triggered by infection. Similarly, schizophrenia has genetic and environmental associations and has been cautiously connected with MHC genes other than those perhaps involved in RA. In addition to gene products accountable for antigen presentation, the MHC gene complex holds a multitude of genes-controlling aspects of immune response. Hypothetically, depending on the set of genes an individual has inherited at the MHC complex, a viral assault will lead the immune system to an immune cascade toward the development of RA, or along a genetically-predetermined path with a network of cytokines and immune mediators and directed against CNS components, resulting in schizophrenia. [17]

The negative rheumatoid connection may be attributable to two mutually-exclusive alleles of the same gene. Such associations may lead to novel treatment strategies; sickle cell anaemia patients are thought to be less affected by malaria. Of note, the combined research of Karolinska Institute in Sweden and John Hopkins's University School of Medicine in the United States have recently discovered the genes and the specific deoxyribonucleic acid (DNA) sequences that regulate them plot together to the progress of RA; rheumatology may be inching close to an early detection method and effective treatments. Such a development could hopefully happen in the schizophrenia research.

Commonalities

Even though ADs superficially seem different, the vast majority of them share several similarities. Like ADs, schizophrenia, as such, is neither infectious nor congenital. Schizophrenia and ADs have well-established genetic propensities, and a combination of genes, rather than a single gene, is thought to be responsible for their manifestations. Both schizophrenia and ADs can be triggered by environmental toxins and they have a remitting and relapsing course. Worsening of symptoms is observed when patients are exposed to stress and both conditions have a peak increase in late adolescence or early adulthood. These similarities argue in favour of an autoimmune aetiological model of schizophrenia. [18]

Apparently, there is an interesting epidemiological dissimilarity between ADs and schizophrenia. The incidence of ADs is on the increase in developed countries, whereas schizophrenia has a consistent incidence of 1% globally. According to the hygiene hypothesis of ADs, the widespread practice of hygiene, vaccination, and antibiotic therapy in rich countries have disabled children's immune systems to deal with proper infections and are more geared to charge with one's own tissues in highly-destructive ways. [19] The incidence between the sexes was thought to be almost similar in the case of schizophrenia, but a recent study shows that for every three males with schizophrenia, there are two females with the disease. [20] ADs are slightly higher among the female population.

Immune Modulation of Clozapine

Antipsychotics may have an immunosuppressant effect; plasma levels of IL-6, soluble IL-6R and transferrin-receptor (TfR) were significantly lower after antipsychotic drug treatment. Activation of cell-mediated immunity may occur in schizophrenia; neuroleptic agents may modulate this through suppression of IL-6 or IL-6R-related mechanisms. [21] The antipsychotic effect may involve a counter-effect on the brain-mediated immune system.

Clozapine, the gold standard for refractory schizophrenia, is a dibenzodiazepine and lowers D2 receptor occupancy and is also a 5-hydroxytryptamine antagonist. Studies indicate that among the atypical antipsychotics, clozapine seems to have an immunosuppressant effect along with neuro-modulatory effect. It has been suggested that clozapine may diminish antibody synthesis in hematopoietic cells and also argued that a possible immunosuppressive action may contribute to its superior antipsychotic efficacy. [22] The long-term immunosuppressive effects of antipsychotics may inhibit putative autoimmune responses against neurological sites and could, thus, act synergistically with the direct antagonistic action on brain receptors for the evident improvement of psychotic symptoms. [23] It is also conjectured that the increase of soluble IL-2 receptor levels in Clozapine-treated patients indicates an immunosuppressant mechanism. [24]

Haloperidol may also be a neuro-immune-modulating drug. A study of in-vitro effects of clozapine and haloperidol on cytokine production by human whole blood suggested that both drugs, at concentrations within their therapeutic range, may exert immunosuppressive effects through an enhanced production of IL-1 receptor antagonists. [25]

It is well recognised that unlike other antipsychotics, clozapine works better over time, as immune modulation may take longer than neuro modulation. In addition to the neuro modulation, antipsychotics may be working on the principles of immune modulation, as well. If a derivative of clozapine, without its haematological and metabolic side effects is discovered, such a drug would become the first line of choice among the antipsychotics, and that could be a significant event in schizophrenia research. The immunosuppressant effects of clozapine seem to have public health awareness that patients on clozapine are advised to have the winter flue jab. Elderly patients on antipsychotic medications are more prone to get pulmonary infections, indicating that such drugs have a delicate immunosuppressant property.

Autoimmune-Neuropsychiatric Disorder?

If schizophrenia is an AD, a higher rate of other ADs may be expected among schizophrenics. Most studies confirm that it is tied to irregularities affecting multiple levels of the immune axis.There are multiple interlinked causative factors in the aetiology of schizophrenia. There are suggestions that the neuro-behavioural changes follow an abnormal response to microbial invasion, but that does not necessarily lead to an autoimmune process. The literature deciphering the role of viruses in neurotransmitter abnormalities linking neurodevelopment assaults and the neuropsychological manifestations of schizophrenia is unhelpful. For those who adhere to the autoimmune model of schizophrenia, the simplest suggestion would be that the pathogenesis of the subset of schizophrenia studied may be caused by antibodies in the plasma and CSF that react with brain proteins, resulting in a neuro-autoimmune process.

Lessons from Viral Infections

The concept that certain psychiatric disorders are the neuro-behavioural sequel of the body's immune response to viral infections was prevalent in the early part of the 20th century. That was an outcome of research conducted into rabies in the late 1880s, which revealed the affinity of viruses for the nervous system. Research into tertiary syphilis also provided evidence of an infectious aetiology for specific psychiatric disorders. Investigation of the encephalitis lethargica pandemic (1919 - 1928) contributed to recognition of viral causation on account of similarities apparent between the psychotic symptoms associated with encephalitis lethargica and the clinical presentation of schizophrenia. [26]

Post-influenza depression, depression following mononucleosis, and hallucination associated with herpes encephalitis are well recognised. Menninger, who studied post-influenza psychosis, promulgated the first acceptable viral hypothesis for schizophrenia. [27] In the mid-twentieth century, psychodynamic studies began to encompass the origins of schizophrenia and viral aetiology lost its novelty. Dementias associated with Acquired Immune Deficiency Syndrome (AIDS) have reawakened interest in the correlation between virology and psychiatric disorders, and different authors have revisited these hypotheses in the last three decades. [28-36]

The immune response to influenza and other viruses involves cell-mediated immunity and cytokine activity, which tend to turn tryptophan into kynurenic instead of serotonin. The outcome of this deviation is mood disturbance. It is the body's immune response that blocks the conversion of tryptophan into serotonin, thereby resulting in post-influenza depression. It is

arguable that there may be other psychiatric disorders consequential to a slow immune response of the body to viral infections. The possibility of viral oncogenesis was originally ridiculed, but now there is some evidence to support the view that viruses are responsible, at some stage, for approximately 20% of human malignant diseases. [31]

In theory, a virus could induce schizophrenic symptoms or depression by stimulating antibodies that cross-react with brain tissue, without necessarily gaining entry into the brain. At different developmental stages, the immune response may become less efficient and viral agents may become potentiated, leading to neuropsychiatric conditions. The supposedly inflammation-mediated brain diseases occur at different stages—for instance, schizophrenia in late adolescence or early adulthood, and Alzheimer's typically at an advanced age. It is well established that the human immunodeficiency virus (HIV) may lead to a form of AIDS dementia, and other common viruses that infiltrate the neurons may cause other types of dementia. HIV/AIDS and Borna Disease Virus (BDV) in animals help to bring the infection-based model of schizophrenia to the realm of scientific imagination

Viruses can influence the human genome. After becoming effective, viral sequences are integrated into the genome of brain cells. These sequences are not thought to be inheritable, but may cause mutations that interfere with brain functions and contribute to the development of psychiatric disorders. [37] It may be arguable that the combination of the body's sustained immune response and the constant release of antigens of a hypothetical slow virus (schizovirus) may account for the neuro-behavioural alterations. In the following paragraphs, the author discusses how viral pathogens and other potential contributors could interact and lead to schizophrenic psychopathology.

Immune Responses

Neuro-developmental theories of schizophrenia fit the hypothesis that viral insult occurs early in sufferers, not proximally to a psychotic episode. The interaction between host and virus is affected by coordinated activity of the immune system and the brain. There is evidence that schizophrenia is accompanied by mutations in the immune system. Innate immunity is the first defence against microbes; infection results in invasion by live microorganisms and their toxic products, stimulating an inflammatory response. Neuronal functions are disrupted by pathogens and the brain's inflammatory responses. Non-cytolytic viruses may affect neurones without causing cyto-architectural alteration, but disturbing neurotransmitter production and weakening hormones involved in neurodevelopment. [38] In schizophrenia, immune infiltration is absent, as are vital inclusion bodies and minimal gliosis. There is subtle disruption of neuronal function and brain development, but no significant loss of neuronal cells. Thus, the schizophrenia subset may have a viral aetiological origin, bringing about anomalous, specific immune responses, an autoimmune basis, or both. What triggers the autoimmune process is uncertain, but microbial triggers are a strong possibility.

Immune dysfunctions including lymphocytic abnormalities, protein abnormalities, auto-antibodies, and cytokines have been suggested in seriously-ill patients [39]. One study showed significantly higher plasma levels of interleukin-6 (IL-6) in schizophrenics, and soluble IL-6R and soluble IL-2R were significantly high in mania. [40] A few early investigators claimed to have microscopically visualised virus-like particles in the cerebrospinal fluid (CSF) of patients or in chicken embryos inoculated with CSF. Studies of viral antibodies, viral antigens, viral genomes, the cytopathic effect of specimens on cell cultures, and animal transmission experiments are other avenues for exploring the viral infection hypothesis.

The subset of schizophrenics in question may have a highly-sensitive surveillance system, but a less-discerning immune mechanism than the general population. It could be the over-reaction of the immune system to the microbial adversary that may eventually lead to the schizophrenia pathogenesis. The fault may lie in the surveillance system, as well as in the body's anomalous response to the microbial invasion. [17] In general, innate and acquired immune mechanisms interact and cooperate, but any derangement can lead to deviant immune responses that may result in neuropsychiatric abnormalities.

From an evolutionary perspective, innate immunity is less evolved and the mammalian brain is endowed with a complex immune response system, implying that the neurobehavioral aberrations of schizophrenia could be more linked with deviant and vigorous specific immune responses. [17] It is possible that the proposed subset of schizophrenia may have either an autoimmune basis or a viral aetiological origin, bringing about anomalous, specific immune responses, or both. It has been argued that a gene family involved in the specific immune system and autoimmunity is involved in schizophrenia. [41] The genome-wide association studies (GWAS) have been disappointing in schizophrenia, whereas the major histocompatability complex (MHC) region continues to be the best replicated.

Epidemiological Findings

Epidemiological studies offer useful supporting evidence for viral aetiology (see Table 4). Epidemiological studies characterised by certain broad patterns of incidence and distribution of schizophrenia offer evidence to suspend the scepticism of the viral causal hypothesis. In a study of adults at risk of exposure in utero to the 1957 influenza A2 epidemic in Helsinki, those at risk during the second trimester had significantly more hospitalisations for schizophrenia than those potentially exposed during the other trimesters or immediate years. [42] Researchers for nine subsequent epidemiological studies scrutinised the risk of schizophrenia after possible intrauterine exposure to influenza in Europe and the USA; these identified a small majority claiming to find an association.[43] Falsifying the influenza link with the origin of schizophrenia does not

altogether make the viral aetiology null and void. There could still be an unknown virus (schizo-virus) as the causative agent. The Hepatitis C virus came to medical attention only 15 years ago. At least these epidemiological studies illustrated that viruses can help set the stage for schizophrenia as a long-term sequel

Table 4 - Suggested Evidences for Viral aetiology

A. Direct evidences:
1.Neuropathology
2.Transmission to laboratory animal
3.Detection of viral genome
4. Sero-epidemiological studies-Detection of Antigen or antibody
B. Indirect evidences:
1.Seasonality of schizophrenic births
2.Prevalence studies
3. Immune alterations
4.Antiviral effects of antipsychotic drugs
5.Possible immunosuppressant effect of antipsychotic drugs
6.Studies of identical twins
7. Migration and high risk
8. Gender differences-males are younger at disease onset and have a more severe course.

A worldwide average of 1% prevalence of "core schizophrenia" is generally accepted, [44] even though such a concept of universal distribution and gender equality has opposition. [45] However, there is evidence to assume that there may not be gross variations in this global prevalence. Cross-culturally stable rates, despite decreased fecundity in affected individuals, support an external biological aetiology. These point toward biologically-interlinked and multifactorial causation including an evolutionary genetic factor, as a single biological factor would be insufficient. The preservation of susceptibility genes for schizophrenia in the human gene pool is an evolutionary enigma; gene carriers or first-degree relatives may have some compensatory evolutionary advantage. [46] In a multifactorial aetiological model of schizophrenia, infectious theories are contestable. [17]

Such a consistent prevalence, if true, could also be argued in favour of a biologically-inter-linked and multi-factorial causation of schizophrenia, as it is obvious that a single biological factor would be insufficient to maintain a delicate and consistent global prevalence of a disease. Many viruses are relatively constantly distributed, while genetic diseases present distinct geographical clustering due to inbreeding. One may hypothesise that where viral loading is high, genetic input may be less and vice versa. The consistent global incidence points toward universal microbes, a readily-available environmental factor, or, more specifically, a "schizovirus" . The interaction of vulnerable host genes with a virus could yield epidemiology like that of schizophrenia.

Birth patterns rank highly among epidemiological observations in schizophrenia. [47] Many more schizophrenics are born in winter and spring than in summer and fall. [48] Infectious aetiology is a plausible explanation, as many viruses show a surge in the same months and viral aetiology is a more convincing explanation of the consistency in question. While gene coding for particular proteins is inherited, environmental and developmental factors are undoubtedly implicated in modulating genes' expression.

Exposure to prenatal infections and other obstetric complications are neuro-developmental assaults that increase vulnerability to schizophrenia. [49-52] In obstetrics, infection in the mother generates antibodies transmitted to the foetus, producing auto-antibodies that upset neural development and increase the schizophrenia risk. [53]

Schizo-Virus or any Microbe?

It is not certain whether it is body's abnormal response to any virus and other microbes or a specific unknown virus that results in "schizophrenic reactions." It is even unclear that the unbeatable antigens of this hypothetical virus alone are capable of inducing the neuro-behavioural changes associated with schizophrenia. The hepatitis C virus came to medical attention only 15 years ago. The rotavirus was isolated in 1973 and the HIV virus was isolated in 1983. Non-detection of a pathogen does not exclude its role in the pathogenesis. If a specific virus is responsible for schizophrenia, it should have been with human society for a very long time, as the illness has been reported from the beginning of recorded human history. Some people may have a genetic vulnerability to the hypothetical schizovirus; inheritability would lie in contracting the specific virus. Poliomyelitis has a concordant rate of 36% among monozygotic twins; the rest are attributed to environmental factors. The majority of children exposed to the polio virus may not develop poliomyelitis and a genetic propensity may be required for the viral manifestation. It is even reported that 10% of the world population rarely catch influenza, in spite of its yearly mutation.

Cardiac disease due to endocarditis (caused by an autoimmune process affecting many parts of the body), a sequel to acute rheumatic fever, is an analogy to demonstrate how, theoretically, a microbial infection may lead to impaired neurodevelopment and psychiatric disorders in a different scenario. Endocarditis is triggered by a reaction to streptococcal bacteria, not a bacterial infection. It may begin a chronic process, leading to valvular cardiac disease. Generally, rheumatic heart diseases are diagnosed 10 - 20 years following rheumatic fever. Similarly, schizophrenia could be an autoimmune complication of a subtle microbial infection; finding and countering the antigenic triggers of ADs may lead to an effective cure.

HIV/AIDS

Patients with HIV are at risk for developing psychiatric symptoms and disorders similar to those seen in the general

population, as well as those that are direct effects of HIV. HIV is a neurotropic and lymphotropic virus that causes immune suppression and allows the entry of opportunistic pathogens with an affinity for the CNS. There is some evidence that HIV may trigger a psychotic episode and contribute to first-onset schizophrenia. [54] Serious CNS complications occur late in the course of HIV infection, when the immunity function has diminished considerably. The viral load is closely associated with the degree of cognitive impairment. HIV-associated dementia (AIDS dementia complex) is defined as acquired cognitive abnormality in two or more domains and is associated with functional impairment and acquired motor or behavioural abnormality in the absence of other aetiology. It is estimated that 30% to 60% of patients experience some CNS complications during the course of their illness and 90% reveal neuropathological abnormalities at autopsy.

Pearce argued that HIV-related encephalitis could engender a scenario for a viral aetiology of schizophrenia. [17] HIV produces symptoms after being latent for several years. HIV was not identified as the aetiological agent of AIDS until the conditions for viral replication in lymphoid cell lines were identified. Prior to the evolution of PCR serology techniques, it was debatable whether the virus was in circulation at all. This indicates that the absence of a demonstrable virus does not mean the absence of a subtle virus-induced disease process. No virus, as such, is currently detectable in the schizophrenia disease process. Even in the absence of opportunistic infections, HIV infection of the brain causes severe neuro-behavioural syndromes, such as AIDS dementia, without infecting neurons, but by complex interaction with host molecules and non-neuronal cells. All these suggest that a rare or unknown infectious agent is involved; it would not be identified unless it was specifically tested for.

The finding that the neurophysiological and psychological stress of HIV infection can aggravate an underlying psychotic illness implies that viruses, without being a direct causative agent in psychotic episodes, can unmask pre-existing psychiatric vulnerabilities, acting on the brain physiology through unknown pathways. A curious aspect of HIV-related psychosis is that it responds to anti-psychotic treatment and to anti-retroviral drugs. Several anti-psychotic drugs have been shown to have antiviral properties, both in vitro [55] and in vivo. [56] The deduction is that a virus could initiate events resulting in psychosis, and anti-psychotic drugs can interrupt that sequence. All these features of HIV infections are consistent with the idea that a virus can cause neurobehavioral abnormalities after several years.

Borna Disease Virus

It has been recognised that Borna disease virus (BDV) could cause neuropsychiatric complications including neurological, behavioural, and mood alterations in animals. [57] A ribonucleic acid (RNA) virus from the family *Bornaviridae*, it is a neurotropic virus with an affinity to a variety of hosts, particularly hoofed animals, and can cause persistent infection of the CNS. Such an infection may be either latent or chronic and slow, but BDV presents with the latent type, characterised by a lack of viral particles. It may resemble the alleged pathogens in non-affective psychosis. The severity of clinical symptoms depends on the immune response of the host.BDV can directly influence the CNS through the binding of viral proteins with neurotransmitter receptors and indirectly through immune response and inflammatory reactions.

Depending on the host's age and the integrity of the immune response, an infection may be asymptomatic or involve a broad spectrum of behavioural disorders. The severity of clinical symptoms depends on the immune response of the host.[58, 59] Unusual features of BDV biology include nuclear localisation of replication and transcription, varied strategies for the regulation of gene expression, and interaction with signalling pathways, resulting in subtle neuropathology.[60] BDV can directly influence the CNS through the binding of viral proteins with neurotransmitter receptors and indirectly through immune response and inflammatory reactions. The issue of human BVD infection has been recently questioned by American researchers who reported an absence of association of psychiatric illness with antibodies to BDV or with nucleic acids in serially-collected serum and white blood cell samples from 396 participants. [61] However, BDV in animals helps to bring the infection-based model of schizophrenia to the realm of the scientific imagination.

Neurotransmitters

It is an overstatement to say that schizophrenia is a neurotransmitter disease, although it is well established that it incorporates a derangement of dopamine activity. Some viruses have been shown to alter dopamine metabolism. [62] The literature deciphering the role of viruses in bringing about neurotransmitter abnormalities linking neurodevelopment assaults and the neuropsychological manifestations of schizophrenia is unhelpful. [63] It has been reported that in rodents, BDV could crash neurotransmitter systems, including dopamine, neuropeptides, and glutamate. [64] How viruses alter neurotransmitters is a central issue. Communication between the immune system and the brain is crucial to defend against viral infection; this is mediated through neurotransmitters. Viruses are bound to tamper with the intrinsic communication system as part of their cellular offensive. Some viruses have been shown to alter dopamine metabolism. [65]

Genetics

The undisputed genetic factor in schizophrenia may be posited to discount the viral hypothesis. However, genetic factors do not exclude environmental contributions. Monozygotic twins have a concordance rate of only 48%. Brief reactive psychosis due to acute sequels to viral infection, though regarded as unrelated to schizophrenia, may still be schizophrenic reactions and they do not progress to schizophrenia only because the sufferers are not genetically predisposed to schizophrenia.

Genetic predilection may be attributable to genes that determine idiosyncratic differences in immune responsiveness to common viral pathogens.

Susceptibility and immune response to infectious agents are known to be subject of genetic control and may involve multiple interacting susceptibility genes.[66] The genetic component of schizophrenia may engross multiple interacting susceptibility genes. These together or singularly may moderate the virus, and the virus and gene product may act at different points. Many cases would have a genetic foundation and it may be extremely rare to develop schizophrenia independently of a genetic anomaly. A small subset of patients may have a purely genetic form. Research should also be directed at identifying risk genes and why they assert themselves and cause the disease. Any future research which sheds more light on some people are affected more readily than others would bring researchers closer to more effective treatments and early intervention (see Table 5).

Table 5 - Future Directions

1. Critical research studies should target in establishing the viral and autoimmune aetiology of a subset of schizophrenia as the illness may be due to both factors. Detection criteria/ tests are vital in isolating this subset from the rest of schizophrenia syndromes 2. Robust epidemiological studies to be conducted to find putative infectious agents and possible models of transmission.
3. Developing new methods for detection of viral agents, directed at the analysis of previously identified pathogens and identification of novel viruses. Vigorous studies with PCR and other sensitive methods for nucleic acid detection to be carried out for the detection of viral nucleic acids in the body fluids of schizophrenia sufferers.
4.To find a method to turn off autoimmune attacks from the body or selectively disable the immune response
5. Identify risk genes and to find the specific DNA molecules and their tagging patterns vital for the progress of the illness.
6. To develop drugs to target specific genes which would mean they would be far more effective and have fewer side effects.
7. Finding psycho-physiological parameters for early detection to minimise the damage.
8. In the event of future discovery of effective antiviral agents, the subset of schizophrenia in question could take advantage of the clinical benefits of such discoveries.
9. Viral aetiology, if proven true, could lead to finding a vaccine against the disease.
10. Selective immune-suppressants could be a future addition into the psychiatric armamentarium.
11. A derivative of cloazapine without its haematological and metabolic side effects would be highly promising.

Summary

There are multiple interlinked causative factors in schizophrenia and viral infection may be only a trigger. Viral infections may be the cause of vigorous immune responses or triggering an autoimmune process that lead to neuro-behavioural aberrations and a subset of schizophrenia would emerge as viro-immuno-neuropsychiatric disorder or autoimmuno-neuro-psychiatric disorder. If such a subset of schizophrenia contains an autoimmune component, either triggered by infectious agents or due to unidentified intrinsic factors, the disease process would be determined by genetic vulnerability. There is not sufficient evidence established to identify viruses as being implicated in the aetiology of schizophrenia, but researchers have reason to anticipate further laboratory studies, as newer, more sensitive laboratory technologies are evolving. A viral or autoimmune model of schizophrenia may illuminate its pathogenesis, but not necessarily the diversity of psychiatric symptomatology. In the last few decades, schizophrenia research has been focussed on neurotransmitter derangements and neuro-developmental anomalies. The cause of a tsunami is not in the sea water, but due to the tectonic shifts under the sea bed; the aetiology of schizophrenia may be similarly due to immune alterations.

Pellagra psychosis due to niacin deficiency was hidden under the schizophrenia umbrella.[67] There may be other psychotic disorders grouped under schizophrenia, and they may have a pure biological aetiology—chemical or infectious—but with genetic vulnerability. No one can be sure whether it is the toxic chemical of the pathogens or the immune response of the host, or both, that may lead to the psychopathology. Searching for this hypothetical virus is a challenging task, but if researchers found it, the benefits would be enormous. A viral aetiology of certain types of schizophrenia, if demonstrable, could affect radical changes in treatment and management. In fact, the hypothesis of viral aetiology is more promising than any other biological hypothesis, as it gives a message of potential drug cure. In this contest, it is interesting to note that the antigenic similarity between components of the streptococcus and cardiac tissue resulted in rheumatic heart diseases, but with the advent of penicillin, this disease has virtually disappeared. Only time will determine the validity and therapeutic prospects of the viral and autoimmune aetiology of schizophrenia.

Davison opined that as evidence accumulates about the autoimmune basis of at least a subset of psychiatric disorders, clinicians should keep abreast of immune-neuropsychiatric research.[68] Psychiatry must constantly expand to meet the growing needs with the emergence of novel ideas in other medical specialities and it is high time to introduce a new terminology—"Psycho-immunovirology"—to study the viral aetiological mechanisms involved in psychiatric disorders like schizophrenia. Neuro-virology and psycho-immuno-virology could develop as an interdisciplinary field which represents a melding of virology, psychiatry, the neurosciences and immunology.

Competing Interests
None declared

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Case Report

BJMP 2015;8(4):a838

An unusual cause of inspiratory stridor: NG tube insertion under anaesthesia

Kristofor Inkpin and Matthew Daunt

Abstract

Insertion and use of nasogastric (NG) tubes is not without risk. We report a case of inspiratory stridor following NG tube insertion whilst under general anaesthesia. We describe its diagnosis, treatment and precautions to prevent further incidents.

Keywords: NG tube, Stridor, Airway, Emergency, blind.

Abbreviations: NG - Nasogastric, NHS - National Health Service, AF - Atrial Fibrillation, CT - Computerised Tomography.

Introduction

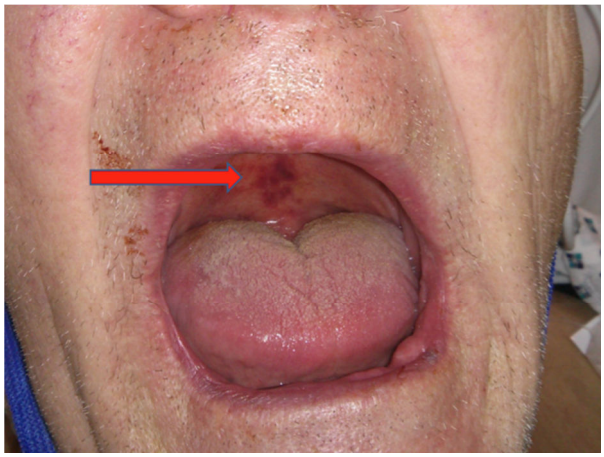
The NHS is supplied with approximately 300 000 NG tubes per year[1]. There are approximately 800-1000 incidents reported to the NPSA every year related to the insertion and use of NG tubes. Difficulties are often encountered with their insertion, especially in the setting of general anaesthesia. Whilst stridor and injury related to the use of NG tubes has been previously reported[2,3], it has been related to prolonged siting. We describe a case acute stridor occurring in the recovery room due to direct trauma of the airway upon NG tube insertion.

Case report

A 61-year-old male presented with clinical symptoms of bowel obstruction. His medical history included atrial fibrillation (AF) treated with flecainide, and a 30-pack year smoking history. He was previously independent with a World Health Organisation performance status of 0. After CT confirmation of bowel obstruction, he was scheduled for an emergency laparotomy. A predicted P-Possum 30 day mortality was calculated at over 10%. He required no organ support pre-operatively, although his AF was poorly controlled. He had a low thoracic epidural sited awake, followed by induction of general anaesthesia with a rapid sequence induction. An arterial line, a central venous line, and an NG tube were inserted once anaesthetised. The NG tube was documented as difficult to site, and there were several attempts at a blind insertion via the oral and nasal route, before successfully inserting under direct vision using a laryngoscope.

The operative finding was that of an unresectable caecal tumour, and a defunctioning loop colostomy was formed. The total duration was 150 minutes. Following peripheral nerve stimulation and administration of 2mg/kg Sugammadex, he was woken, extubated and escorted to recovery.

Within minutes of being in the recovery area, he was acutely stridulous. Emergency assistance was called, and after assessment he was given nebulized adrenaline (1mg diluted in 4mls 0.9% saline), and 200mg of intravenous hydrocortisone. The nasogastric tube was removed, and his breathing was then supported with CPAP via a Mapleson C circuit and 100% oxygen. Direct examination of his airway, and indirect nasendoscopy with a Storz fibre-optic scope were performed. Significant bruising of his soft palate was seen, in addition to bruising and oedema of the soft tissues around the arytenoid cartilages with a small haematoma within the valleculae [Figure 1]. After approximately twenty minutes his stridor settled.



He was transferred to a level 2 high dependency unit later that day. He did not suffer from any further airway compromise, and his symptoms completely resolved.

Discussion

The insertion of an NG tube, whilst often deemed low risk, may result in life threatening consequences[4]. There even exists a "NG tube syndrome" [5], the pathophysiological mechanism of which is thought to be paresis of the posterior cricoarytenoid muscles secondary to ulceration and infection over the posterior lamina of the cricoid. There is no doubt that insertion of an

NG tube in the anaesthetised patient can prove to be difficult, with a failure rate of up to 50% on first pass[6], with repeated attempts at insertion being required. However, this case highlights the need for a controlled and ordered approach to managing the difficulties that can be encountered. Medical training incorporates NG insertion as a basic skill within the curriculum, but this affords new anaesthetic trainees little help with the anaesthetised and intubated patient.

There are several techniques described to insert NG tubes in anaesthetised, intubated patients[7]. There is evidence to suggest that modified techniques such as a reverse Sellick's manoeuvre or neck flexion with lateral pressure are better than blind insertion in the neutral position. In the right hands, insertion under direct vision can overcome most difficulties, but is again not without risk.

We feel it is important to remember that NG insertion can cause patient harm, and potentially lead to life threatening consequences. Whatever the approach or technique that is chosen, having a logical and ordered approach is paramount. Using suitable alternative methods for insertion, or abandoning the procedure, as opposed to blindly continuing to repeat the same unsuccessful method must be key for success, as would be the case for approaching any clinical encounter.

Published with the written consent of the patient.

Competing Interests
None declared

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Case Report

Tumefactive Multiple Sclerosis Masquerading as Cancer

Kamran Khan, Susan E. Wozniak, JoAnn Coleman

Abstract

Tumefactive Multiple Sclerosis (MS) is a rare variant of MS that is extremely difficult to diagnose. It can resemble malignancy and perplex the clinician until all diagnostic tests are exhausted. A brain biopsy is not required to treat for the disease, as it is in CNS malignancy. Newer diagnostic tests are available that allow diagnosis to be attained and treated presumptively. Presented is a case of a 48-year-old female that mimicked metastatic malignancy. We were able to use surveillance MRI and CSF analysis to diagnose our patient.

Keywords: Tumefactive Multiple Sclerosis, MS, Demyelinating lesion

Abbreviations: ECG- Electrocardiogram, CSF- Cerebrospinal Fluid, CN- Cranial Nerve, V/Q- Ventilaion/Perfusion, CA- Cancer Antigen, AFP- Alpha Feto Protein

Introduction

Multiple Sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system (CNS) that affects approximately 400,000 people in the United States and 2.5 million worldwide.[1] There are rare variants of this disease that can profoundly delay diagnosis and treatment. Examples of such variants include: Tumefactive MS, Acute Disseminated Encephalomyelitis, Neuromyelitis Optica, Marburg's MS and Balo Concentric Sclerosis.[2] These variants have a uniquely aggressive presentation and do not exhibit classic MS features.[2] Classic MS features include relapsing and remitting sensory and motor impairments, optic neuritis and pain. These aggressive variants are more likely to present with symptoms similar to neoplasm such as motor impairments and seizures. When dealing with these aggressive MS variants diagnostic options include Magnetic Resonance Imaging (MRI), Single Photon Emission Computed Tomography (SPECT) scan, MR spectroscopy and Cerebrospinal Fluid (CSF) analysis.[3]

Invasive tests such as brain biopsy are not warranted unless absolutely necessary. In MS, a biopsy must not be completed in order to confirm a diagnosis. However, to confirm a diagnosis of cancer a biopsy is required.

We present a rare case of Tumefactive MS that exhibited a clinical picture identical to brain metastasis. This was diagnosed with surveillance MRI and CSF analysis in the absence of a brain biopsy.

Case presentation

A 48-year-old African American female was brought in by emergency medical services after falling with a brief loss of consciousness. Associated symptoms included dull chest pain, diaphoresis and shortness of breath. While in the emergency department she also developed nausea, vomiting and dizziness. The patient reported no similar previous episodes and denied precipitating events. There was nothing else to note on review of systems. The past medical history included hypertension with no previous surgeries and family history included breast cancer of the mother diagnosed at age 47. The patient denied tobacco, alcohol and intravenous drug use. She noted an allergy to iodine.

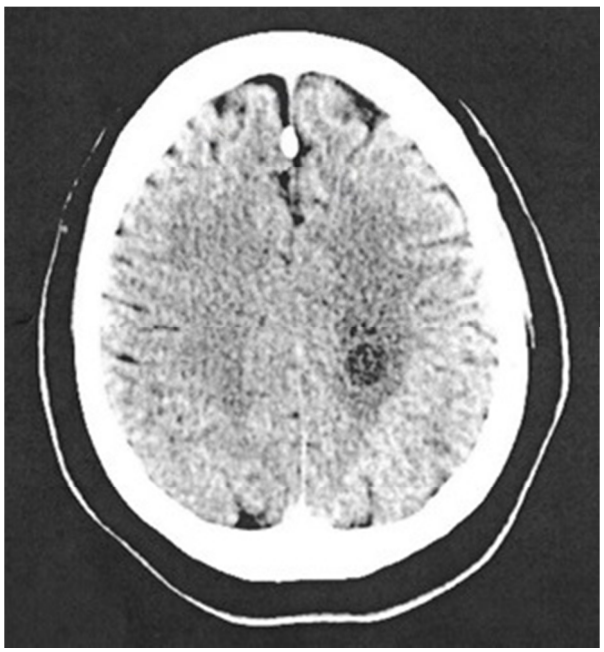

Figure 1. Head CT without contrast: left centrum semiovale round hypodense lesions measures 1.4 cm with perilesional vasogenic edema

On physical examination the patient was afebrile, normotensive and tachycardic with an oxygen saturation of 89% on room air. She was alert and oriented but pale and diaphoretic with mild

left sided chest pain. Cardiac examination revealed a normal rhythm tachycardia and no murmurs were heard. Her neurological examination showed a normal mental status, normal cognition/comprehension and that Cranial Nerves II-XII were intact.

Laboratory findings included haemoglobin of 9.8 g/dL, 30.8% haematocrit and potassium of 3.3 mmol/L. Electrolytes were otherwise normal. Cardiac workup showed a normal ECG and slightly elevated cardiac enzymes of 0.319 ng/mL.

Given the patients tachycardia and desaturation, a stat Ventilation-perfusion (V/Q) scan was completed (patient had an iodine allergy). The V/Q scan revealed a perfusion defect suggesting pulmonary embolism (PE) as the cause of symptoms. Subsequently the patient was placed on appropriate anticoagulation.

Head CT (computed tomography) showed a left centrum semiovale round hypodense lesion measuring 1.4 cm, a left basal ganglia round hypodense lesion measuring 1.0 cm and a left occipital lobe round hypodense lesion measuring approximately 1.0 cm (Figure 1). No midline shift was seen. MRI showed multiple hypointense T1/hyperintense T2 nonenhancing lesions, mainly within the left cerebrum (Figure 2 A-F). The three largest lesions within the left posterior centrum semiovale (2A), left globus pallidus (2B) and left posterior corona radiata adjacent to the occipital horn (2C) measured 1.5 cm, 1.0 cm and 1.0 cm respectively. Perilesional vasogenic oedema was seen in all except the basal ganglia lesion. There were bilateral cerebral scattered foci of hyperintense FLAIR/T2 signals (D-F). The imaging suggested a differential diagnosis which included metastasis, infection or primary CNS malignancy.

Further work up in search for possible malignancy was completed. Skin map revealed no concerning nevi. Mammogram showed no tumor. CT of the abdomen and pelvis revealed a 2.6 cm indeterminate hypodense lesion in the left lobe of the liver (Figure 3A) along with an enlarged fibroid uterus (17x 7 x 14 cm). Liver biopsy was considered but a repeat MRI and ultrasound showed the lesion to be cystic, so this was deferred following surgical oncology recommendations (Figure 3B). For the hypertrophic uterus found on imaging, gynecology felt no further workup was necessary as they attributed the findings to a fibroid uterus.

Tumor markers CA 27-29, CA 19-9, CA 125 and AFP were all sent and came back negative. Initial lumbar puncture with CSF analysis was not completed secondary to possible complications that could be incurred while on necessary PE anticoagulation.

Due to a non-focal neurological examination, she was discharged on Levetiracetam 500 mg for seizure prophylaxis and Dexamethasone 4 mg for perilesional oedema. Over subsequent months the patient did well without headaches, vision changes or seizure like activity. On subsequent visits to the clinic, she had no evidence of focal neurological deficits except for mild bilateral symmetric hyperreflexia. Given that the metastatic work up remained negative, we considered obtaining a baseline Positron emission tomography (PET) scan to ensure we were not missing any possible metastasis.

She subsequently went back to work full-time and reported no symptoms. Repeat MRI of the head (Figure 4 A-C) showed predominantly T1 hypointense and T2 hyperintense (A-B) lesions with significant decrease in size from MRI done three months ago. These lesions demonstrated no enhancement to incomplete ring enhancement, with diminished vasogenic oedema (A). These findings suggested an inflammatory demyelinating process so a lumbar puncture was obtained after anticoagulation was held. CSF analysis was done using Isoelectric Focusing (IEF) and immunoblotting methodology. This revealed a normal myelin basic protein but with eight oligoclonal bands restricted to the CSF. These findings solidified the suspicion of Tumefactive MS.

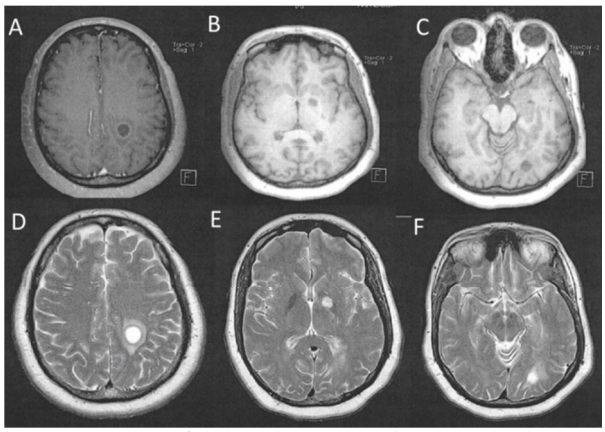

Figure 2. MRI of brain showing axial T1-weighted (A-C) hypodense lesions of the left centrum semiovale(A), left basal ganglia(B) and left occipital lobe(C). Axial T2-weighted (D-F) views show multiple hyperdense lesions corresponding to the same locations. Perilesional vasogenic edema is seen.

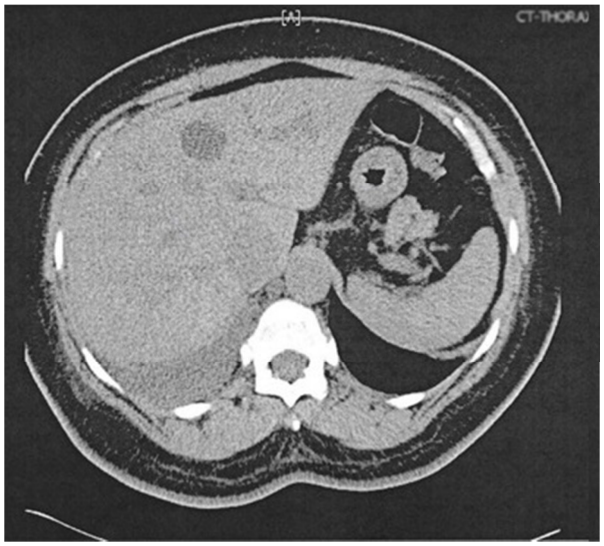

Figure 3A. Thorax CT without contrast. 2.6 cm left lobe liver lesion.

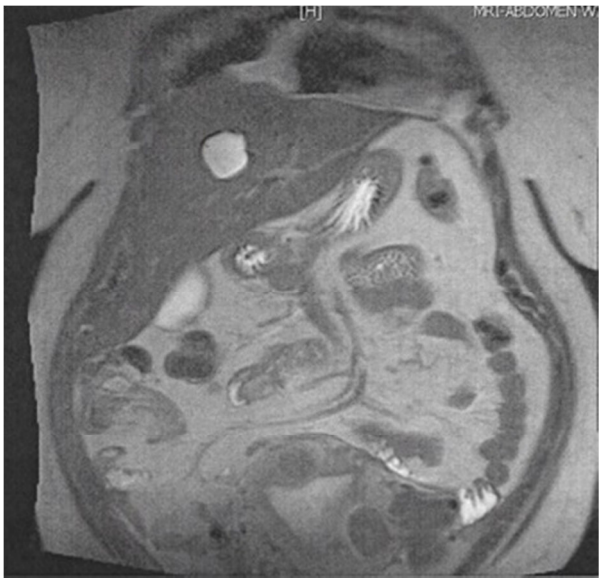

Figure 3B. MRI of abdomen showing coronal T2-weighted half-Fourier acquisition single-shot turbo spin-echo (HASTE) hyperdense lesion. A mildly enlarged liver measuring 18.7 cm in craniocaudal span. Simple 2.8 x2.4 cm cyct in the medial segment of left lobe.

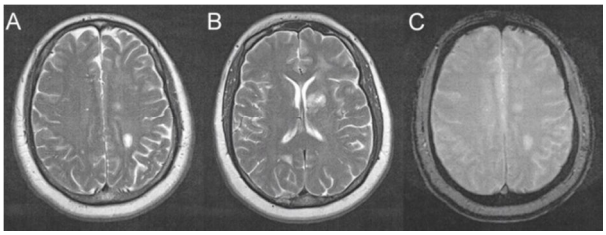

Figure 4. MRI of brain (3 month after initial scans) showing axial T-2 weighted (A-B) hyperdense lesions of the left centrum semiovale(A) and left basal ganglia(B). There is irregular peripheral enhancement. Considerable decrease in size is seen from previous MRI (Figure 2). Left posterior centrum semiovale, left globus pallidus and left occipital lobe lesion measure 1.3 cm, <1 cm and <1 cm respectively. Vasogenic edema is diminished in comparison to previous study.

Discussion

Tumefactive MS lesions are defined as solitary demyelinating plaques greater than 2 cm.[5] Lesions are difficult to distinguish between primary or metastatic given similarity of imaging features.[5] Imaging features suggestive of Tumefactive MS include incomplete ring enhancement, absence of mass effect and absence of cortical involvement.[6] [7]Kim describes that CT hypoattenuation of magnetic resonance enhancing lesions was found to be highly specific for distinguishing Tumefactive MS lesions from CNS cancer pathology.[6] It has been shown that SPECT using I-IMP is useful for diagnosing CNS malignancy.[3] This is because there would be increased uptake in comparison to the MS lesions - implying increased metabolic activity.[3] However this study has its limitations in diagnosis. In a few isolated cases I-IMP was found in greater quantities in MS tumor-like lesions.[3]

The imaging studies for this patient established a concern for metastasis, infection or primary malignancy. Extensive cancer workup was completed as previously discussed. Since all tumor markers were negative a baseline PET scan was considered however, was not done secondary to insurance denial. Due to the asymptomatic presentation of her disease, a primary differential diagnosis of brain metastasis and anticoagulation therapy for PE, a CSF analysis was not considered until much later. We were able to use surveillance MRI and CSF analysis to see some resolution of these lesions and confirm the diagnosis. Brain biopsy was never warranted but in unique symptomatic cases it may have been.[6]

The cornerstone of diagnosing MS is the demonstration of lesions in both time and space - termed the McDonald Criteria.[8]The revised criteria allow a diagnosis of MS, "possible MS" or "not MS".[8] This is what made the diagnosis of our patient difficult, as no clinical symptoms or attacks were evident. It was demonstrated that over the course of three months the lesions seen on MRI evolved. From the size of 1.5 cm, 1.0 cm and 1.0 cm they became 1.3 cm, <1.0 cm and <1.0 cm respectively (Figure 2, Figure 4). This was likely the effects of steroids that the patient was on due to her vasogenic oedema. Here an evolution in time and space is demonstrated which excluded brain metastasis and infection. This brings into discussion the diagnostic value of surveillance MRI, which in our case was helpful and appropriate as the patient did not have clinical symptoms.

Conclusion

The diagnosis of Tumefactive MS can be extremely difficult and time consuming. As seen in our case, it can mimic other conditions. Our patient was able to be diagnosed with MRI surveillance and CSF analysis. The definitive diagnostic test for MS is a brain biopsy but this is not preferred due to the invasiveness of the procedure. With the advent of newer diagnostic tests such as SPECT, MR Spectroscopy, surveillance MRI and CSF analysis, diagnosis can be attained and treated presumptively.

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Case Report

BJMP 2015;8(4):a830

Acute reversible cardiomyopathy due to methamphetamine overdose

Ashok Raj Devkota, Alix Dufrense and Premraj Parajuli

Abstract

Methamphetamine abuse is associated with various cardiac complications like acute coronary syndrome, cardiomyopathy and sudden cardiac death. We report a case of patient who presented with cardiomyopathy and acute heart failure due to intravenous methamphetamine abuse. His cardiac function recovered fully after medical management.

Keywords: Methamphetamine, cardiomyopathy, heart failure

Abbreviations: EKG: Electrocardiogram, ECHO: Echocardiogram, CT: Computed tomography, LVEDP: Left ventricular end diastolic pressure

Introduction

Methamphetamine and related compounds are the most widely abused drugs in the world after cannabis [1]. Methamphetamine is a synthetic stimulant which acts both on central and peripheral nervous system. It causes the release and blocks the reuptake of dopamine, norepinephrine, epinephrine and serotonin in neuronal synapse. Methamphetamine can be smoked, snorted, injected or ingested orally. Methamphetamine is more potent, and its effects last longer than cocaine [2, 3].

Methamphetamine intoxication causes various systemic complications like sympathetic over activity, agitation, seizure, stroke, rhabdomyolysis and cardiovascular collapse. Acute cardiac complications of methamphetamine like chest pain, hypertension, arrhythmias, aortic dissection, acute coronary syndrome, cardiomyopathy, and sudden cardiac death have been reported [4, 5]. Chronic methamphetamine use is associated with coronary artery disease, chronic hypertension and cardiomyopathy [6].

Here we present a case of methamphetamine overdose, which presented with cardiomyopathy and severe systolic heart failure whose cardiac function was normalized after treatment.

Case presentation

A 38-year-old male presented with shortness of breath, chest tightness and sweating which started after he used intravenous crystal meth the day before presentation. He was an active poly substance abuser and used different drugs like marijuana, alprazolam, amphetamine, cocaine, percocet (oxycodone and acetaminophen) and clonazepam regularly. He was on methadone maintenance program as well. The patient did not have any cardiac problem in the past. He had a seizure disorder but he was not on medication. He had an episode of a seizure after methamphetamine use. His review of system was otherwise unremarkable.

On presentation he was tachycardic, his pulse was 128/min and his temperature was 98 degree Fahrenheit. He had bilateral diffuse crackles on lung bases. Troponin I was high 4.23 ng/ml (reference 0.01-0.05 ng/ml) and BNP was high 657 pg/ml (reference 0-100pg/ml). His electrolytes, renal function, liver function and creatinine kinase were normal. Urine toxicology was positive for opiate, methadone, amphetamine, benzodiazepine, cocaine and cannabinoid. Electrocardiogram showed sinus tachycardia at rate 130/min and QTc was prolonged at 488ms (Figure 1).

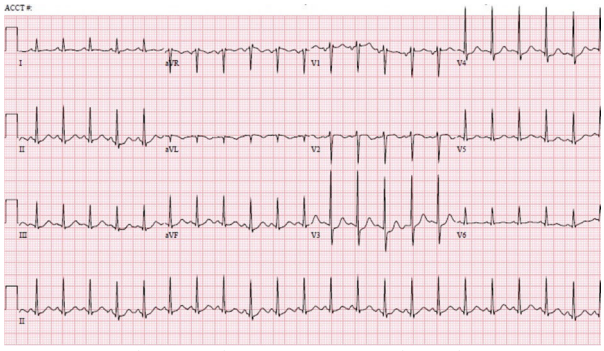

Figure 1 - Electrocardiogram: Sinus tachycardia at 130/min with prolonged QTc

Subsequently the patient became tachypnoeic and hypoxic, was intubated, put on a mechanical ventilator, and sedated with versed, fentanyl and propofol. Arterial blood showed respiratory acidosis and hypoxia. The patient was in cardiogenic shock and dopamine drip was started and intravenous Lasix was given. A subsequent chest X-ray showed newly developed pulmonary congestion. Echocardiogram showed left ventricular dilatation with diffuse hypokinesis and depressed systolic function. The

left atrium was dilated. He had moderate diastolic dysfunction, mild mitral regurgitation and tricuspid regurgitation with a pulmonary artery pressure of 38mmHg. There was global left ventricular function was reduced and ejection fraction was 25-30%. His CT head was negative for an infarct or hemorrhage. He was managed in the cardiac care unit and responded very well to treatment. He became haemodynamically stable and dopamine was discontinued; aspirin, clopidogrel and carvedilol were started. The patient gradually improved and was extubated. Cardiac catheterization showed normal coronaries and normal left ventricular function. LVEDP was 18mmHg. His repeat echocardiogram one week later showed normal left ventricular systolic and diastolic function with an ejection fraction of 70%. The patient was discharged to drug rehab after eight days of treatment.

Discussion

This patient used intravenous crystal meth after which his problem started, so the most likely culprit was methamphetamine. Although he used multiple drugs including cocaine and amphetamine, which have acute and chronic effects on the heart, his cardiac function was normal before. Different mechanisms for cardiac injury due to methamphetamine have been proposed which include catecholamine excess, coronary vasospasm and ischaemia, increase in reactive oxygen species, mitochondrial injury, changes in myocardial metabolism, and direct toxic effects[3].Methamphetamine use is known to cause acute and chronic cardiomyopathy and the reversal of cardiac failure has been documented after discontinuing the drug. In one case report, a patient with chronic methamphetamine-associated cardiomyopathy did not demonstrate late gadolinium enhancement, consistent with an absence of significant fibrosis, and had left ventricular function recovered with 6 months of medical therapy and decreased drug abuse [7]. Another case of a female 42 year old methamphetamine user who had transient left ventricular dysfunction and wall motion abnormalities and an index ventriculogram showed apical ballooning consistent with Takotsubo cardiomyopathy; her left ventricular function significantly improved after 3 days of medical treatment [8]. In our patient, acute cardiomyopathy resolved quickly with intensive medical management. It is not clear how long it takes for cardiomyopathy to revert to normal after discontinuing the drug, or at what stage cardiac damage is irreversible. Many patients who use methamphetamine also ingest other drugs as well. It is unclear to what extent the use of multiple drugs play synergistic role in the cardiac complications that occur. Among patients who present with cardiomyopathy and cardiogenic shock, the usage of drugs like methamphetamine and co-ingestion of other drugs should be considered. Further study is needed to recommend treatment for methamphetamine and related drugs induced cardiomyopathy.

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Education and Training

Causation in medical litigation and the failure to warn of inherent risks

Jem Barton-Hanson and Renu Barton-Hanson

Abstract

Patients who have not been warned of risks involved in a course of treatment traditionally had to establish that, had they been properly informed, they would have opted for a different path. This paper demonstrates that there has been a shift in judicial attitudes; it is no longer enough that medical professionals satisfy their duties to patients, rather they must ensure their patients have the knowledge required to make an autonomous decision. It further shows that the law on causation has been extended on policy grounds to give remedies to a greater class of patients.

Keywords: Causation, Failure to warn, Medical Negligence, Inherent Risks, Informed Consent

Abbreviations: cauda equine syndrome (CES)

Introduction

Claimants in medical negligence cases are increasingly making use of negligent failure to warn of risk in claims for compensation following medical mishaps when an inherent risk in a medical procedure has manifested itself resulting in injury. In order to succeed the claimant must establish firstly that the failure to warn was negligent and secondly that the negligence has caused a loss. This paper focuses on causation in failure to inform cases but briefly considers the shift in judicial attitudes to the requirement to give warnings in order to explain how the duty to inform and the available remedies have diverged.

Members of the medical profession commonly believe that to find a negligent failure to inform has caused a loss to the claimant a court must be satisfied that the patient would not have consented to the treatment had they been told of the risk. This was probably true until 2004 when the House of Lords came to a surprising decision which has since received a mixed reception.

The Changing nature of the requirement to give warnings

In the early days of medical litigation whether non-disclosure amounted to negligence was left to the standards of the medical profession. A medical professional was under a duty to at least equal the standards of a reasonably skilled and competent doctor; this would be assumed if s/he had acted in accordance with a body of professional opinion. This is referred to as the Bolam test.[i] There was disquiet amongst academic lawyers that doctors were being allowed to set their own standards and over time the courts have been wrestling back control.[ii],[iii] Following the Recent Supreme Court ruling in Montgomery[iv] there is now no doubt that patient autonomy is paramount and the need to inform will now be judged by reference to a reasonable person in the patient's position.

In Montgomery the claimant, a diabetic, alleged she had been given negligent advice during her pregnancy. In particular she was not warned of risk of shoulder dystocia, the inability of the baby's shoulders to pass through the pelvis, assessed at 9-10% for diabetic mothers and not informed of the possibility of delivery by elective caesarean section. The Consultant responsible for her care gave evidence (at paragraph 13) that she would not routinely advise diabetic mothers of this risk because if mentioned, "most women will actually say, 'I'd rather have a caesarean section.'" The Supreme Court in finding (at paragraph 87) for the claimant held, "The doctor is therefore under a duty to take reasonable care to insure that the patient is aware of any material risks involved in any recommended treatment, and of any reasonable alternative or variant treatments. The test of materiality is whether, in the circumstances of the particular case, a reasonable person in the patient's position would be likely to attach significance to the risk, or the doctor is or should reasonably be aware that the particular patient would be likely to attach significance to it." Although expressed as, "a duty to take reasonable care," the medical professional is expected to, "ensure," that the patient has the requisite knowledge. The test in failure to inform cases now focuses, not on the actions of the medical professional but, on the patient's knowledge of the risks.

Chester v Afshar[v]

On 21st November 1994 Mr Afshar carried out a microdiscectomy at three disc levels on Miss Chester. There was no complication during the operation and the surgeon was

satisfied that his objectives had been met. When Miss Chester regained consciousness she reported motor and sensory impairment below the level of L2. A laminectomy shortly after midnight the next day found no cause and the surgeon's only explanation was cauda equine contusion during the retraction of the L3 root and cauda equine dura during the L2/L3 disc removal. During the legal proceedings Miss Chester brought against Mr Afshar it was found that the operation carried an unavoidable 1-2% risk of cauda equine syndrome (CES) and that the surgeon had not warned the patient about this risk. It was further found that, had the warning been given, Miss Chester would have sought a second (and possibly third) opinion meaning that the operation would not have taken place on 21st November.

The surgeon and the patient did not agree what was said about the risks of the operation before consent was obtained but the issue was decided in favour of the patient: the surgeon had failed to give a proper warning about the risk of CES. In order to succeed in her claim Miss Chester needed to establish that this failure had caused her loss but her lawyers did not argue that she would have refused consent if she had been informed. They took a different approach; the 1-2% risk of CES is not patient specific and is realised at random. If warned of the risk Miss Chester would have sought a second opinion meaning that the operation would have happened at a later date and possibly with a different surgeon. This subsequent operation would have carried the same 1-2% risk of CES. The High Court of Australia had previously accepted (in a different case) that the claimant can satisfy the burden by showing that, if informed, s/he would have chosen a different surgeon with a lower risk of adverse outcome but there was no evidence in this case that by choosing another surgeon Miss Chester could have reduced the risk.[vi]

At the time Mr Afshar failed to advise Miss Chester of the risks two paths should have been open to her. She could choose to have the operation with the defendant on 21st November which resulted in CES or to seek a second opinion and undergo the operation at a later date giving her a 98-99% (a better than balance of probabilities) chance of avoiding CES. Thus the failure to inform did not increase the 2% risk of CES but the court found, as a matter of fact, that it did cause the CES. Although the physical harm that Miss Chester had suffered (because of the inevitable risk) did not fall within the scope of the doctor's duty to inform (to allow the patient to minimise risk) a majority of the House of Lords felt that the surgeon should be held liable because otherwise the patient would be left without a remedy for the violation of her right to make autonomous decisions about treatment.

There are two leaps in Chester the first is the notion that negligence causes a loss if it induces the claimant to follow a path with an associated risk that is realised when they could have followed another path with exactly the same risk. The second is that violating a patient's right to make autonomous decisions should, as a matter of policy, make the surgeon liable for personal injury which happens after the patient is deprived of their right to make a decision about treatment. The next two paragraphs will consider these leaps in turn.

Equally risky paths: The first leap

In Wright[vii] the patient had developed a streptococcus pyogenes infection that had seeded into her proximal femur resulting in osteomyelitis. Her admission to hospital was delayed for two days by the defendant clinic's negligent handling of her first presentation. On admission to hospital the patient had the additional misfortune to receive woefully inadequate treatment resulting in septic arthritis and permanently restricted mobility. The patient took the questionable decision to sue the clinic but not the hospital. One of the patient's arguments against the clinic was that had she been admitted to hospital without the two day delay she would have been treated by different staff who would, almost certainly, not have been negligent. The claimant argued that, as in Chester, although the clinic's negligence did not increase the random risk of receiving negligent hospital care it had, as a matter of fact, caused the negligent care. Lord Justice Elias rejected this suggestion precisely because the delay had not increased the risk that the hospital would provide the patient with inadequate treatment. However, the other members of the Court of Appeal found for the patient but for another reason; given two extra days the hospital would probably have realised their mistakes and been able to correct them before any permanent harm resulted.

Violated autonomy and personal injury: The second leap

There have been attempts to expand the scope of the majority reasoning in Chester. In Meiklejohn[viii] the patient was treated for suspected non-severe acquired apastic anaemia with Anti Lymphocyte Globulin and Prednisolone the latter causing an avascular necrosis. At an initial consultation a blood sample was taken from the patient for "research purposes" but possibly to exclude dyskeratosis congenital, the condition from which he was actually suffering. The patient argued he had not given informed written consent to the taking of a blood sample for research purposes and that had he been told about the uncertainty in the diagnosis he would have delayed treatment pending the result of the blood test or asked to have been treated with Oxymetholone instead. He further argued these violations of his autonomy required that he be given a remedy for the injury which had actually occurred through a reasonable misdiagnosis of his rare condition. Lady Justice Rafferty sitting in the Court of Appeal dismissed this argument stating at paragraph 34 that, "Reference to [Chester] does not advance the case for the Claimant since I cannot identify within it any decision of principle."

Conclusion

Courts deciding failure to warn cases have shifted the emphasis from the reasonable practices of the medical profession to the autonomy of the patient; from the duty of the medical

professional to the rights of the patient. Medical professionals are now required to give enough information to allow a reasonably prudent patient to make an informed decision about their own treatment. While this change has been taking place there has been no corresponding revision of the remedies available when a patient's autonomy is infringed. If autonomous decision making is to be properly protected a remedy should be vested in every patient who has had their autonomy infringed whether or not that patient has suffered physical injury; autonomy infringements should be actionable per se (without proof of loss) and result in the award of a modest solatium (a small payment representing the loss of the right to make an informed decision about treatment.) Under the present arrangements the wrong that the patient complains of (infringement of autonomy) is not what they are seeking damages for (personal injury.)

In a small way, the court in Chester has sought to close this gap between the patient's right and the remedy available by extending the existing law and widened the circumstances in which damages can be recovered by a patient following an infringement of autonomy. Medical professionals who fail to warn patients of small risks may be held liable if disclosing the risk might cause the patient to delay treatment while further deliberations take place. Paradoxically it could conceivably be argued that medical professionals who fail to disclose significant risks (greater than 50%) should escape liability because the loss was more likely than not to happen anyway!

Both Chester extensions to the law have been tested independently in Wright and Meiklejohn and rejected but this does not mean that it has been overruled. The two subsequent cases were heard by the Court of Appeal which cannot overrule the House of Lords (now the Supreme Court.) Both cases were distinguished meaning that the court was satisfied that they were not factually the same as Chester. Clearly Wright is not concerned with rights to autonomy and Meiklejohn is a failure to warn of uncertainties in diagnosis or failure to obtain written informed consent to research rather than risks inherent in treatment. If the facts of Chester were to come before the Courts again the decision would have to be the same; a surgeon could not necessarily escape liability by proving that, informed of the risk, the patient would have consented to the operation.

Summary points

- Patients have a right to be informed of material risks inherent in medical treatment
- An injured patient does not necessarily need to prove they would not have consented to the operation if the risks had been disclosed
- A legal claim against a health care professional may be successful if the patient would have delayed the operation to a later date
- This extension of the law has critics but the situation is unlikely to change in the near future

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6. Chappel v Hart [1998] HCA 55.
7. Wright (A Child) v Cambridge Medical Group [2011] EWCA Civ 669.
8. Meiklejohn v St George's Healthcare NHS Trust [2014] EWCA Civ 120.

Viewpoint

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Formal Psychiatric Treatment: advantages and disadvantages

James Paul Pandarakalam

Abstract

This paper discusses the merits and undesirable effects of compulsory detention on psychiatric patients and the dilemmas of the mental health staff. It also points out the added risk and the iatrogenic stress psycho geriatric patients in particular may be subjected in instances of mental health act assessments. There is a scarcity of research specifically concerned with the identification of the ill effects of compulsory detention and detection of a subset of highly vulnerable patients who are likely to respond negatively to compulsory care. The author does acknowledge the advantages of mental health acts. The objective is to enhance the awareness among mental health professionals for the need to upgrade the quality of research on the effects of involuntary admission and find more sophisticated alternatives.

Keywords: Key words: Mental health acts; suicides; PTSD, merits; demerits.

Introduction

The closure of asylums in the last century has resulted in an increased number of compulsory hospital admissions for psychiatric patients. Psycho-geriatric patients are highly vulnerable in this respect. Although the traditional buildings instituted for the care of the mentally afflicted have gone, misconceptions about provision and anecdotes about incarceration continue to haunt the community. Recent legislative changes have further extended the occurrence of involuntary hospital admission.[1] Compulsory community care is under constant review. Concurrently the validity of the concept of mental illness, psychiatric classification and diagnostic dilemmas all continue to be debated. Confinement has regained respectability in the discourses of present-day British mental health system because of violent offences committed by psychiatric patients and the public media portraying them as a reflection of failure of community care.

Table 1, Advantages of Mental Health Acts

1. Mental health acts secure the safety of vulnerable people
2. Helps to regain control on their lives
3. Compulsory treatment helps to prevent further deterioration of mental health
4. Aimed to provide effective care and treatments
5. Ensure better after care
6. Protects the safety of other people
7. Prevents suicides
8. Provides opportunities for assessments and diagnosis
9. Can be therapeutic by unburdening personal responsibilities to an institution.

Numerical quantitative studies imply that generally involuntarily admitted patients show clinical improvement and retrospectively view their compulsory admission rather positively.[2] It is an unquestionable fact that Mental Health Acts prevent suicides and homicides (table 1). Mental Health Acts have some unsatisfactory outcomes particularly on a subset of patients including senior citizens admitted formally. It is important to identify such patients and take additional precautions in their management as they run the risk of leaving hospital feeling inferior and inadequate. Patients' specific characteristics, thought processes and past treatment experiences, colour their attitude towards coerced treatment and determine the gains and shortcomings of compulsory care.

Disadvantages

The Mental Health Acts are open to social abuse and elderly patients can be more defenceless in this respect. Specifically they may be: invoked to control behaviour; misused for material gain and implicated in subtle expressions of revenge. They are sometimes invoked to hasten divorce proceedings and to secure the custody of children by a specific parent. They are also used to control the behaviour of children by their parents. Mental Health Acts designed to control psychiatric patients are being enacted and enforced in some underdeveloped countries that lack an efficient tribunal system to monitor their effects.

A patient who has been detained is at risk of repeat detention and someone who has been inappropriately assessed becomes increasingly vulnerable to control on psychiatric grounds. The experience of being detained involuntarily has a reductive effect on behaviour after discharge – it may induce anxiety or post-psychiatric depression. The awareness of being deemed to require compulsory detention generates such negative attitudes as self-denigration, fear and unhealthy repression of anger. It may also impede self-direction and the normal sense of internal control and may encourage the view that in a world perceived as

being divided into camps of mutually exclusive 'normal' and 'abnormal' people, the patient is in the latter category. Compulsory detention may lead to suicide because the patient loses their sense of integration within their own society. Furthermore, the fear and anxiety associated with involuntary admission delays the recovery process. There are other frequently occurring barriers to recovery for those affected such as, loss of capabilities, whether real or imagined, ineffectual medication due to poor elicitation of symptoms because of patient's lack of cooperation and negative drug side effects.

Depressed patients have a higher suicide risk than the population at large and one of the reasons for detention is suicidality. Some of the subjective symptoms of depression can be ameliorated by denying them, while compulsory detention may reinforce depressive symptoms. Detention gives carers a false sense of security and this may lead them to relax their vigilance towards the patient. The Mental Health Acts increase the stigma associated with psychiatric illness and with the exuberant expression of emotions. Patients who are under section or are frightened of being placed under section may deliberately mask their symptoms in an attempt to have the section lifted or to avoid sectioning.

Trans-cultural studies

Trans-cultural studies show that members of migrated cultures, particularly the elderly, are more at risk of inappropriate sectioning than the rest of the population because of the lack of knowledge on part of professionals about the patient's culture. For instance, the debate of over diagnosis of schizophrenia among Afro-Caribbean patients is still unsettled. A study conducted in South London has concluded that Black Africans and Black Afro-Caribbean patients with psychosis in that area are more likely than White patients to be detained under the Mental Health Act 1983.[3] GreatBritain has become a multicultural society and a significant percentage of professionals working in psychiatric units have been trained overseas, in a wide range of countries. This creates further risk of inappropriate diagnosis. There needs to be more emphasis on the significance of trans-cultural psychiatry in the United Kingdom. In particular, psychiatrists should be aware that psychiatry is a medicine of language and culture as well as of the mind.

Medical Dilemmas

Countries in which Mental Health Acts are widely enforced have not achieved any reduction in suicide rates through their implementation. Sectioning is perceived by many patients affected as a psychological guillotine – a form of psychiatric terrorism. The medical profession is invested by the Acts with undue power over society. This is of particular concern because training in psychiatry does not include the study of free will and allied philosophical issues and also because there is no clear definition or description of mind and consciousness. In psychiatry there is a lack of clinical indicators and psycho-physiological parameters so the criteria for diagnosis are imprecise, with a concomitant risk of the Acts being erroneously implemented. It has been postulated that once a person has been classified as having deviant behaviour, that categorisation has a potent effect on the subsequent actions of the person concerned and those interacting with them.

Is it not justifiable to argue that even if a few mentally ill patients are underdiagnosed and not subjected to psychiatric admission, someone whom we would regard as normal should not be detained in a psychiatric hospital against their will? Such a view is analogous to the judicial view regarding capital punishment where even if ninety-nine murderers escape capital punishment because there is no death penalty, one innocent person should not be sentenced to death. Mental Health Acts may be a necessary evil but they present a dilemma for mental health professionals: the morality of helping patients and protecting the society from the consequences of their illness against the immorality of restricting their freedom. Clinicians become torn between the ideals of curing mental illness and defending the sanity of patients.

Patients' Perception

A small survey conducted by the author revealed that no sectioned patient in the group studied sent a thank-you card after discharge to the ward in which they were confined. However, many voluntary patients expressed appreciation in that way. This is an indicator of the attitude of sectioned patients towards the Mental Health Acts. One reason must be that a record of being sectioned limits their freedom to travel and also affects their employment opportunities adversely. A patient has commented that it is easier for an ex-convict to gain employment than it is for a once-sectioned psychiatric patient.

There is anecdotal evidence illustrating the panic that may be generated with the word 'section' in psychiatric patients. A recovering elderly hypomanic patient explained that he misconstrued the word on hearing it when he was ill, taking it in relation to sectioning in Obstetrics and General Surgery. He remembered that as he resisted entering a taxi while being persuaded to agree to admission, the driver said that he was going to be sectioned if he refused hospital admission. The patient misunderstood this and interpreted it as he was going to be cut into pieces and tried to jump out of the vehicle.

Post-traumatic stress disorder

Any loss of intrinsic importance to an individual constitutes bereavement. Denial, anger and depression experienced in compulsory detention are comparable to bereavement.[4] In the case of a detained patient, the loss of self-identity and of social functioning causes a grief reaction. It has been hypothesised that there are high levels of Post-traumatic Stress Disorder (PTSD) symptoms in detained patients.[5] Very few repeat detainees become habituated to the implementation of the

Mental Health Acts. The vast majority become increasingly frustrated and develop a pessimistic outlook towards their mental health. There is a high incidence of suicide among patients who have multiple detentions.

Post-hospitalisation Stress Disorder is much more common than generally recognised. Formal admission may lead to fear, anger, frustration, depression or loss of self-esteem, depending upon the individual's psychological response.[6] Involuntary admission may result in pervasive distress in any patient – this kind of hospital admission may be perceived as threatening and even as a catastrophe. Detained psychotic patients are less aware of their environment because of the preoccupation with their symptoms. Non-psychotic patients, when detained for instance because of a risk of suicide, are fully aware of their immediate environment and the chaos they have caused to themselves. They have a high risk of PTSD.

Preventive detention

Fear of liability may lead to compulsory hospitalisation solely to prevent violence on the part of patients who otherwise do not require in-patient care.[6] Psychiatrists are not trained to police society and may lack sufficient knowledge and experience to participate in the social control responsibilities that are part of the remit of the criminal justice system - they are sometimes involved in that function. Psychiatry has to be safe and secure in the hands of individual psychiatrists and psychiatrists have to be protected when practising psychiatry. Mentally ill patients are sometimes mistakenly processed through the criminal justice system rather than the mental health system. When that happens, compulsory detention may be perceived as a form of criminalisation of mental illness. Unless there is scrupulous monitoring, mandatory treatment impinges on civil liberties. Preventive detention is legally ambiguous and clinically impractical.

Assessment

Amongst the government's fundamental powers and responsibilities are, protecting people from injury by another and caring for less able people, whether physically or mentally incapacitated. These functions encompass the welfare and safety of both the individual concerned and the public.

A decision about compulsory detention is made on the basis of three considerations: loss of emotional control; psychotic disorder and impulsivity with serious thoughts, threats or plans to kill oneself or others. Any perceived risk must be imminent and provocative. The clinician is legally required to determine the least restrictive environment to which a patient may be safely assigned for continued care. To fulfil these requirements while implementing the Mental Health Acts, a psychiatrist needs the skills of a physician, lawyer, judge, detective, social worker and philosopher. The decision-making process is influenced by multiple factors such as: the clinician's propensity to detain patients; the record of past untoward incidents involving the patient; attitude towards risk taking and availability of hospital beds and alternative safe treatment facilities. It is regrettable that in section 5(2) assessments, often it is a junior doctor, the least experienced person in the team, who is called upon to conduct the evaluation.[4] A multitude of interviews with mental health staff, a social worker and solicitor will have to be endured by the patient - these are regarded as ordeals by most of them.

Non-detainable patients

Since the introduction of the Mental Capacity Act 2005, the number of assessments that are followed by a decision against compulsory detention is increasing. Patients who are assessed for formal admission but not found to be detainable may develop new risks subsequently as a result of the assessment procedure itself. Before assessment, mental health professionals may place themselves in covert locations around the patient's house and neighbours may watch eagerly behind their curtains. Thereby the patient's social image is damaged. After meticulous assessment, it may be a relief for the patient that they are not detained and that euphoria may continue for a short while but all too often damage has been done. The patient who is tormented by psycho-social stressors may find the assessment experience intensifies the injury. The decision about whether it is appropriate to assess someone is therefore an area in which more clarification and some management guidelines are much needed. In situations such as these, untoward incidents have been periodically reported. That may mean that the professionals involved and perhaps also family members who initiated the assessment, blame themselves and endure severe guilt feelings or blame each other. Furthermore, psychiatrists are not mind readers. It is possible that a patient will cleverly deny any suicidal intent during assessment, intending to fulfil a suicidal urge afterwards and that may falsely appear to be a reaction to the assessment. An interview for assessment may be the factor that takes them beyond their limit. Because of all these circumstances, the patient may need intensive home care and counselling after an assessment that does not lead to hospital care. In addition to treating mental illness, it is the duty of the psychiatrist to defend the sanity of patients. The difficulty of defining normalcy is notorious: it is easier to detect psychiatric symptoms than to describe normal behaviour.

Tribunals

Mental health tribunals are demanding and may be humiliating and intimidating. They are highly stressful for the patient and clinician and they involve the breach of patient confidentiality. Tribunals are often emotionally charged scenes for the patient and psychiatrist, they may result in traumatisation. The largely professional make-up of a tribunal is often perceived as intimidating by patients, who tend to be suspicious of collusion between professionals and above all of their reluctance to challenge the decision of a psychiatrist.[7] Psychiatrists who are aware of legal profession's ignorance on psychiatric issues

dominate the tribunal scene by flamboyant linguistic expressions, while lawyers question the objectivity of psychiatry and the expertise of psychiatrists in legal matters. Tribunals are concerned with the legality of detention and not with the appropriateness of treatment. However, one study has shown that patients who appear before tribunals find it easy to accept they require compulsory admission. [8] Psycho-geriatric patients find it extremely distressing to attend tribunals. Hospital managers' review hearings are often arranged and carried out promptly. Managerial hearings involve local people too which may make them less intimidating for detained patients.

Involuntary treatment

Although mental health staff usually have the best of intentions, when mandatory treatment is applied to patients it may prove traumatic and counter-therapeutic. The experience of undergoing forced treatment adds to the patient's perception of stigma and discrimination. Involuntary psychiatric drug treatment is bound to be less effective than voluntary treatment. An outcome may be misdiagnosis, long-lasting and disabling side effects. Forced treatment potentially violates a person's right to respect private life under Article 8 of the European Convention on Human Rights. Article 8 is violated only if patients can prove the treatment given is more harmful than the claimed therapeutic benefits, yet the clinician can administer the treatment if he thinks it is therapeutically necessary. Compulsory treatment makes patients feel infantilised, especially because forced psychiatric treatment often involves coercion, emotional intimidation, bullying and threats.

Community Treatment Order (CTO) is being constantly evaluated in terms of its merits and demerits. The results have been inconclusive and warrant more systematic studies. It was Section 41 of the Mental Health Act that inspired the introduction of CTO - the main purpose being to protect the community from the aggressive behaviour of some of the psychiatric patients as in the case of the successful Section 41. There are indications that CTO has fulfilled such a goal. It was also targeted to enhance compliance and concordance with the mental health services and to prevent suicides but studies indicate that those goals were not achieved.[9,10] The Oxford Community Treatment Order Evaluation Trial (OCTET) substantiates a lack of any evident advantage in dropping relapse.

The "knee jerk" reaction from part of community service has apparently resulted in spontaneous readmissions of patients under CTO. It has also contributed to prolonged detention of patients awaiting community placement under CTO. This is because detained patients must stay on section 3 or 37 to allow the Mental Health Act to be converted to CTO upon discharge. Obviously, such a scenario curtails liberty. Patients always feel bitter about the "hanging feelings" of continued detention. Coercion runs the risk of weakening therapeutic alliance. It may be true that if fewer conditions are imposed, CTO could serve as a "memory knot" for patients with limited insight. Despite all the controversies surrounding the benefits of CTO, its use is increasing worldwide. [11]

Assertive Human Rights

All human beings have individual rights and mental health professionals in particular must be mindful of those rights. Table 2 presents the list of assertive human rights, as modified from Gael Lindenfield (2001). [12]

Table 2, Assertive Human Rights

1. The right to ask for what we want (realising that the other person has the right to say "No").
2. The right to have an opinion, feelings and emotions and to express them appropriately.
3. The right to make statements which have no logical basis and which we do not have to justify (e.g. intuitive ideas and comments).
4. The right to make our own decisions and to cope with the consequences.
5. The right to choose whether or not to get involved in the problems of someone else.
6. The right to know about something and not to understand.
7. The right to be successful.
8. The right to make mistakes.
9. The right to change your mind.
10. The right to privacy.
11. The right to be alone and independent.
12. The right to change ourselves and be assertive people.
13. The right to be neutral.
14. The right to be empathetic and apathetic.

Discussion

Community care is more innovative than compulsory detention in hospital. For majority of patients, the best way forward is having high quality home treatment facilities as it is least restrictive and using compulsory detention should be the last resort. In some cases, forced psychiatric admission is indicative of failure in the supply of quality home treatment. One thing that sometimes leads to in-patient admission is lack of confidence in the service available. The perception of home treatment may be at fault here - it needs to be understood as more than merely staying outside hospital. Forensic patients and treatment resistant psychotic disorders lacking insight may be a different state of affairs. CTOs have serious impact on the autonomy and privacy interests of individuals and should not be applied to compensate for under-resourced community services.

Caring and supportive relationships between mental health staff and patients during involuntary in-patient care have considerable bearing on the outcome of compulsory detention.

A recent study has revealed that among patients who have been detained involuntarily, perceptions of self are related to the relationships with mental health professionals during their inpatient stay. [13] Perceived coercion at admission predicts poor engagement with mental health staff in community follows up. When professionals demonstrate their genuineness and encourage patient participation in the treatment options, coercive treatment would be perceived as less of an infringement to the autonomy of patients and their sense of self-value. [14] If patients maintain both positive and negative views about detention, interventions should be designed to enhance positive experiences by focussing on respect and autonomy.Patients admit only compulsory detention gave them an opportunity to receive medication in a time of crisis and report it did not necessarily prevent thoughts relating to self-harm. It simply reduced the opportunities for impulsive acts.

'Rooming-in' is worth debating as an alternative to compulsory detention. This is the voluntary participation of so-called confidants, who may be chosen family members or trusted friends. They provide a 24-hour vigil for the patient in a safe hospital environment. An Australian study has suggested this system is highly valued by nursing staff, patients and their families.[15] It is an initiative that needs further testing and evaluation. The resolution of angry feelings towards the mental health professionals has a significant bearing on their future compliance. The post-detention period tests the attention given to patients by mental health professionals. Here the staff members have to take the initial steps required to repair damaged relationships which may have developed in particular with angry patients. Detained patients should be offered counselling in post-discharge follow-ups and should be given satisfactory explanation of the circumstances for formal admission. Detained patients should be given the support to enable them to: rewrite their life story; reconstruct a sense of self; achieve healing of the assault of their illness and the treatment procedures inflicted on their personality. Specific interventions should be designed and evaluated in order to deal with any unresolved PTSD symptoms relating to formal psychiatric admission.

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None declared

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