Case Report

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Case report: DiGeorge syndrome presenting with hypoparathyrodism and Learning Difficulties in adulthood

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Abstract
We report a 40 year old female with mild dysmorphic facial features, learning difficulties, epilepsy and chronic dermatitis, presenting with symptomatic hypocalcaemia. The laboratory investigations confirmed the diagnosis of hypoparathyroidism. The hint to DiGeorge syndrome was the hypoparathyroidism in association with learning difficulties and dysmorphic features. Chromosomal analysis using fluorescence in situ hybridization (FISH) analysis showed a deletion of chromosome 22q11.2 and confirmed the diagnosis of DiGeorge syndrome. This case report demonstrates that DiGeorge syndrome should be considered while investigating hypocalcaemia and Hypoparathyroidism in adulthood as this syndrome has very important implications for health and future family planning for patients and their families.

Case Report

Our patient is a 40-year-old lady who presented to our department feeling unwell with fever and numbness in both hands. Past medical history showed recurrent urinary tract infections, rheumatoid arthritis, chronic eczema and epilepsy .She was taking Levetiracetam 500mg twice daily and Clobazam 5 mg twice daily for the epilepsy. She is also known to have learning difficulties. Mild hypocalcaemia was documented few years back in a previous admission in other hospitals, but the cause was unclear. On admission, she was hemodynamically stable with mild facial dysmorphism, and positive Trousseau's and Chvostek's signs.

Blood tests showed a low corrected calcium 1.5 mmol/L (NR 2.25-2.5 mmol/L), high C-reactive protein, Leukocytosis, and 3.0 mmol/L serum potassium level (NR 3.5-5.0 mmol/L). Other routine blood tests were normal. Further investigations showed low Serum parathyroid hormone levels, normal magnesium levels and normal TSH level. A CT scan of the brain was unremarkable. Electrocardiogram showed QT prolongation (with QTc of 520 ms). The diagnosis of hypoparathyroidism and urinary tract infection was established and the patient was treated with antibiotics to cover urinary tract infection and calcium supplements for hypocalcaemia. The patient symptoms improved significantly and was discharged on calcium supplements and Calcitriol (Rocaltrol 0.25 mcg) with a calcium level of 2.1 mmol/L. The presence of hypoparathyroidism in association with learning difficulties, eczema and epilepsy prompted chromosomal analysis for DiGeorge syndrome. The microdeletion of chromosome 22q11.2 was confirmed by FISH (fluorescent in situ hybridization) analysis. Cardiac echo examination demonstrated no abnormalities and abdominal ultrasound examination showed no renal abnormalities. The patient was offered Genetic counselling together with her family.

Discussion:

DiGeorge syndrome is a well-known genetic disorder with a prevalence of 1:4000 live births[1.] It was initially described by Angelo DiGeorge a physician and paediatric endocrinologist in 1968 [2]. DiGeorge is a developmental defect caused by a microdeletion of chromosome 22q11.2; it is also known as velocardiofacial syndrome or CATCH 22 syndrome to describe the classical features of this syndrome (C-Congenital heart disease, A-Abnormal facies, T-Thymus hypoplasia, C-Cleft Palate and H- Hypocalcaemia due to Hypoparathyroidism. Autoimmune disorders, skeletal defects, renal abnormalities, psychiatric and behavioural disorders are also associated with this syndrome.

DiGeorge is an autosomal dominant syndrome but the majority of patients have de novo mutations caused mainly by the microdeletion of chromosome 22q11.2 which leads to developmental disorders such as the failure of development of pharyngeal pouch system [3, 4.] These developmental disorders are the main cause of the classic features and presentation of DiGeorge syndrome such as congenital heart diseases, hypoplasia of the parathyroid glands and thymus, congenital immune deficiency and renal abnormalities[5] .

Congenital Conotruncal cardiac defects that involve truncoaortic sac can present in 70% patients with DiGeorge Syndrome. The most common cardiac anomalies are interrupted aortic arch, Tetralogy of Fallot, Atrial septal defect and ventricular septal defects [4, 5, 6] .

Hypocalcaemia is due to hypoparathyroidism and is present in about 60 % of patients [5, 7] . Hypocalcaemia is a strong predictor of DiGeorge syndrome if it is associated with other clinical features such as cardiac defect and immunodeficiency. Hypocalcaemia commonly presents as muscle cramps,

numbness, tetany, focal or generalized seizures, prolong QT and hypotension.

Immunodeficiency is rare in adults and but it may present in up to 70-80% of the children with DiGeorge syndrome. Immunodeficiency occurs because of the low T cell count due to thymus hypoplasia. The function of T cells is however, usually preserved. Patients with immunodeficiency may have recurrent viral chest infection, systemic fungal infections frequent bacterial infections [8] .

The characteristic facies of DiGeorge include long face, narrow palpebral fissures, broad nasal bridge, micrognathia and asymmetrical crying face.

Psychiatric disorders have been reported with 22q11.2 deletion syndromes such as schizophrenia, bipolar disorder, anxiety and affective disorders.

Other conditions that may be associated with DiGeorge are atopic disorders (asthma and eczema) rheumatoid arthritis, autoimmune thyroiditis, renal abnormalities (such as multicystic kidneys andVesicoureteral reflux).

Conclusion:

Due to the variety of symptoms and the de novo mutations, DiGeorge Syndrome should be considered in adults presenting with hypocalcaemia due to hypoparathyroidism even in the absence of the classical features. The syndrome has significant health implications, and confirming the diagnosis is important for future family planning.

Competing Interests
None declared
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