# BJMP

### Volume 7 Number 2 June 2014

# British Journal of Medical Practitioners

www.bjmp.org ISSN: 1757-8515

# British Journal of Medical Practitioners

Volume 7 Number 2 (June 2014)

http://www.bjmp.org

#### Editorial Staff

#### **Managing Editors**

- Dr Javed Latoo, UK
- Dr Nadeem Mazi-Kotwal, UK

#### Associate Editors

- Professor Ken Brummel-Smith, USA
- Dr Nasseer Masoodi, USA

#### **Specialty Editors**

- Dr Francis Dunne, Consultant Psychiatrist and Honorary Senior Lecturer, UK
- Dr M Y Latoo, Consultant Anaesthetics and Critical Care, UK
- Prof Claudio Puoti, Chief of Internal Medicine and Liver Unit, Marino, Italy
- Mr Yadu K Shankarappa, Consultant Trauma and Orthopaedic Surgeon, UK
- Dr Daljit Sura, General Practitioner and Family Physician, UK
- Dr Sandeep Tripathi, Assistant Professor of Paediatrics, USA

#### **Editorial Advisors**

Editorial Advisors suggest names of other peer reviewers, suggest topics to be covered and provide ongoing advice to the editors. The advisory board members will be reviewed annually. No person, including editors, will be involved in the peer review process of an article in which they have a conflict of interest.

- Prof Raman Bedi, Director of Global Child Dental Health Taskforce, UK
- Prof Rajan Madhok, Medical Director of NHS Manchester, UK
- Prof Elisabeth Paice, Dean Director of Postgraduate Medical & Dental Education for London, UK
- Prof Arnie Purushotham, Professor of Surgery, UK
- Prof Khalid J Qazi, Professor of clinical Medicine, USA
- Dr Abid Rajah, Consultant Anaesthetics and Critical Care Medicine, UK
- Prof A A Riaz, Professor of Surgery, UK
- Prof Robert Thomas, Professor of Oncology, UK

#### Editorial Board

No person, including editors, will be involved in the peer review process of an article in which they have a conflict of interest. Peer reviewers helps editors decide which manuscripts are suitable for our journal and helps authors and editors to improve the quality of reporting

#### Internal Medicine and allied Specialties

- Dr John Ellis Agens, Jr, Associate Professor of Medicine, USA
- Dr Mohammed Azher, Consultant Physician, UK
- Dr Rajith deSilva, Consultant Neurologist, UK
- Dr Indrajit Gupta, Consultant Physician, UK
- Dr Amir Jaffer, Associate Professor of Internal Medicine, USA
- Dr Roop Kaw, Assistant Professor of Internal Medicine, USA
- Prof G V Sherbet, Cancer and Molecular Medicine, UK
- Dr Yili Zhou, Neurologist and Interventional Pain Management Specialist, USA

#### Surgery and allied Specialties

- Mr Habib Charfare, Consultant Surgeon, UK
- Prof Jorg Haier, Professor of Surgery, Germany
- Mr Patrick Omotoso, Consultant Surgeon, Canada
- Mr Harbinder Sharma, Consultant Surgeon and Urologist, UK
- Mr Manoj Sood, Consultant Orthopaedic Surgeon, UK

#### Anaesthesia and Critical Care Medicine

- Dr Altaf Bukhari, Cardiac Anaesthetist, UK
- Dr Mehmood A Durrani, Vice Chair of Anaesthesia and Chief of Cardiiac Anaesthesia, USA
- Dr Faisal Salim, Consultant Anaesthetics, UK
- Dr Asquad Sultan, Consultant Anaesthetist and Pain Specialist, UK

#### Psychiatry

- Dr Chris McEvedy, Consultant Psychiatrist, UK
- Dr Minal Mistry, Consultant Psychiatrist, Canada
- Dr Kabir Padamsee, Consultant Child Psychiatrist, UK
- Dr Aadil Jan Shah, Consultant Psychiatrist, UK

- Dr Saoud Sultan, Consultant Psychiatrist and College Tutor, UK
- Dr Ovais Wadoo, Consultant Psychiatrist, UK
- Prof Malcolm Weller, Emeritus Consultant Psychiatrist, UK

#### Family Medicine

• Dr Anita Sharma, Family Physician, UK

#### Pediatrics

• Dr Ramesh Mehta, Consultant Pediatrician, UK

#### Gynaecology & Obstetrics

• Mr Dilip Patil, Consultant Obstetrician & Gynaecologist, UK

#### Research & Development Advisors

- Dr Sam Tothill, Associate Dean of the Faculty of Medicine & Biosciences Crainfield University, UK
- Dr Mohammed Wasil,Assistant Director of Research & Development & Clinical Fellow Crainfield University , UK

#### **Other Editorial Staff**

#### Section Editors

- Dr Trinisha Govender, UK (E-Interview section)
- Dr Mehraj Shah, UK ( Education & Training)

#### **Proof Readers**

- Dr Ruth St John, UK
- Dr Diana Ayoola Mabayoje, UK
- Dr Tabassum Malik, UK
- Dr Arafat-Ur-Ibrahim Mulla, UK
- Dr Cristal Oxley, UK
- Dr Claire Pocklington, UK
- Dr Natasha Quader, UK
- Dr Farheen Zulfiquer, UK

#### Legal Advisor

• Fazl Syed, Consultant International law, UK; Attorney at Law, New York, USA; Solicitor-Supreme Court of England & Wales, UK.

#### Further Information

Instructions to authors Please visit: http://bjmp.org/content/guidance-authors

Submit an article Please visit: http://bjmp.org/content/submit-articles

Contact us Please visit: http://www.bjmp.org/contact

#### Publishers

JMN Medical Education Ltd 1 Waltham Drive Elstow Bedford, United Kingdom MK429FY

The British Journal of Medical Practitioners (BJMP) is a quarterly peer-reviewed online international medical journal published by JMN Medical Education Ltd UK. The information, opinions and views presented in the British Journal of Medical Practitioners reflect the views of the authors and contributors of the articles and not of the British Journal of Medical Practitioners or the Editorial Board or its publishers. The British Journal of Medical Practitioners and/or its publisher cannot be held responsible for any errors or for any consequences arising from the use of the information contained in this journal.

http://www.bjmp.org

# British Journal of Medical Practitioners

Volume 7 Number 2 (June 2014)

#### BJMP June 2014 Volume 7 Number 2

Editorial	
Health care quality and hospital acquired infection in Intensive care: Bundles and checklists Sandeep Tripathi	4
Research Articles	
Extended spectrum beta lactamase positive uropathogenic E. coli - Epidemiological Factors and Resistance Priya Datta, Varsha Gupta and Shailpreet Sidhu	7
Case Reports/Series	
Lamotrigine-induced hallucination in patient with bipolar disorder and no history of epilepsy or psychosis: a case report and literature review Yasir Hameed and Jacobus Hamelijnck	10
<b>Carbimazole induced ANCA Positive Vasculitis</b> Yasmeen Ajaz and Sameem Matto	14
Liver Veno-Occlusive Disease (VOD) in a patient given 6-Thioguanine for Crohn's Disease Agata Salerno, Marco Vacante, Donatella Pollina, Benedetta Stancanelli, Silvia Martini, Ezio David, Lorenzo Malatino	16
Medical Images	
<b>Tracheo esophageal fistula</b> M Suresh Babu, Deepak Suvarna, Chandrashekhar Shetty and Aditya Nadella	19
The twitching leg Jose A Egido and Ana M Garcia	21
<b>Spotted Bone - A Spot Diagnosis</b> Abdul Rehman Arshad, Asif Rahman, Shafqat Hussain	23
Miscellaneous	
"Of Psychosis" - A Poem by Dr Javed Latoo Javed Latoo	25
A Very Important Doctor Francis J Dunne	26

# Health care quality and hospital acquired infection in Intensive care: Bundles and checklists

#### Sandeep Tripathi

BJMP 2014;7(2):a715

Hospital acquired infections (HAI) are one of the most common complications involving hospital care and are the leading cause of death in U.S. Central line associated Blood stream Infection (CLABSI), Ventilator Associated Pneumonia (VAP), Surgical site infection (SSI) and Catheter associated urinary tract infection (CAUTI) represent 75% of all HAI<sup>1</sup>. HAI prevention is one of the 20 'priority areas' identified in the Institute of Medicine (IOM) 2003 report 'transforming health care quality'<sup>2</sup>. Certain HAI are preventable, but as the prevention efforts become more defined, there remains a lack of evidence of a strong return of investment for hospitals and health care payers in preventing these infections. This lack of evidence presents potential obstacles in advancing efforts to prevent infections.

#### Central Line Associated Blood Stream Infection (CLABSI)

CLABSI is a primary blood stream infection that develops in a patient with a central line in place within the 48 hour period before the onset of blood stream infection, which is not related to infection at another site. Central line associated blood stream infection occurs up to 80,000 times per year resulting in 28,000 deaths among patients in the Intensive Care unit (ICU). Average cost of CLABSI is approximately \$ 45,000 per incidence<sup>3</sup>. CLABSI reduction is also one of the success story of how inexpensive interventions, grouped as a checklist could reduce the rate of nosocomial infections to a median rate of zero. Although quality control interventions in many areas of ICU have been studied, the idea of integrating quality indicators with group of interventions known as bundles has been validated in the ICU most successfully in CLABSI. The landmark study on reduction of CLABSI was the 'Keystone ICU' project funded by the Agency for Health care Research and Quality (AHRQ)<sup>4</sup>. One hundred and three ICUs in Michigan participated in this state wide safety initiative. The study intervention recommended five evidence based procedures that were identified as having the greatest effect on the rate of catheter related BSI and the lowest barriers to implementation. The interventions were remarkably successful, nearly eliminating CLABSI entirely in most ICUs over an 18 month follow up period.

lead to improved outcomes, in long term the biggest impact on decreasing HAI, is of the safety climate of the unit. Studies have linked safety climate to clinical and patient outcomes in addition to showing that the safety climate is responsive to interventions. A large study targeting the culture of safety was a follow up of the Michigan Keystone study. The study was a prospective cohort study to improve quality of care and safety culture by implementing and evaluating patient safety interventions in participating ICUs and showed large scale improvements in safety climate among diverse organizations<sup>5</sup>. As part of the national effort to reduce the HAI, the Department of Health and Human Services (HHS) launched the HHS action plan to reduce the health care associated infections in 2009. The project was titled 'On the cusp: Stop BSI', designed to apply the principles of comprehensive unit based safety program (CUSP) to improve the culture of patient safety and implement evidence based best practices to reduce the risk of infection. The initiative ultimately reduced mean rates of CLABSI in participating units by an average of 40%, preventing more than 2000 CLABSI, saving more than 500 lives and avoiding more than \$34 million in excess health care costs<sup>6</sup>.

Although in short term intensive training and monitoring can

#### Ventilator Associated Pneumonia

Optimizing the care of mechanically ventilated patients is an important goal of health care providers and hospital administrators. An easily acquired and reliable marker for medical quality has been elusive for this patient population. VAP has historically been used as a marker of the quality of care associated with mechanically ventilated patient and is associated with worse outcomes7. However the diagnosis of VAP is nonspecific, the clinical diagnosis by the widely used American College of Chest Physicians (ACCP) criteria includes a new progressive consolidation on chest radiography plus at least two of the following clinical criteria: fever > 38, leucocytosis or leucopenia and purulent secretions. Unfortunately, all these findings alone or in combination can occur in other noninfectious conditions, making the diagnosis of VAP subjective and prone to bias. In fact, for the last many years, the surveillance rates of VAP are decreasing, whereas the clinical

diagnosis of VAP and tracheobronchitis as well as antibiotic prescribing remains prevalent. External reporting pressures may be encouraging stricter interpretation of the subjective signs that can cause artifactual lowering of the VAP rates. The result is that, it is almost impossible to detangle the relative contribution of quality improvement efforts in the ICU versus surveillance efforts as explanation for the currently observed lower rates of VAP<sup>8</sup>.

To eliminate the subjectivity and inaccuracy and to create an objective, streamlined and potentially automatable criteria, Center of Disease Control (CDC) now recommends surveillance of ventilator associated events (VAE) as a more general marker and defines it as sustained increase in patient's ventilator settings after a period of stable or decreasing support . There are three definition tiers within the VAE algorithm; 1) Ventilator Associated Condition (VAC); 2) Infection Related Ventilator Associated Complication (IVAC); and 3) Possible and probable VAP. The screening for VAC captures a similar set of complications to traditional VAP surveillance, but it is faster, more objective and potentially a superior predictor of clinical outcomes9. In a CDC funded study of 597 mechanically ventilated patients on use of VAC as an outcome predictor, it was noted that 9.3% of the study population had a VAP, whereas 23% had VAC. VAC was associated with increased mortality (odds ratio of 2.0) but VAP was not. VAC assessment was also faster (mean 1.8 minutes vs 3.9 minute per patient) 10.

Similar to the CLABSI bundles, prevention of VAP by utilization of evidence-based bundles of care has proved to be a very successful. Heimes and colleagues recently conducted a study examining 696 consecutive ventilated patients in a level 1 trauma center to evaluate a VAP prevention bundle with 7 elements. They found a VAP rate of 5.2/1000 days of ventilator support in the pre intervention phase, while a 2.4 /1000 and 1.2/1000 days (p= 0.085) in the implementation and enforcement periods respectively<sup>11</sup>.

#### Catheter Associated Urinary Tract Infection (CAUTI)

Health care associated UTI account for up to 40% of infections in hospitals and 23% of the infections in the ICU. The vast majority of UTIs are related to indwelling urinary catheters. CAUTI result in as much as \$ 131million excess direct medical costs nationwide annually<sup>12</sup>. Since October 2008, Center of Medicare Services (CMS) no longer reimburses hospitals for the extra costs of managing a patient with hospital acquired CAUTI.

There are certain factors like Diabetes mellitus, old age or severe underlying illness that places patients at a greater risk of CAUTI, but there also are modifiable factors like non adherence to aseptic catheter care recommendations and duration of catheterization that can be targeted by quality improvement efforts, to decrease the risk<sup>13</sup>. The key strategies for prevention of CAUTI include avoiding insertion if possible, early removal by implementation of checklists, nurse based interventions or daily electronic reminders, utilization of proper techniques for insertion and maintenance and considering alternatives to indwelling catheters like intermittent catheterization, condom catheters and portable bladder ultrasound scanner. Most of these strategies have been utilized in quality improvement efforts to decrease CAUTI. Assessment of the need is essential as Munasinghe et al have found urinary catheter placed in 21 to 50% of patients for inappropriate reasons<sup>14</sup>. A nurse based reminder to physician to remove unnecessary urinary catheters in a Taiwanese hospital resulted in reduction of CAUTI from 11.5 to 8.3 /1000 catheter days<sup>15</sup>. Similarly utilization of electronic urinary catheter reminders system and stop orders have been shown to reduce the mean duration of catheters by 37% and CAUTI by 2%<sup>16</sup>. Utilization of condom catheter has also been shown to be effective in reducing bacteriuria, symptomatic UT and mortality as compared to indwelling catheter<sup>17</sup>.

#### Final word

Health care is often compared with airline industry with six sigma efficiency. This would translate to 0.002 defective parts or errors/million, obviously we are not close to that and may not be realistic. However this also cannot be an excuse to rationalize poor practice culture. As in any industry, in health care to establish change it is essential to regulate interpersonal interactions. With behaviors change leading to changes in processes of care, change is not only possible, it is sustainable.

Competing Interests None declared Author Details SANDEEP TRIPATHI, MD, Consultant, Pediatric Intensive Care Unit, Assist Professor of Pediatrics, Mayo Clinic, Rochester, MN. CORRESSPONDENCE: DR SANDEEP TRIPATHI, 3107 Avalon Cove Court NW, Rochester, MN 55901 Email: sandeeptripathi2000@yahoo.com

- Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care associated infections and deaths in U.S. hospitals, 2002. Public Health Rep 2007;122:160–166.
- National Research Council. Priority Areas for National Action: Transforming Health Care Quality. Washington, DC: The National Academies Press, 2003.
- Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infections in critically ill patients. Excess length of stay, extra costs, and attributable mortality. JAMA 1994;271:1598–601.
- Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. N Engl J Med 2006;355(26): 2725–2732.
- Sexton JB, Berenholtz SM, Goeschel CA, et al. Assessing and improving safety climate in a large cohort on intensive care units. Crit Care Med 2011;39:934–9.
- AHRQ Patient Safety Project Reduces Bloodstream Infections by 40 Percent. September 2012. Agency for Healthcare Research and Quality,

Rockville, MD. http://www.ahrq.gov/news/newsroom/pressreleases/2012/20120910.html

- Kollef MH, Hamilton CW, Ernst FR. Economic impact of ventilatorassociated pneumonia in a large matched cohort. Infect Control Hosp Epidemiol 2012;33: 250–6.
- Klompas M. Is a ventilator-associated pneumonia rate of zero really possible? Curr Opin Infect Dis 2012;25:176–82.
- Marin H. Kollef. Ventilator-associated Complications, Including Infection-related Complications: The Way Forward. Crit Care Clin 2013;29:33–50.
- Klompas M, Khan Y, Kleinman K, et al. Multicenter evaluation of a novel surveillance paradigm for complications of mechanical ventilation. PLoS One 2011;6: e18062.
- Heimes J, Braxton C, Nazir N, et al. Implementation and enforcement of ventilator-associated pneumonia prevention strategies in trauma patients. Surg Infect (Larchmt) 2011;12:99–103.
- Burton DC, Edwards JR, Srinivasan A, et al. Trends in catheterassociated urinary tract infections in adult intensive care units-United States, 1990-2007. Infect Control Hosp Epidemiol 2011;32:748–56.
- Umsheid CA, Mitchell MD, Doshi JA, et al. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality costs. Infect Control Hosp Epidemiol 2011;32:101–14.

- Munasinghe RL, Yazdani H, Siddique M, et al. Appropriateness of use of indwelling urinary catheters in patients admitted to the medical service. Infect Control Hosp Epidemiol 2001;22(10):647–9.
- Huang WC, Wann SR, Lin SL, et al. Catheter-associated urinary tract infections in intensive care units can be reduced by prompting physicians to remove unnecessary catheters. Infect Control Hosp Epidemiol 2004;25:974–8.
- Meddings J, Rogers MAM, Macy M, et al. Systematic review and metaanalysis: reminder systems to reduce catheter-associated urinary tract infections and urinary catheter use in hospitalized patients. Clin Infect Dis 2010; 51:550–60.
- Saint S, Kaufman SR, Rogers MA, et al. Condom versus indwelling urinary catheters: A randomized trial. J Am Geriatr Soc 2006;54:1055– 61.

## Extended spectrum beta lactamase positive uropathogenic E. coli - Epidemiological Factors and Resistance

Priya Datta, Varsha Gupta and Shailpreet Sidhu

#### Abstract

Introduction: There is increasing incidence of ESBL producing E. coli causing community urinary tract infections. The primary objective of this study was to study the epidemiological factors associated with ESBL (Extended spectrum beta lactamases) positive community acquired uropathogenic E. coli isolates and to determine their susceptibility to newer oral drugs including mecillinam.

Materials & Method: In this prospective study, from total of 140 community isolates of E. coli causing UTI, ESBL was detected by CLSI criteria. Drug susceptibility was done by Kirby-Bauer method disc diffusion method for various oral antimicrobial agents. Various epidemiological factors associated with ESBL for each patient were recorded on individual forms. This included age, presence of diabetes mellitus, renal calculi, pregnancy, history of urinary instrumentation, recurrent UTI and antibiotics intake.

**Results:** Out of total of 140 strains of E. coli, which were screened for ESBL production, 30 (21.4%) isolates were positive. High-level resistance 94 (70%) was seen for many antimicrobial agents. Only 4.5% of uropathogenic E. coli were resistant to Mecillinam. Various epidemiological factors associated with ESBL causing infections were female patients, H/o antimicrobial intake, elderly age > 60 years, renal calculi and H/o recurrent UTI. Conclusions: The epidemiology of ESBL positive uropathogenic E. coli is becoming more multifaceted.

Keywords: ESBL, Community UTI, E.coli, epidemiology

Abbreviations: ESBL - Extended spectrum beta lactamases, UTI - Urinary tract infection

#### Introduction

Community acquired urinary tract infection (UTI) due to Escherichia coli is one of the most common form of bacterial infections, affecting people of all ages. Originally ESBL (extended spectrum  $\beta$ -lactamases) producing E. coli was isolated from hospital setting but lately this organism has begun to disseminate in the community.<sup>1</sup>

In India community presence of ESBL producing organisms has been well documented. However, various epidemiological factors associated with ESBL producing strains need to be documented. This will allow clinicians to separate patients with community UTI with these factors so that appropriate and timely treatment can be given.<sup>2</sup>A community UTI when complicated may be a potentially life-threatening condition. In addition, for deciding the empirical treatment for patients with a UTI a thorough knowledge of local epidemiology is required. Therefore, the primary objective of this study was to determine the epidemiological factors associated with ESBL positive community acquired uropathogenic E. coli isolates and to determine their susceptibility to newer oral drugs. Mecillinam is a novel β-lactam antibiotic that is active against many members of family Enterobacteriaceae. It binds to penicillin binding protein (PBP 2), an enzyme critical for the establishment and maintenance of bacillary cell shape. It is given as a prodrug that is hydrolyzed into active agent. It is well tolerated orally in the treatment of acute cystitis.3

#### Material and Methods

This prospective study was conducted, from Jan 2012- July 2012, in our tertiary care hospital, which caters to medical needs of the community in North India.

#### Study Group:

The study group included patients diagnosed as having a UTI in outpatient clinic, or the emergency room or patients diagnosed within 48 hrs after of hospitalization. These patients and were labeled as patients having a community UTI. A diagnosis of symptomatic UTI was made when patient had at least one of the following signs or symptoms with no other recognized cause: fever  $\geq 38.8^{\circ}$ C, urgency, frequency, dysuria or suprapubic tenderness and a positive urine culture (i.e.  $\geq 10^{5}$  microorganisms/ml of urine).<sup>4</sup> Various epidemiological factors for each patient were recorded on individual forms. This included age, presence of diabetes mellitus, renal calculi, pregnancy, history of urinary instrumentation, recurrent UTI (more than 3 UTI episodes in the preceding year) and antibiotics intake (use of  $\beta$ -lactam in the preceding 3 months).<sup>2</sup>

Patients with a history of previous or recent hospitalization were excluded from study.

Antibiotic susceptibility testing was carried out following Clinical Laboratory Standards Institute (CLSI) guidelines using the Kirby-Bauer disc diffusion method.<sup>5</sup> The antibiotics, which were tested included Amoxyclav (30/10µg), Norfloxacin (10µg), Ciprofloxacin (5µg), Tetracycline (30µg), Nitrofurantoin Trimethoprim-sulfamethoxazole (23.75/1.25µg), (300µg), Cephalexin (30µg), Cefaclor (30µg), Cefuroxime (30µg), Mecillinam (10µg) (Hi-Media, Mumbai, India).

#### Detection of ESBL

ESBL detection was done for all isolates according to latest CLSI criteria.5

Screening test - According to latest CLSI guidelines, zone diameter of E. coli strain for Ceftazidime <22mm and for Cefotaxime < 21mm is presumptively taken to indicate ESBL production.

Confirmatory test - As per CLSI guidelines, ESBLs were confirmed by placing a disc of Cefotaxime and Ceftazidime at a distance of 20mm from a disc of Cefotaxime /Clavulanic acid (30/10µg) and Ceftazidime/Clavulanic acid (30/10µg) respectively on a lawn culture of test strain (0.5 McFarland inoculum size) on Mueller-Hinton agar. After overnight incubation at 37° C, ESBL production was confirmed if there was a  $\geq$ 5mm increase in zone diameter for either antimicrobial agent tested in combination with Clavulanic acid versus its zone when tested alone

Control strain - Standard strain of Klebsiella pneumonia ATCC 700603 was used as ESBL positive controland Escherichia coli ATCC 25922 was used as ESBL negative control.

#### Results

Out of total of 140 strains of E. coli, which were screened for ESBL production, 30 (21.4 %) isolates were found to be positive. High-level resistance was seen for many antimicrobial agents like Cephalexin (92.8%), Cefaclor (90%), Amoxyclavulanate (88.57%), Cefuroxime (75.7%), Sulfamethoxazoletrimethoprim (72.8%), Norfloxacin (75.71%) and Ciprofloxacin (70%). Sensitivity to Nitrofurantoin was found to be 90%. Only 4.5% of uropathogenic E. coli were resistant to Mecillinam.

Various epidemiological factors seen in ESBL producers include female patients (n =24, 80%), history of antimicrobial intake (n = 17,57 %), elderly age >60 years (n =16 53%), renal calculi (n =15, 50%), history of recurrent UTI (n =11, 37 %), pregnancy (n = 11,37%), diabetes mellitus (n = 7, 23%) and history of urogenital instrumentation (n = 7, 23%).

#### Discussion

The epidemiology of ESBL positive uropathogenic E. coli is becoming more multifaceted, with increasingly indistinct boundaries between the community and hospital.<sup>6</sup> In addition, infection with an ESBL producing organisms causing community UTI is associated with treatment failure, delayed clinical response, higher morbidity and mortality. These

organisms are multi-resistant to other antimicrobials like Aminoglycosides, Quinolones and Co-trimoxazole. Therefore, empirical therapy with Cephalosporins and Fluoroquinolones often fail in patients with community UTI.7

The rate of ESBL producers in our study is lower than that described by other authors. In a similar study Mahesh E et al. reported higher rate (56.2%) of ESBL positivity from E. coli, which were causing UTIs from a community setting.<sup>8</sup> Additionally Taneja N et al. described a higher rate (36.5%) of ESBL positivity in uropathogens. 9,10

A high rate of resistance was seen to almost all antimicrobial agents. This is in agreement with other authors like Mahesh et al. and Mandal J et al.<sup>8,11</sup> Mecillinam showed very good results with only 4.5% resistance. Wootton M et al. reported similar high activity of Mecillinam against E. coli(93.5%).<sup>3</sup> Auer S et al. reported that Mecillinam can be a good oral treatment options in patients with infections due to ESBL organisms.7

A limitation of our study was that being a developing country with limited resources, molecular typing and determination of antimicrobial resistance profiles of the isolates was not done. In our study female patients, elderly, patients with a history of antimicrobial intake, renal calculi and history of recurrent UTI were important factors for infection due to ESBL producers. These findings are similar to risk factors studied by other authors.<sup>2</sup> In conclusion; this study confirms that ESBLproducing E. coli strains are a notable cause of community onset infections especially in predisposed patients. The widespread and rapid dissemination of ESBL-producing E. coli seems to be an emerging issue worldwide. Further clinical studies are needed to guide clinicians in the management of community onset infections caused by E. coli.

Competing Interests
None declared
Author Details
PRIYA DATTA, MD, Assistant Prof, Dept Of Microbiology, Govt
Medical College Hospital, Sec 32, Chandigarh, India. VARSHA
GUPTA, MD DNB, Professor, Dept Of Microbiology, Govt Medical
College Hospital, Sec 32, Chandigarh, India. SHAILPREET SIDHU,
MD, Senior Resident, Dept Of Microbiology, Govt Medical College
Hospital, Sec 32, Chandigarh, India.
CORRESSPONDENCE: DR SHAILPREET SIDHU, Senior
Resident, Dept Of Microbiology, Govt Medical College Hospital, Sec
32, Chandigarh, India.
Email: shailpreet78@hotmail.com

#### REFERENCES

- 1. Rodríguez BJ, Alcalá CJ, Cisneros MJ, Grill F, Oliver A, Juan P et al. Community Infections Caused by Extended-Spectrum B-Lactamase-Producing Escherichia coli. Arch Intern Med. 2008; 168: 1897-1902.
- 2. Azap OK, Arslan H, Serefhanoglu K, Colakoglu S, Erdogan H, Timurkaynak F et al. Risk factors for extended-spectrum β -lactamase positivity in uropathogenic Escherichia coli isolated from communityacquired urinary tract infections. Clin Microbiol Infect .2010;16: 147-51.

- Wootton M, Walsh TM, Macfarlane L, Howe R. Activity of mecillinam against Escherichia coli resistant to third-generation cephalosporins. J Antimicrob Chemother. 2010; 65: 79-81.
- Dong SL, Chung BL, Seung-JL. Prevalence and Risk Factors for Extended Spectrum Beta-Lactamase-Producing Uropathogens in Patients with Urinary Tract Infection. Korean J Urology. 2010; 51:492-7.
- Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: Twenty First Informational Supplement M100-S21. CLSI, Wayne, PA, USA, 2011.
- Nesher L, Novack V, Riesenberg F, Schlaeffer F. Regional communityacquired urinary tracts in Israel; diagnosis, pathogens, and antibiotics guidelines adherence: A prospective study. International J Infect Dis 2007; 11:245-50.
- Auer S, Wojna A, Hell M. Oral Treatment Options for Ambulatory Patients with Urinary Tract Infections Caused by Extended-Spectrum beta-Lactamase-Producing Escherichia coli. Antimicro Agents Chemo. 2010,54: 4006-8.
- Mahesh E, Ramesh D, Indumathi VA, Khan MW, Kumar PS, Punith K. Risk Factors for Community Acquired Urinary Tract Infection caused by ESBL-producing Bacteria. J Indian acad clinl med.. 2010; 11:271-6.

- Taneja N, Rao P, Arora J, Dogra A. Occurrence of ESBL & Amp-C βlactamases & susceptibility to newer antimicrobial agents in complicated UTI. Indian J Med Res 2008; 127: 85-8.
- Taneja N, Singh G, Singh M, Madhup S, Pahil S, Sharma M .High occurrence of bla CMY-1 Amp C lactamase producing Escherichia coli in cases of complicated urinary tract infection (UTI) from a tertiary health care centre in north India. Indian J Med Res 2012; 136: 289-91.
- Mandal J, Acharya NS, Buddapriya D, Parija SC.Antibiotic resistance pattern among common bacterial uropathogens with a special reference to ciprofloxacin resistant Escherichia coli. Indian J Med Res 2012; 136: 842-9.

# Lamotrigine-induced hallucination in patient with bipolar disorder and no history of epilepsy or psychosis: a case report and literature review

#### Yasir Hameed and Jacobus Hamelijnck

#### Abstract

We report a rare case of hallucinations in a patient with bipolar affective disorder BAD without any history of psychosis or epilepsy following the introduction of lamotrigine as an add-on medication to her current treatment with lithium carbonate. The patient has been on two previous medications (quetiapine and sodium valproate) without significant improvement and only showed partial response to lithium. Lamotrigine was introduced as an adjunctive medication with her lithium carbonate. Her dose of lithium was 800 mg once daily with satisfactory lithium levels.

She started to report complex auditory and visual hallucinations which started two days after starting lamotrigine (25 mg once daily) and increased with its dose increase to 50 mg once daily two weeks later and resolved completely with stopping it. Hallucinations following lamotrigine treatment in non-epileptic patients are an extremely rare reaction and only few similar case reports are reported in literature.

Awareness of this rare but serious side effect is important to avoid confusion with other psychotic symptoms related to mental illness and avoid unnecessary treatment.

Keywords: Anticonvulsants; Bipolar Affective Disorders; Drug interactions and side effects; Education and training; Mood stabilisers Abbreviations: BAD: Bipolar affective disorder. ICD 10: International Classification of Disesases. Tenth Edition. DSM 5: Diagnostic and Stastical Manual. Fifth Edition.

#### **Case Presentation:**

We report the case of 36 year old white Caucasian female who used to work as a driving instructor and living with her parents.

She has a diagnosis of congenital adrenal hyperplasia (21 hydroxylase deficiency) and is on long term corticosteroid replacement (prednisolone 4 mg once daily and fludrocortisone

100 mcg once daily) and she is under the care of an endocrinologist.

She was referred for psychiatric evaluation with "anxiety and depressive symptoms" and failure to respond to antidepressant treatment which was prescribed by her General Practitioner.

During the psychiatric assessment, she reported long history of recurrent episodes of elevated mood and depression dating back to her late teens with clear description of distinct periods of mood elevations lasting for few weeks and longer periods of persistent low mood. There was no history of psychotic symptoms and no family history of mental illness.

She was diagnosed with bipolar affective disorder and failed to achieve remission of symptoms on two different antipsychotic medications (quetiapine and olanzapine) and anticonvulsant medication (sodium valproate) before starting lithium carbonate. The introduction of lithium and gradual titration resulted in significant improvement in her symptoms and mood stability. However, few months later, she reported relapse in her symptoms (mainly reporting features of bipolar depression) despite adequate lithium levels.

She agreed on the introduction of lamotrigine as an adjunctive medication to lithium. The initial dose of lamotrigine was 25 mg daily for two weeks in line with dose recommendation from manufacturer and drug guides.

On the same day of lamotrigine introduction, the patient started to experience visual hallucinations that she never had before (please see patient's perspective for detailed description of her hallucinations).

With the dose of lamotrigine increased to 50 mg daily after the initial two weeks, she started to report worsening of these abnormal perceptions which developed into more complex visual and auditory hallucinations.

More importantly, there was no evidence of accompanying manic symptoms or severe depressive symptoms to explain these symptoms and also no alcohol or drug use.

Following a psychiatric review, the dose of lamotrigine was reduced to 25 mg which resulted in immediate reduction in the intensity of the abnormal perceptions. When the lamotrigine was eventually stopped after one week, there was complete cessation of abnormal perceptions.

Lamotrigine was never re-started again and she was maintained on a combination of lithium and quetiapine with good effect.

#### Investigation:

We used the Naranjo Adverse Drug Reaction Probability Scale (1) to determine the likelihood of whether an adverse drug reaction is related to this specific drug or may be related to other factors. This tool examine factors such as the temporal association of drug administration and event occurrence, alternative causes for the event, drug levels, dose – response relationships and previous patient experience with the medication.

The probability of the adverse drug reaction is concluded from the total score (Definite if the overall score is 9 or greater, Probable for a score of 5-8, Possible for 1-4 and Doubtful if the score is 0).

#### Questionnaire

1. Are there previous conclusive reports on this reaction? Yes (+1)

2. Did the adverse events appear after the suspected drug was given? Yes (+2)

3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?

Yes (+1)

4. Did the adverse reaction appear when the drug was readministered? Do not know or not done (0)

5. Are there alternative causes that could have caused the reaction? No (+2)

6. Did the reaction reappear when a placebo was given? Do not know or not done (0)

7. Was the drug detected in any body fluid in toxic concentrations?

No (0)

8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?

Yes (+1)

9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?

No (0)

10. Was the adverse event confirmed by any objective evidence? Do not know or not done (0)

Scoring 7 (Probable Adverse drug reaction)

#### Discussion:

Lamotrigine is a phenyltriazine derivative used as an anticonvulsant drug with established mood stabilising properties. In the United Kingdom, it is recommended for use in bipolar affective disorder according to the guidelines from the National Institute of Health and Care Excellence (2) and the British Association for Psychopharmacology (3).

We performed a literature search to find similar case reports. We searched the following databases using the keywords (lamotrigine AND hallucinations): Complementary Medicine (AMED), British Nursing Index BNI), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Excerpta Medica Database (EMBASE), Health Business Elite (HMIC), Medline, PsycINFO and Health Management Information Consortium (HMIC).

The search returned 57 results. Only 8 articles discussed hallucinations and other psychiatric symptoms as side effects associated with lamotrigine and therefore were included in this review.

Psychotic symptoms have been reported with the use of lamotrigine (both as an anticonvulsant or mood stabiliser) but this reaction is mainly seen in patients with history of epilepsy. One study reported 4.8% incidence of psychiatric and behavioural side effects with lamotrigine in 546 patients with epilepsy. (4)

Another study on paediatric patients showed that reversible visual and auditory hallucinations were reported in one patient among 9 patients with epilepsy who received lamotrigine treatment (mean age 5 years). (5)

Villari et al published a literature review on psychiatric symptoms related to lamotrigine and included case reports documenting full acute psychotic episodes hallucinations and affective switching in patients with and without history of epilepsy.(6)

They found one case report on hallucination with lamotrigine in bipolar patient without epilepsy. In patients with epilepsy, they reported two cases reports and one case series (total number of patients 9) developing psychotic symptoms following lamotrigine and one randomised controlled trial in which four out of 216 patients stopped lamotrigine due to psychotic symptoms (including hallucinations and delusions).

The authors concluded that majority of the case reports concluded that these symptoms were lamotrigine-induced due to the temporal association with lamotrigine treatment and favourable outcome following drug withdrawal. It also appeared that more case reports were from patients with epilepsy, suggesting lower incidence in patients without this condition.

Chistyakova and Amos (7) reported a case of delirium associated with lamotrigine use. The dose of lamotrigine was increased from 200 to 400 mg over two weeks prior to her admission. The patient reported visual and auditory hallucination with confusion. She took an accidental overdose of her medication (200 mg of fluoxetine and 2800 mg of lamotrigine) due to her confusion and medications were stopped.

The authors concluded that delirium may result from lamotrigine toxicity or drug interaction with fluoxetine.

Uher and Jones in 2006 (8) reported a case of a 42-year-old woman with bipolar affective disorder with comorbid alcohol abuse and no history of neurological illness.

The patient tolerated an initial dose of lamotrigine 50 mg/day but following a dose increase to 100 mg/day, she reported vivid dream-like experiences and subsequently she reported visual hallucinations. These symptoms subsided over a few days when the dose was decreased to 50 mg/day.

The authors suggested a causal association through this dose dependent effect but also pointed out that the concurrent alcohol abuse may have been a contributing factor.

They also highlighted the paucity of case reports documenting this rare adverse reaction and identified two similar case reports in their references (which we were unable to get their full text) and a third paper reporting hallucination in 2 out of 108 patients with epilepsy on a combination of lamotrigine and sodium valproate (9)

Hallucination with lamotrigine when combined with valproic acid was also reported in a case report by Roberts et al (10) in 14 year old girl with epilepsy when it was added to valproic acid and it was suggested that this adverse effect may be due to an interaction between the two medications causing lamotrigine half-life to triple with valproic acid.

#### Learning points:

- Lamotrigine is an anticonvulsant with an established role in management of bipolar affective disorder, particularly for the treatment and prevention of depressive episodes.
- However, it appears to be associated with variable incidence of psychiatric symptoms which should be known to the prescriber and patient.
- These adverse effects are mainly seen in patients with history of epilepsy but can occur in patients with mental health problem without epilepsy.
- Different mechanisms for inducing these psychiatric symptoms have been suggested, including idiosyncratic reaction, lamotrigine toxicity as a result of concomitant use of another drug that affect lamotrigine metabolism (e.g., valproic acid) and delirium.
- Examples of these psychiatric symptoms including affective switches in depressed patients with bipolar disorder, hallucinations in depressed patients, delirium and psychotic symptoms (mainly hallucinations and delusions) in patients with or without epilepsy.

- Reversible and severe psychiatric disturbances associated with lamotrigine therapy are rarely reported in literature and more research is needed to identify population at risk.
- Patient education about these rare but frightening side effects is essential to improve medication adherence and better outcome of the management of the mental disorder.

#### Patient perspective:

"The first hallucination I had was one hour roughly after taking lithium and lamotrigine. It was the Pope which appeared as bright light on my wall. He was wearing a white gown and he had gold jewellery. The picture was so clear and very detailed. I'm not religious and this image would not be something I would think of.

Every day on lamotrigine I had black spots moving quickly around the walls. They were in size of about an inch, 20-30 moving around at one time. Like spiders but without legs. I was really scared at first because I hate spiders. It was very unsettling and I changed my whole bed, away from my wall, and had trouble sleeping.

There was another night when I had similar to the black dots, where instead I had smaller black dots like bees moving into the corner of my room. They were all slightly moving as if they were getting their places. There were hundreds of them.

The scariest incident that happened was hearing voices downstairs. I was so sure that people had broken into the house; I went downstairs armed with razors. I was going to cut DNA from the burglars to give to the police as evidence. When I checked the house, there was no one there.

When I was taking lamotrigine with the lithium, it made me very unsettled, more anxious and mentally unstable. I was so tiered for not sleeping and my decisions irrational. It wasn't a pleasant place to be for me personally."

#### **Competing Interests**

None declared.

Author Details

Yasir Hameed (MRCPsych), Specialist Registrar, Old Age and General Adult Psychiatry, Norfolk and Suffolk NHS Foundation Trust. Jacobus Hamelijnck (MRCPsych), Consultant Psychiatrist, Northgate Hospital, Norfolk and Suffolk NHS Foundation Trust, Great Yamrouth, Norfolk, UK, NR30 1BU.

CORRESSPONDENCE: Yasir Hameed (MRCPsych), Specialist Registrar, Old Age and General Adult Psychiatry, Norfolk and Suffolk NHS Foundation Trust, Northgate Hospital, Great Yamrouth, Norfolk, NR30 1BU.

- Naranjo CA, Busto U, Sellers EM et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981. 30 (2): 239–245.
- 2. National Institute of Health and Clinical Excellence. Bipolar disorder. The management of bipolar disorder in adults, children and

adolescents, in primary and secondary care. NICE clinical guideline CG38. http://guidance.nice.org.uk/CG38

- Goodwin GM. Evidence-based guidelines for treating bipolar disorder: revised second edition-recommendation from the British Association for Psychopharmacology. Journal of Psychopharmacology 2009;23(4):346–388.
- Weintraub D, Buchsbaum R, Resor Jr SR, et al. Psychiatric and behavioural side effects of the newer antiepileptic drugs in adults with epilepsy. Epilepsy Behav 2007; 10: 105-10
- Cardenas J.F., Rho J.M., Ng Y.-T. Reversible lamotrigine-induced neurobehavioral disturbances in children with epilepsy. Journal of Child Neurology 2010; 25 (2): 182-187.
- Villari V. Roccab P, Frieria T, Bogettob F. Psychiatric symptoms related to the use of lamotrigine: a review of the literature. Funct Neurol 2008. 23(3):133-136.
- Chistyakova Y, Amos J. Delirium associated with lamotrigine and fluoxetine treatment. Am J Psychiatry2008;165(7):918.

- Uher R, Jones HM. Hallucinations during lamotrigine treatment of bipolar disorder. Am J Psychiatry 2006;163:749-750.
- Faught E, Morris G, Jacobson M, et al. Adding lamotrigine to valproate: incidence of rash and other adverse effects: Postmarketing Antiepileptic Drug Survey (PADS) group. Epilepsia 1999; 40:1135– 1140.
- Roberts C, Davenport R, Patel H, et al. Hallucinations during lamotrigine treatment. The Nurse Practitioner 2008;33:12-13.

#### Carbimazole induced ANCA Positive Vasculitis

Yasmeen Ajaz and Sameem Matto

BJMP 2014;7(2):a712

#### Abstract

Anti-throid drugs like propylthiouracil and carbimazole are the main drugs prescribed for hyperthyroidism worldwide. Vasculitis related to anti-thyroid medication is very rare and can be potentially life threatening, if not recognized early. We report a female patient with Graves' Disease who developed ANCA positive vasculitis due to carbimazole. The episode was characterized by a Raynaud's Phenomenon of hands and feet and small joint arthritis. To our knowledge this is the first ANCA positive carbimazole induced vasculitis case reported from United Arab Emirates.

Keywords: Carbimazole, ANCA, Vasculitis, Hyperthyroidism, Raynauds Phenomenon, Graves Disease, Antithyroid Drugs. Abbreviations: TSH-Thyroid stimulating hormone, FT3-Freetri-iodothyronine, FT4-Free thyroxine, ANCA-Antineutrophilic cytoplasmic antibodies, CRP-C reactive protien, ESR-Erythromicin sedimentation rate, ECG-electrocardiogram, ATD-Antithyroid drugs, PTU-Proplythiouracil, ANTI-TPOthyroperoxidase, MPO-Myeloperoxidase

#### Introduction

Hyperthyroidism is a common endocrine disorder and is mainly treated with anti-thyroid medications like propylthiouracil (PTU) and carbimazole. These medications have a large number of adverse effects, the commonest being skin rashes, and some are rare like agranulocytosis. Vasculitis is uncommon, but ANCA positivity is reported more in propylthiouracil and rarely with carbimazole or methimazole (1).We report a female patient with Graves' disease who developed ANCA associated vasculitis while on carbimazole treatment.

#### Case report

A 29 year old female Filipino patient came to us with history of palpitations, tremors and weight loss for the last one month. Her thyroid profile showed severe hyperthyroidism (TSH <0.005, FT3-11.5, FT4-45.6) She was diagnosed with Graves' disease as her anti-TSH receptor positive and was started on carbimazole 10mg tds. After three weeks of treatment, she developed macular rash over arms and legs and swelling of small joints of both hands. She noticed pain and colour change of both the hands and experienced typical Raynaud's phenomenon. She had no renal or lung involvement.

On examination her blood pressure was 120/84mmHG, pulse 104 beats per min, temperature -37.1°C. She had a mild diffuse goiter. Her X-ray chest, ECG and urine dipstick routine were all normal. Her CRP and ESR were raised. X-rays of the hands were normal. P-ANCA was positive. Antimyeloperoxidase antibody was positive. Anti-TPO and TSH receptor antibodies were positive.

Diagnosis of carbimazole induced vasculitis was made. The patient was treated with prednisolone 40mg daily once daily

which was tapered over three weeks. She improved within 48hours and was asymptomatic after three weeks. She was treated successfully with radioiodine ablation. Her MPO-ANCA after 6 months was negative.



Figure 1. Pictures of the hands showing Raynaud's phenomenon



Figure 2. Pictures of the hands showing Raynaud's phenomenon

#### Discussion

ANCA positive vasculitis in association with antithyroid drugs was first reported in 1992 (2). There has been 32 cases of ANCA positive vasculitis associated with antithyroid medications reported up until now (3). The presenting symptoms are variable and may include renal involvement (67%), arthralgias (48%), fever (37%), skin involvement (30%), respiratory tract involvement (27%), myalgias (22%), scleritis (15%) and other manifestations (18%) (3).

In these patients the underlying thyroid disease is most commonly Graves' disease but ANCA positive vasculitis has also been seen with association with toxic multinodular goitre (4). Recent studies have shown high frequency of ANCA positivity in patients with Graves' disease treated with antithyroid medications, especially with PTU. Most cases of ANCA positivity are seen in patients on long term therapy (greater than 18 months) or in those with recent commencement of therapy as seen in our patient. However, a small percentage of these go on to develop features of vasculitis (3).

The majority of cases of vasculitis (88%) have been reported in association with PTU, vasculitis associated with carbimazole is very rare (5, 6, and 7). The pathogenesis of ATD associated vasculitis is not clearly understood. PTU has been shown to accumulate within neutrophils (8) and bind myeloperoxidase (9). The binding alters the configuration of myeloperoxidase (9) and may promote formation of autoantibodies in susceptible people. There has been no data with regards to whether carbimazole can alter the configuration of myeloperoxidase. ANCA positive vasculitis may be more common in patients of Asian ethnic origin, with half of cases reported from Japan (3). Our patient was from Philippines.

Wadw et al have reported 25% of patients were positive for MPO-ANCA in PTU group whereas in methimazole group 3.4% were positive (10).

This case highlights the awareness of this relatively rare adverse effect of a thyroid medication which may lead to fatal renal and pulmonary complications. Early diagnosis and withdrawal of the offending medication is important. In asymptomatic patients the significance of ANCA positivity is not clear but early definitive therapy in the form of radioiodine ablation or surgery should be considered.

Acknowledgements
NONE
Competing Interests
None declared
Author Details
YASMEEN AJAZ (M.D, F.A.C.E, PGDD, SCE) Specialist Internal
Medicine And Endocrinology, Belhoul Speciality Hospital, Dubai,
UAE. SAMEEM MATTO (M.D, PGDD, SCE) Specialist Internal
Medicine And Endocrinology, Canadian Specialist Hospital, Dubai,
UAE.
CORRESSPONDENCE: DR SAMEEM MATTO, Canadian
Specialist Hospital, Abuhail Deira, PO BOX 15881, Dubai, UAE.
Email: sameematto@hotmail.com

- Sera N, Ashizawa K, Ando T, et al. Treatment with propylthiouracil is associated with appearance of antineutrophil cytoplasmic antibodies in some patients with Graves' disease. Thyroid 2000; 10:595-9.
- Stankus SJ & Johnson NT. Propylthiouracil-induced hypersensitivity vasculitis presenting as Respiratory failure. Chest 1992 102, 595–1596.
- Gunton JE, Stiel J, Clifton-Bligh P, et al. Prevalence of positive antineutrophil cytoplasmic antibody (ANCA) in patients receiving antithyroid medication. Eur J Endocrinol 2000; 142: 587-96.
- Gunton JE, Stiel J, Caterson RJ & McElduff A. Anti-thyroid drugs and antineutrophil cytoplasmic antibody positive vasculitis. A case report and review of the literature. Journal of Clinical Endocrinology and Metabolism1999 8413–16.
- Day C, Bridger J, Rylance P, et al. Leukocytoclastic vasculitis and interstitial nephritis with Carbimazole treatment. Nephrol Dial Transplant 2003; 18: 429-31.
- Sève P, Stankovic K, Michalet V, et al. Carbimazole induced eosinophilic granulomatous vasculitis localized to the stomach. J Intern Med 2005; 258: 191-5.
- Calañas-Continente A, Espinosa M, Manzano-García G, et al.Necrotizing glomerulonephritis and pulmonary hemorrhage associated with carbimazole therapy. Thyroid 2005; 15: 286-8.
- Lam DCC & Lindsay RH. Accumulation of 2-[14C]-propylthiouracil in human polymorphonuclear leukocytes. Biochemical Pharmacology 1979 282289–2296.
- Lee H, Hirouchi M, Hosokawa M, Sayo H, Kohno M & Kariya K.Inactivation of peroxidase of rate bone marrow by repeated administration of propylthiouracil is accompanied by a change in the heme structure. Biochemical Pharmacology 1988 372151–2153.
- Bonaci-Nikolic B, Nikolic MM, Andrejevic S, et al. Antineutrophil cytoplasmic antibody (ANCA)-associated autoimmune diseases induced by antithyroid drugs: comparison with idiopathic ANCA Vasculitides. Arthritis Res Ther 2005; 7:1072-81.

### Liver Veno-Occlusive Disease (VOD) in a patient given 6-Thioguanine for Crohn's Disease

#### Agata Salerno, Marco Vacante, Donatella Pollina, Benedetta Stancanelli, Silvia Martini, Ezio David and Lorenzo Malatino

#### Abstract

6-Thioguanine (6-TG) is being given to patients with Crohn's disease failing conventional immunosuppression, but cases of hepatotoxicity have been reported. We report the case of a patient who developed acute sinusoidal obstruction syndrome after 3 months of successful 6-TG treatment. A complete regression of liver injury was observed after withdrawal of 6-TG. Our case-report underscores the risk of hepatic injury due to the administration of 6-TG for Crohn's disease. We strongly recommend alternative therapeutic options in patients intolerant or resistant to conventional thiopurines. Keywords: 6-thioguanine, Crohn's disease, hepatotoxicity, veno-occlusive disease.

A 44-yr-old patient with history of ileal Crohn's disease was admitted to our Department because of asthenia, subclinical jaundice, painful hepatomegaly, fluid retention and ascites. In 2008 the patient was diagnosed with bladder cancer and was treated by surgical resection of the cancer and intravesical chemotherapy with mitomicyn C. In 2010 he was given azathioprine (AZA) at 2 mg/kg for Crohn's disease and 3 months later he developed an increase in serum alkaline phosphatase, gamma-glutamyl transpeptidase and transaminases. He was then started on 1.5 mg/kg 6mercaptopurine (6-MP) once daily. After 9 months he stopped 6-MP because of nausea, vomiting and abnormal liver function tests; 6-MP was therefore discontinued until the normalisation of markers of liver function. Two months later, when the transaminases were within the normal range, he received 6thioguanine (6-TG) 25 mg a day, that was progressively increased to 80 mg a day. Three months later, the patient was referred to our Department with painful hepatomegaly, ascites and asthenia. Laboratory tests on admission revealed an elevation in AST 198 U/l and ALT 209 U/l. Total bilirubin was 3 mg/dl (direct bilirubin 1.5 mg/dl), LDH 784 U/l, alkaline phosphatase 191 U/l and ammonia 112 umol/l. Virological markers (HBsAg, HBcAb, anti HCV, HBV DNA) were negative. Patient was apyrexial, showed normal blood pressure (130/80 mmHg), tachycardia (110 bpm) and 97% SaO2 on room air. Physical examination revealed right hypochondrial tenderness, abdominal distension and shifting dullness, suggesting the presence of ascites. The rest of the physical examination was unremarkable. An echo-Doppler evaluation revealed thin linear suprahepatic veins and confirmed the presence of ascites. A CT scan of the abdomen showed hepatomegaly with dishomogeneous enhancement after dye injection (mosaic pattern). There was no evidence of any



FIGURE 1A. CT scan of the abdomen on admission: Dishomogeneous enhancement of the liver after dye injection (mosaic pattern) (arrow). Suprahepatic veins are not detectable.



FIGURE 1B. Histological pattern of the liver biopsy specimen: marked centrilobular congestion (arrows) with hepatocyte dropout. There is no evidence of centrolobular veins thrombosis.

venous thrombosis or splenomegaly (Figure 1A); 6-TG was withdrawn empirically and the patient was started on therapy with albumin 25 g/day and spironolactone 200 mg/day. The average serum Na+ level during diuretic treatment was 134 mEq/l. An abdominal paracentesis of two litres was necessary, due to the progressive increase of ascites.



FIGURE 2A. Echography of the liver at follow up. No evidence of ascites.



FIGURE 2B. Echography of the liver at follow up. No evidence of ascites. Suprahepatic veins are detectable (arrow)

A routine laboratory investigation of ascitic fluid showed < 500 leukocytes/ $\mu$ L and < 250 polymorphonuclear leukocytes (PMNs)/ $\mu$ L. The ascitic fluid total protein level was 2.1 g/dl and serum-ascites albumin gradient (SAAG) was > 1.1 g/dL. No neoplastic cells were found. A transjugular liver biopsy was then performed, showing marked centrilobular hemorrhage with hepatocyte necrosis. There was mild ductular reaction, with no evidence of centrilobular vein thrombosis. The histologic diagnosis confirmed veno-occlusive disease (VOD) (Figure 1B). Screening for thrombophilia was also done, showing low levels of serum protein C and protein S. There was no mutation of

JAK-2 V617F. The patient was then treated with a hyposodic diet, mild hydric restriction, enoxaparin,spironolactone, lactulose and omeprazole. He was discharged two weeks later, and after 3 months a complete regression of ascites and hepatomegaly occurred, and echography of the liver was unremarkable (Figure 2A and 2B).

#### Discussion

Although VOD was known among complications of 6-TG in childhood, this case-report emphasises the occurrence of VOD in adults with Crohn's disease, as first described by Kane et al. in 2004<sup>1</sup>. The thiopurine drugs were developed more than 50 years ago, and 6-MP was first used as a drug in 1952<sup>2</sup>. Since then, 6-MP and 6-TG have been widely used to treat acute lymphoblastic leukemia in children. VOD mimicking Budd-Chiari like disease was then described as a frequent complication of 6-TG in pediatric patients given the drug for lymphoblastic leukaemia. Later on, in 1976, Griner et al. described the cases of two adult male patients with acute leukaemia developing a fatal Budd-Chiari-like disease while receiving 6-TG<sup>3</sup>. Since patients were given 6-TG plus cytosine arabinoside, authors were unable to ascribe this complication solely to 6-TG3. VOD exclusively related to 6-TG was first described by Gill et al., who observed a clinically reversible liver VOD developing in a young man with acute lymphocytic leukemia after 10 month administration of 6-TG<sup>4</sup>. Furthermore, sinusoidal obstruction was also reported in a patient with psoriasis treated with 6-TG and other cytotoxic therapy<sup>5</sup>. In 2006, a European 6-TG Working Party established that 6-TG should be considered a rescue drug in stringently defined indications in inflammatory bowel diseases (IBD). The indication for administration of 6-TG should only include its use for maintenance therapy as well as intolerance and/or resistance to aminosalicylates, azathioprine, 6-mercaptopurine, methotrexate and infliximab. Moreover, 6-TG must be withdrawn in case of overt or histologically proven hepatotoxicity<sup>6</sup>. Although Ansari et al <sup>7</sup> found no nodular regenerative hyperplasia (NRH) in the liver of patients given 6-TG, Dubinsky et al.8 described NHR as a common finding in 6-TG-treated patients with inflammatory bowel disease in the absence of VOD. By contrast, in our case report we showed histological pattern of VOD and, in accord with Gisbert et al.9, would suggest that 6-TG should not be administered out of a clinical trial setting. Given that the proportion of patients with Crohn's disease achieving an improvement of symptoms during 6-TG treatment is similar to that after methotrexate<sup>10</sup> or infliximab6, these drugs should therefore be considered as second line therapy in patients intolerant or resistant to azathioprine and 6-mercaptopurine.

#### Competing Interests None declared Author Details

AGATA SALERNO MD, Department of Internal Medicine, University of Catania, c/o Cannizzaro Hospital, Via Messina 829, 95126 Catania, Italy. MARCO VACANTE, MD, Department of Internal Medicine, University of Catania, c/o Cannizzaro Hospital, Via Messina 829, 95126 Catania, Italy. DONATELLA POLLINA, MD, Department of Internal Medicine, University of Catania, c/o Cannizzaro Hospital, Via Messina 829, 95126 Catania, Italy. BENEDETTA STANCANELLI, MD, Department of Internal Medicine, University of Catania, c/o Cannizzaro Hospital, Via Messina 829, 95126 Catania, Italy. SILVIA MARTINI, MD, SSCVD Insufficienza Epatica e Trapianto, Azienda Ospedaliera Città della Salute e della Scienza - Molinette, C.so Bramante 88, 10126 Turin, Italy. EZIO DAVID, MD,SCDU II Anatomia Patologica, Azienda Ospedaliera Città della Salute e della Scienza – Molinette, C.so Bramante 88, 10126 Turin, Italy. LORENZO MALATINO, MD, PROFESSOR OF MEDICINE Department of Internal Medicine, University of Catania, c/o Cannizzaro Hospital, Via Messina 829, 95126 Catania, Italy.

CORRESSPONDENCE: MARCO VACANTE, Department of Internal Medicine, University of Catania, c/o Cannizzaro Hospital, Via Messina 829, 95126 Catania, Italy.

Email: marcovacante@yahoo.it

- Kane S, Cohen SM, Hart J. Acute sinusoidal obstruction syndrome after 6-thioguanine therapy for Crohn's disease. Inflamm Bowel Dis. 2004;10:652-4.
- Elion G, Burgi E, Hitchings G. Studies on condensed pyrimidine systems, IX. The synthesis of some 6-substituted purines. J Am Chem Soc 1952;74:411-4.
- Griner PF, Elbadawi A, Packman CH. Veno-occlusive disease of the liver after chemotherapy of acute leukemia. Report of two cases. Ann Intern Med. 1976;85:578-82.
- Gill RA, Onstad GR, Cardamone JM, Maneval DC, Sumner HW. Hepatic veno-occlusive disease caused by 6-thioguanine.Ann Intern Med. 1982;96:58-60.
- Kao NL, Rosenblate HJ. 6-Thioguanine therapy for psoriasis causing toxic hepatic venoocclusive disease. J Am Acad Dermatol. 1993;28:1017-1018.
- de Boer NK, Reinisch W, Teml A, van Bodegraven AA, Schwab M, Lukas M, et al; Dutch 6-TG working group. 6-Thioguanine treatment in inflammatory bowel disease: a critical appraisal by a European 6-TG working party.Digestion. 2006;73:25-31.
- Ansari A, Elliott T, Fong F, Arenas-Hernandez M, Rottenberg G, Portmann B, et al. Further experience with the use of 6-thioguanine in patients with Crohn's disease.Inflamm Bowel Dis. 2008;14:1399-405.
- Dubinsky MC, Vasiliauskas EA, Singh H, Abreu MT, Papadakis KA, Tran T, et al. 6-thioguanine can cause serious liver injury in inflammatory bowel disease patients.Gastroenterology. 2003;125:298-303.
- Gisbert JP, González-Lama Y, Maté J. Thiopurine-induced liver injury in patients with inflammatory bowel disease: a systematic review. Am J Gastroenterol. 2007;102:1518-27.
- Feagan BG, Rochon J, Fedorak RN, Irvine EJ, Wild G, Sutherland L, et al. Methotrexate for the treatment of Crohn's disease. The North American Crohn's Study Group Investigators. N Engl J Med. 1995;332:292-7.

#### Tracheo esophageal fistula

#### M Suresh Babu, Deepak Suvarna, Chandrashekhar Shetty and Aditya Nadella

A 40 year old patient presented to the hospital outpatient department with one year history of cough, choking sensation following swallowing, hoarseness of voice and loss of weight. History revealed his previous hospital admission 1 year back for management of organophosphorus poisoning during which he was intubated and put on mechanical ventilator for 10 days. Patient developed the symptoms a month after his discharge from the hospital. Cranial nerve examination was within normal limits.



Fig 1: Barium swallow illustrating a dilated oesophagus and the TOF with resultant contamination of the trachea and bronchial tree



Fig 2: Oesophagoscopy showing TOF

What is the possible diagnosis?

- 1. Gastro-oesophageal reflux disease
- 2. Tracheo-oesophageal fistula
- 3. Oesophageal diverticula
- 4. Oesophageal rupture

#### Correct answer:

2. Tracheo-oesophageal fistula

#### Discussion:

A tracheo-oesophageal fistula (TOF) is a communication between the trachea and oesophagus which can be congenital or acquired. Congenital and acquired TOFs are associated with multiple complications, including poor nutrition, recurrent pneumonia, acute lung injury, acute respiratory distress syndrome, lung abscess, bronchiectasis from recurrent aspiration, respiratory failure, and death. Acquired TOFs occur secondary to malignant disease, infection, ruptured diverticula, and trauma.<sup>1, 2</sup> Acquired TOFs are quite rare, and incidence rates have not been well documented. Post intubation TOFs uncommonly occur following prolonged mechanical ventilation with an endotracheal or tracheostomy tube. TOFs caused by endotracheal tube intubation depend on several factors, including prolonged intubation, an irritating or abrasive tube, and pressure exerted by the cuff. Pressures exceeding 30 mm Hg can significantly reduce mucosal capillary circulation and result in tracheal necrosis. Cuff pressure is particularly risky when exerted posteriorly against a rigid nasogastric tube in the oesophagus. Poor nutrition, infection, and steroid use cause tissue alteration, which predisposes patients for the development of TOFs. As a result of laryngeal bypass, spillage of oesophageal contents occurs into the trachea. Saliva, food and gastric juice contaminate the airways. This leads to congestion, infection, pneumonia, bronchial obstruction, and respiratory distress. The severity atelectasis of contamination depends on the width and length of the fistula as well as the posture of the patient. Spontaneous closure of nonmalignant TOFs is exceptional.

Patients with acquired TOFs have high mortality and morbidity rates because of critical illnesses and co-morbidities. Acquired TOFs may occur in individuals of any age, and elderly individuals are at increased risk if they become ventilator dependent because of respiratory failure. Acquired TOFs can be diagnosed by instillation of contrast media into the oesophagus (Fig.1) or during direct visualization by flexible oesophagoscopy (Fig.2) or bronchoscopy. A high index of suspicion is needed to diagnose tracheo-oesophageal fistula in a post intubated patient presenting with symptom of cough following deglutition. Since acquired TOFs do not close spontaneously, surgical repair is needed if the patient is stable enough.<sup>3, 4</sup> Critically ill patients are managed conservatively until stable enough for a major surgical procedure.

Typical oesophageal symptoms of gastro-oesophageal reflux disease include heartburn, regurgitation and dysphagia. The classic presentation of spontaneous oesophageal rupture is chest pain and subcutaneous emphysema after recent vomiting or retching (Mackler's triad) in a middle-aged man with a history of dietary over-indulgence and over consumption of alcohol. Oesophageal diverticula presents with oropharyngeal dysphagia, usually to both solids and liquids, which is the most common symptom. Retention of food material and secretions in the diverticulum, particularly when it is large, can result in regurgitation of undigested food, halitosis, cough, and even aspiration pneumonia. The patient may note food on the pillow upon waking up in the morning.

None declared Author Details M SURESH BABU, MBBS MD FCCP FICP FICS FIMSA FIACM FISE FACP(USA), Associate Professor, Department of Internal Medicine, JSS Medical College and Hospital, JSS University, Mysore, Karnataka, India. DEEPAK SUVARNA, MBBS MD DNB(Gastroenterology), Professor, Department of Gastroenterology, JSS Medical College and Hospital, JSS University, Mysore, Karnataka, India. CHANDRASHEKHAR SHETTY, MBBS MD(Radiology), Professor and Head of Department, Department of Radiology, JSS Medical College and Hospital, JSS University, Mysore, Karnataka, India. ADITYA NADELLA, MBBS, Junior Resident, Department of Internal Medicine, JSS Medical College and Hospital, JSS University, Mysore, Karnataka, India. CORRESSPONDENCE: Dr. M. Suresh Babu MBBS, MD, FCCP, FICP Associate Professor, Department of Internal Medicine, JSS Medical College and Hospital, JSS University, Mysore, Karnataka, India-570004 PH: +91-9448052680 Email :drmsureshbabu@yahoo.co.in Postal Address: #739, E and F Block, Kuvempunagar, Mysore-570023, Karnataka, India Email: drmsureshbabu@yahoo.co.in

#### REFERENCES

**Competing Interests** 

- Diddee R, IH Shaw IH Continuing Education in Anaesthesia, Critical Care & Pain | Volume 6 Number 3 2006
- 2. Sharma S Tracheoesophageal fistula e medicine.medscape.com/article Medscape reference 2012
- Reed MF and Mathisen DJ "Tracheoesophageal fistula," Chest Surgery Clinics of North America, vol. 13, no. 2, pp. 271–289, 2003.
- Chauhan SS, Long JD, "Management of tracheoesophageal fistulas in adults," Current Treatment Options in Gastroenterology, vol. 7, no. 1, pp. 31–40, 2004

#### The twitching leg

#### Jose A Egido and Ana M Garcia

#### Abstract

A 87-year-old man was admitted to the Acute Stroke Unit and incidental spontaneous movements were seen at rest. Differential diagnosis and ancillary tests are discussed in this article.

Keywords: Fasciculation, neurological examination, radiculopathy

Abbreviations: ALS: amyotrophic lateral sclerosis EMG: electromyography MRI: magnetic resonance imaging

#### Clinical Scenario / Question

An 87-year-old gentleman was admitted after sudden dysarthria and left facial palsy due to a right internal carotid artery occlusion. On examination, incidental spontaneous movements were seen at rest in the left leg (video), with bilaterally diminished Achilles reflexes. Patient was unaware of this finding. Muscle atrophy and hypoesthesia were not present. When walking on heels, left foot dorsiflexion was impaired.

What kind of physical finding is shown in this video?

#### http://youtu.be/cmhCoYCAC20

- A. Myoclonus
- B. Dystonia
- C. Tremor
- D. Chorea
- E. Fasciculation
- F. Myokymia

#### Answer / Discussion

Focal fasciculations in the tibialis anterior muscle are shown. When walking on heels, left foot dorsiflexion was slightly impaired.

Fasciculation is a brief, twitching, spontaneous involuntary contraction affecting muscle fibres served by one motor unit, which may be visible under skin. When present, they reflect denervation.

A complete history intake and neurological examination will lead to a sensible diagnostic work-up and to set a prognosis. Clinical differential diagnosis is presented in table 1.

*Localization* helps in diagnosis: fasciculations can be *generalised*, in metabolic-toxic conditions, the benign fasciculation syndrome and degenerative disorders of anterior horn of spinal cord, as amyotrophic lateral sclerosis; *segmental*, as in syringomyelia; *or focal*, affecting the muscles controlled by a nerve or spinal root. When fasciculations are in a distribution that cannot be explained by plexus, root or nerve lesion amyotrophic lateral sclerosis (ALS) must be ruled out as soon as possible.

Table 1: Key points for clinical diagnosis

Myoclonus	Brief, shocklike involuntary contraction of a muscle or group of muscles
Dystonia	Involuntary muscle contraction that can cause slow repetitive movements or abnormal postures
Tremor	Involuntary rhytmic contraction of antagonistic muscles
Chorea	Involuntary irregular movement that starts in one part of the body and moves unpredictably and continously to another part, like "dancing"
Myokymia	Involuntary spontaneous quivering, writhing movements within a single muscle not extensive enough to cause a movement of a joint

*Evolution* findings are also pivotal. The absence of muscle atrophy suggests that an acute or subacute nerve lesion is present, although a limited chronic nerve lesion cannot be excluded based on that observation alone. A clinical examination should be repeated at least every six months to assess progression, muscle weakness, upper motor neuron signs and other findings, such as bilateral wasting of the tongue, the "split hand", head drop, emotionality and cognitive or behavioral impairment<sup>1</sup>

It is also very important to rule out any possible *metabolic* disorder, as *toxic conditions*. Earl Grey tea intoxication has been reported as a cause of widespread fasciculations and cramps<sup>2</sup>

Electromyography (EMG) is the recording of the electrical activity of the muscles. It supports the clinical suspicion and

helps in the topographic diagnosis. If ALS is suspected, a systematic examination of clinically uninvolved muscles has to be done for 2 minutes as fasciculations are the hallmark of this condition. As fasciculation potentials in ALS and benign fasciculation syndrome are indistinguishable on grounds of waveform parameters<sup>3</sup> and there is not a reliable biological marker of the disease, a minimum follow-up of 6 months is required before setting a prognosis. When non-progressive isolated fasciculations of the tibialis anterior muscle, it has to been examined the 5<sup>th</sup> lumbar root and the deep peroneal nerve, as localizer sensory symptoms may be absent<sup>4</sup>, and to rule out any more diffuse neurogenic processes.

Magnetic resonance imaging (MRI) is supportive to EMG findings as it is very sensitive in detecting anatomic changes that could be responsible for the radiculopathy, but there are other causes of radiculopathy besides nerve root compression. Moreover, lumbar disk protrusions can be found in asymptomatic patients independent of age<sup>5</sup>. Therefore, MRI is not appropriate if pain or foot drop are not present.

Finally, an isolated chronic left L5 radiculopathy was diagnosed related to lumbar spondyloarthrosis.

Competing Interests None declared Author Details JOSE A EGIDO, MD MPHIL FESO, Stroke Unit and Neurosonology Laboratory Clinical Lead, Hospital Clinico San Carlos, Madrid, Spain. ANA M GARCIA, MD MPHIL, Consultant Neurologist and Stroke Physician, Worcestershire Royal Hospital, Worcester, United Kingdom. CORRESSPONDENCE: ANA M GARCIA, Consultant Neurologist and Stroke Physician, Worcestershire Royal Hospital, Worcester, United Kingdom. Email: amgarciagarcia@gmail.com

- Turner MR, Talbot K. Mimics and Chamaleons in Motor Neuron Disease. Practical Neurol 2013; 13 (3): 153 – 164, doi: 10.1136/practneurol-2013-000557
- Finsterer J. Earl Grey Tea Intoxication. Lancet 2002; 359 (9316): 1484, doi: 10.1016/S0140-6736(02)08436-2
- Mills KR. Characteristics of Fasciculations in Amyotrophic Lateral Sclerosis and the Benign Fasciculation Syndrome. Brain: a Journal of Neurology 2010; 133 (11): 3458–3469, doi:10.1093/brain/awq290.
- Garland H and Moorhouse D. Compressive Lesions of the External Popliteal (Common Peroneal) Nerve. British Medical Journal 1952; 2 (4799):1373–1378.
- Jensen MC, Brant-Zawadzki MN, Obuchowski N, et al. Magnetic Resonance Imaging of the Lumbar Spine in People Without Back Pain. New England Journal of Medicine 1994; 331 (2): 69–73, doi:10.1056/NEJM199407143310201.

#### Spotted Bone - A Spot Diagnosis

Abdul Rehman Arshad, Asif Rahman, Shafqat Hussain

Abstract

A young male was incidentally diagnosed to have a rare disorder on X rays done to rule out a bony injury after trauma to his left wrist. The radiological findings and differential diagnosis are briefly discussed. Keywords: bone dysplasia, osteosclerosis, osteopoikilosis

#### Clinical Scenario / Question

A 26-year-old previously healthy male presented with a two day history of pain in his left wrist following trauma inflicted while playing volleyball. It was aggravated by movements around the affected joint. Clinical examination revealed mild tenderness over the left wrist with full range of movements and absence of any swelling. Distal neurovascular status was intact. X-ray of the left hand and wrist was done to rule out an injury to the bones (Fig. 1).



Fig. 1: X-Rays of left hand and wrist

What diagnosis does the X-ray findings indicate?

- Fracture of left scaphoid bone
- Osteoblastic metastases
- Osteopathia striata
- Tuberous sclerosis
- Osteopoikilosis

#### Answer / Discussion

The X-ray in Fig. 1 shows multiple small hyperdense oval and circular lesions scattered in all small bones of the left hand, with preservation of cortical thickness. These findings are suggestive

of osteopoikilosis. Similar lesions were also present in the contralateral hand and wrist, as well as the pelvis (Fig. 2), on X-rays done subsequently.



Fig. 2: X-Ray Pelvis showing bone islands

Patient was counselled and reassured about the radiological findings. He was prescribed oral Paracetamol and topical Piroxicam for three days and asked to rest the affected joint. Osteopoikilosis (also called spotted bone) is a benign, possibly autosomal dominant dysplasia of bones, occurring in 1 per 50,000 people.<sup>1</sup> Small bones of hand and feet, long tubular bones and pelvis are most frequently affected. The condition is asymptomatic and is diagnosed incidentally on radiographs taken for other problems. The diagnosis is straightforward, based on the typical radiological appearances of small (up to 10mm) hyperdense opacities distributed symmetrically. No further investigations or any specific treatment are indicated. Patients need to be reassured about the benign nature of radiological findings.

Osteoblastic metastases occur in the older age group, are generally larger in size and do not have such a uniformly symmetric distribution. Osteopathia striata is another rare bone dysplasia, characterized by long hyperdense striations mainly in the metaphyses of long bones and pelvis.<sup>2</sup> Sclerotic bone lesions in tuberous sclerosis are frequently seen in the axial skeleton especially calvarias and spine, are at times distributed focally and have irregular borders and variable size.<sup>3</sup> Subperiosteal new bone formation may be present and other clinical features like epilepsy may also provide a clue. As seen in Fig. 1, there is no break in the continuity of scaphoid bone, thus ruling out a fracture.

#### **Competing Interests**

None declared Author Details

ABDUL REHMAN ARSHAD, MCPS, FCPS(Pak). 1 Mountain Medical Battalion, Bagh, AJK Pakistan. ASIF RAHMAN, MCPS, FCPS(Pak). Combined Military Hospital Bannu, Pakistan. SHAFQAT HUSSAIN, MBBS. 1 Mountain Medical Battalion, Bagh, AJK Pakistan. CORRESSPONDENCE: Dr ABDUL REHMAN ARSHAD,

Classified Specialist in Medicine, 1 Mountain Medical Battalion (MDS), Bagh 12500, Azad Kashmir, Pakistan. Email: maj.abdulrehman@gmail.com

- Meena S, Saini P, Chowdhary B. Multiple spots on bone: diagnostic challenge or spot diagnosis? Osteopoikilosis. Neth J Med 2013; 71(7):372, 376.
- Perdu B, de Freitas F, Frints SG, et al. Osteopathia striata with cranial sclerosis owing to WTX gene defect. J Bone Miner Res 2010; 25(1):82-90. doi: 10.1359/jbmr.090707.
- Umeoka S, Koyama T, Miki Y, et al. Pictorial review of tuberous sclerosis in various organs. Radiographics 2008; 28(7):e32. doi: 10.1148/rg.e32. Epub 2008 Sep 4.

#### "Of Psychosis" - A Poem by Dr Javed Latoo

This poem was written with the intention of increasing awareness of psychosis amongst the medical fraternity and general public. It is written in jargon free English language and highlights the important features of this medical condition.

When our beautiful mind feels all muddled up and Ripe with a tendency to draw bizarre conclusions; Hearing or seeing imaginary things as in a dreamland Experiencing unreal things like unwanted intrusions.

When we worry about other people's intentions Suspicious of being followed stirs waves of stress; Carrying a tempest of troublesome mental tensions

Due to a belief that others are talking about us.

Stress of preoccupation with an unfounded belief Of not being in control of our mind and body; Worrying about being controlled invokes a great grief Making us anxious and suspicious of everybody.

Holding an inflated view of being able to communicate With God, aliens and royalty with a pleasure;

Insisting to possess powers to heal, and elucidate Being royal with an ability to control the weather.

Being blissfully ignorant of lack of motivation, idleness And apathy during the spring of our lives;

Often ignoring our daily personal cleanliness With no interest to tidy up due to the lack of strives .

- Soiled and too weary by the lack of enough sleep Grief of our favourite food not appealing anymore;
- Our neglect may even turn a house into a trash heap With a brain too bewildered to focus furthermore.
- This muddled state of mind is an illness called psychosis Not a curse or black magic or witchcraft; beware
- This is a temporary phase rather than an eternal stasis Treatment is available instead of never ending despair.

#### Author Details

Dr JAVED LATOO MBBS DPM MRCPsych, Consultant Psychiatrist and Honorary Lecturer, 5 Borough Partnership NHS Foundation Trust, Hollins Park, Hollins Lane, Warrington, United Kingdom. email: javedlatoo@gmail.com

#### A Very Important Doctor

Frances J Dunne

Once upon a time there lived a quite wealthy young man - in the sense that he was quite smug and comfortable, never really wanting for anything. 'Wealthy people don't have to concern themselves about others or indeed material matters, he used to say to himself, blissfully unaware of the dramatic irony in his statement. He had tons of clothes (which made it difficult to decide what to wear each day), lived on his own in a big house almost the size of a mansion, went on lots of holidays to exotic places, ate in the best restaurants, and by all accounts had no worries whatsoever. He was a man of modest intelligence, quite tall and stout with an arrogant (or should I say confident) manner. He could quite easily win an argument because he would literally wear his opponent down with the ferocity of his delivery, even though it bore little substance. 'I could be a politician because I am so good at debating sensitive issues which affect ordinary people, he would reflect when on his own, which was frequent.

His parents had so much money (from their banking business) to fritter away and therefore had no trouble finding him a suitably big house (almost as large as a mansion as stated) in a fashionable area of London. He also owned a house in Richleymanor, wealthy, а prosperous suburb of Richleyshire. 'Because I have no worries and am in perfect health', he said when he was only 16, 'I am going to become a doctor and heal people who are not rich enough to see me privately and who are a million times less fortunate than me.' Such was his altruistic spirit. And so he studied as hard as he could because he had to (he was not the brightest card in the pack). With the help of his parents' influential circle of friends in the whole of Richleyshire who knew people in high places, he managed to secure a place in an elite medical school where only top doctors were trained - even though he did not possess any outstanding qualifications on leaving school. But that sort of thing doesn't really matter if you possess an altruistic spirit. 'I mean', he reasoned, - 'Lots of famous people (including entrepreneurs) did not pass their final school year exams with Honours and I am just like them in that respect - really downto-earth, a man of the people.'

On the first day of entry to the Royal Breedington University Medical School he was already planning his future career. Not for him the humdrum life of a family doctor. No - he was aiming for prestige and acclaim. He did not need the money though extra money would help 'because you can never have enough, especially if you want to help others less fortunate than yourself, he would say to himself. Such was his determination. 'Should I become a great brain surgeon', he pondered one evening. Should I become an eminent cardiologist or a revered obstetrician? You see, for him it was not enough to be an ordinary doctor - one had to be special in some way. These careers and others (the field of Medicine is huge) he considered. Then one day he decided: 'I know now what to do'; I will get my basic qualifications out of the way and then embark on a career in Mentalology - a subject which was gaining great interest in the popular press. Even students at the University were talking about it. It was a higher degree than Neurodevelopmental Psychobabble (another much sought-after career, normally the reserve of doctors studying cerebrotherapy). So after lots and lots of postgraduate courses in Mentalology he finally passed the higher degree, becoming a member of the Royal College of Mentalologists (MRCM), spent 5 more years in training and became a Consultant Mentalologist at a very prestigious hospital, one which had links to a university, as it happened. His ultimate ambition was to become a Doctor in Medical Politics because he wanted to be in charge of doctors and patients but without the encumbrance of having to care for patients per se or to actually meet doctors. Not for him the drudgery of life in a hospital or general practice - no - one needs to earn as much as possible by doing the least work, rather like Business Executives, he would ruminate.

Initially he enjoyed seeing a few patients here and there as par for the course, but because he felt he was a very important doctor, he needed to move up the ladder to the higher echelons, managing other doctors who might in turn benefit from his great wisdom and enormous insight, accrued in just 8 years training! He decided that he was too important to be seen hanging around hospital wards or in the outpatient department and so spent nearly all his time in the library and at meetings, apart from breakfast and lunch. He always had breakfast in the hospital canteen to show he had the common touch, and sometimes he would make a point of staying on longer after lunch in order to mix with other not-so-important doctors, who would laugh and grovel obsequiously at his every spoken word. Then suddenly he was off, and would be seen bustling and rushing through the canteen doors on his way to a very important event at the prestigious headquarters of the Organization, where he would sit three seats away from the Lord High Superexecutive Chief of the Organization (LHSCO), a very long title indeed but when one is important one usually has imposing if not long titles. Such was the circle the very important doctor was mixing, it explained why he was hardly ever seen in the hospital outside lunch hours or breakfast. Because, you see, in his estimation or rather esteemed opinion, if one is not around much then one must be a very important person indeed.

Sometimes he was seen rushing off to other very important meetings at a top-class hotel where there would be a special Conference Room; sometimes he was at meetings all day. However, often it was difficult to find out exactly what he was doing or where he was because many of the meetings were high level top-secret meetings; for example, a Superexecutive meeting lasting a whole hour might have on the agenda a motion to close down the hospital outpatient department because patients were costing the Organisation too much money. That superfluous-to-requirements money could be better spent on holidays and pay rises for other but not-so-important medical chums as well as serious-minded managers who in turn might do him a favour later on. 'You never know what's around the corner', he always used to say in one of his contemplative moments. The Organization often talked about very big issues such as Doctor Management Downcasting (how to keep those grasping medics in line) and Patient Empowerment, even though patients were never included in any discussions about where they would go when their hospital closed down. Sometimes meetings would extend until the early hours of the morning, which suited the very important doctor because he had no family to worry about or other personal commitments and could come and go as he pleased. Others had to stay on at the very important meetings regardless of their personal circumstances. Sometimes he was so exhausted attending meetings he would spend the following afternoon on the golf course relaxing before attending another evening conference. 'I don't know how he does it', his reverential colleagues would mutter, in hushed tones. 'He deserves another award for taking time off to recharge his batteries for the next meeting'. 'It is quite astonishing how much energy some people have', he would say contentedly to himself.' 'What would the Organisation do without someone of my great leadership skills'?, he asked himself many times in a semi-congratulatory tone.

Nothing would deter the very important doctor from achieving his goals and pleasing the Organisation. After all, this was the way to the top of the medical hierarchy – Doctor of Medical Politics (DMP) and Chief Scientist and Supervisor of the Faculty of Mentalology (CSSFM for short) was his goal. First he set out some decrees or edicts. These would all come under the rubric 'Management Directives', or put in another way, informing his colleagues in a polite but firm manner how he would delegate them to do 'this and that', and therefore no one would blame the very important doctor for say, dismantling any part of the service; besides, his sheer tenacity and doggedness (character traits which he had cultivated from his seniors) gained him further admiration from the legions of subdoctors (doctors who were under his control) who had to yield to his commands. He would sometimes act very humble when questioned about his ruthless tactics and would feign innocence (or was it impotence) in the face of criticism. No, it was the Organization 'calling the shots', as he used to describe it, callously ignoring the plight of his colleagues and patients.

It was strange that he could never recall or at least did not seem to know any of the names of people in the Organization who were responsible for the targets to be achieved. 'Anyway, most patients are not really ill, they just complain and they can jolly well go back to their own general practitioner if they want to bother someone', he would argue in one of his rare insights into the human condition, particularly when colleagues challenged him. His doctor 'associates' (he could never really truthfully call them friends) were stupefied by his perspicacity and visionary zeal and were in no doubt that in order to achieve a change in their practice it was better they were paid less and worked more intensely between 9am and 5pm. They could come in earlier or stay later if they wanted to of course, but no extra money was available for overtime because it was costing the Organization thousands of pounds annually. Best to give the bonuses to those who really deserved them - those Manager Doctors who were extremely busy writing protocols about Best Practice and Risk Assessments - real life-and - death issues, and spending at least 4 hours every six months at very special high-powered meetings drafting 'outcome protocols'. So many emails to send out. This agenda was 'all in a day's work' for the very important doctor who needed to supervise this superhuman task in between meals.

But even the very important doctor himself needed resources and time to carry out all this work. 'I know what', he said to himself one bright sunny Sunday morning on the golf course, -

'I will reduce the amount of time doctors spend seeing patients and cut costs further in this way for all those dedicated doctors because dedication is costing too much'. One hospital inpatient could cost the Organization £1000 a week, even more. 'The doctors can still attend meetings in the hospital (no costs incurred) and do extra administrative work.' 'The bonuses will only go to those who have achieved a special distinction in doing the work of Managers and follow the party line'. 'Yes, that's the way forward', he thought to himself, in one of his rare flashes of brilliance. 'From now on doctors will only have to work 9-5pm'. 'The on-call commitments can be covered by NHS Indirect', the latter being a new company set up to replace doctors and nurses at night-time and weekends, usually manned by staff from one of the local supermarkets. Surgeons would be then free to down tools at 5pm instead of wasting time (and the Organization's money) battling through endless hours of unnecessary exhaustive operations such as cardiac bypasses or hip replacements, which could easily be carried out in the patients' homes anyway. Psychobabble experts could use tickbox rating scales or instruments to assess new referrals (no need to see patients, too costly).

There is no way to describe the tumultuous reception these ideas received at the Managers Annual Conference in Bristol, and the very important doctor received even more accolades. In fact, he was considered for a Rhodium Medal, the highest award in the land given to any doctor. Before being conferred with this precious and prestigious medal (because it can only be worn around your neck, or else it lies on the mantelpiece where nobody really notices it) he was given two lots of pay rises - one for services to the Organisation, the other for keeping the common grasping subdoctors in line by forcing them to sign in and out of work every day and by reducing their salaries. After all, there were rumours that the grasping, greedy subdoctors were beginning to think that perhaps the very important doctor was becoming too very very important. But they kept quiet in any event.

His great achievement was the setting up of SCRAP (Strategic Commission for Rapid Abolition Programme) which set out a one-year plan of how to prevent any patient being seen by a doctor. The patient could be seen by any number of people, from the tea lady to the hospital porter, who were already working flat out on the minimum wage. At least they were not so expensive to keep on the pay roll. The next brilliant idea he concocted was to replace the word 'patient' with 'customer'. 'Patient', he did not like. It gave the impression that someone was ill and needed to see a doctor. But with the New Opinion About Hospital Patients (NOAHPS in short) charter, the word 'patient' did not fit the profile of an enterprising Organisation and so NOAHCS (New Opinion About Hospital Customers) sounded much better. All staff were thence ordered to use this terminology or face the consequences. It was rumoured that it was a sacking offence to use the word patient. He even sent an email to the same effect around the whole Organisation. No one spoke out for fear of reprisal and possible instant dismissal. He was applauded at every Organization meeting from that time on and was rewarded by being given Freedom of the Hospital. This meant he did not have to do anything really just walk around shaking hands with everybody, telling them what a great job they were doing, and so forth. He used the phrase 'Congratulations on a job well done' as many as four times a day to different staff in the hospital. In private he would be irritated because he had to praise other people for what he truly believed were his achievements.

By the end of each week he was so exhausted from sitting on comfortable chairs (some were so comfortable it was a real effort to get out of them) at the many meetings he attended that he would fly off to some far away country for a rest, though of course would endeavour to find out how that country dismantled its health service. Because of his enterprising attitude on behalf of the Organization these trips would be paid for and the very important doctor would not have to spend a penny. 'I deserve it because of all the hard work I am putting in', he used to say, to justify his huge salary and the enormous expenses paid for by the Organization. 'They obviously think very highly of me.' Besides, they know I would get a better salary elsewhere if they did not pay me such gigantic sums of money here', he would rationalise. But this suits me for the time. I have a big house in London near the University and an even bigger house in Richleyshire where I can play golf on the weekends and charge all my expenses to the Organization, even the Golf Club fees. 'Why not? Politicians were doing it', he would argue, in a rare utterance of cognitive dissonance (or pangs of conscience others might think) a term he had picked at one of the many important half-hour psychology conferences he attended (he was much too busy to stay to the end of any conference.

As time passed he was beginning to think he needed a higher salary because time off and holidays were costing him money (domestic shopping, clothes, food, heating bills) despite the freebies. During his days off he would spend lots of time going to museums, visiting the theatre, eating in expensive restaurants and staying in luxury hotels not too far from home, say 10 miles or less. However, for him a real holiday was travelling abroad in a first class seat on a prestigious airline to faraway places. This gave him an edge over his less wealthy colleagues and he would often spend hours on his return recounting his great adventures and experiences abroad in exotic lands. 'He is so broadminded and well-travelled', his managerial associates would say with a feeling of unrequited envy. It is quite remarkable how he manages to be in so many places at the same time - if only he could do the same at this hospital, we would be top of the League Tables for Hospital Risk (LTHR) and gain the recognition we deserve'. 'For all his hard work spent travelling abroad researching better ways of closing down wards and hospitals he now deserves a huge rise in salary'.

And so it came to be. The very important doctor was given an extra allowance (EA for short) worth half his salary and a Credit for Working Hard Allowance (CWHA), both linked to his pension. He was also given a bonus allowance (BA) for sitting twice yearly on a Doctors Work Review Panel (DWRP) set up to deal with those doctors who were not pulling their weight or taking more than one day sick leave or 2 days annual leave at a time. Study leave had already been dropped because the very important doctor argued that if he did not need study leave then no one else did. Besides, 'Who needs study leave when you can look things up on the internet – even how to carry out open heart surgery'. He would argue. Commitment to the Organization was his raison d'être.

And so it continued. After 10 years nearly all the patients had been discharged from the hospital and family doctors were sending them elsewhere into more luxurious, expensive, private hospitals for 'reviews, assessments, and second, third, even fourth opinions'. The Organization would pay for all this from the money it saved closing down the local hospital. This was the very important doctor's finest hour and for his services to the Organization he was awarded the Rhodium Medal at the Annual Convention of Supermanagers Conference. This award was inevitable, given all the time both home and abroad he had invested in this venture. Now the entire hospital could be closed down thereby saving the Organization millions of pounds.

However, there was a problem with this way of operating, he began to think: 'If the hospital were to close down there would be no need for an Organization to run it. There would be no management posts and my post as MDP and CSSFM might be superfluous to requirements. 'I know what I will do' - he decided - 'When that happens I will apply for another post in a different Organisation and I am sure I will be successful given all the accolades I have received, and when that Organisation closes down with my help I will get an even bigger salary and move on to the next post' - maybe Minister for Health?

To be continued

Competing Interests
None declared
Author Details
FRANCIS J DUNNE, FRCPsych, Consultant Psychiatrist and
Honorary Senior Lecturer, University College London, North East
London Foundation Trust, United Kingdom.
CORRESSPONDENCE: FRANCIS J DUNNE, FRCPsych,
Consultant Psychiatrist and Honorary Senior Lecturer, University
College London, North East London Foundation Trust, United
Kingdom.
Email: francis.dunne@nelft.nhs.uk