Case Report

DiGeorge syndrome with microdeletion of chromosome 21

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Abstract

DiGeorge syndrome consists of abnormalities of the parathyroid, thymus and the kidneys. It also includes facial dysmorphism and cardiac defects. It is caused by a microdeletion of the long arm of chromosome 22 and occasionally chromosome 10. The case of a 12-week-old female infant with low set ears, retrognathia, micrognathia, high-arched palate, right-sided aortic arch, hypocalcaemia and truncus arteriosus which are all typical of DiGeorge syndrome and an unusual microdeletion of chromosome 21 is presented.

Keywords: Catch 22, chromosome, DiGeorge syndrome, microdeletion

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INTRODUCTION

DiGeorge syndrome also known as CATCH 22 syndrome (cardiac, abnormal facies, thymic hypoplasia, cleft palate, hypocalcaemia) is a well-studied microdeletion syndrome, with a prevalence of 1 in 4000–6000 live births.[1,2] The clinical manifestations include hypoplasia or aplasia of the thymus and parathyroid gland, palatial and facial dysmorphism, renal abnormality and conotruncal defects of the heart.[3,4]

Most deliveries in Nigeria occur outside the hospital, thus cases of this kind are likely to be missed because of lack of detailed clinical examination.[5] Recurrent infections, tetany from hypocalcaemia and congenital heart disease when present, are often the major abnormalities that bring the condition to light.[6]

DiGeorge syndrome is commonly caused by a microdeletion of the long arm of chromosome 22 (22q11.2) and less frequently by a deletion of the short arm of chromosome 10 (10p13).[3] The case of a 12-week-old female infant with features of DiGeorge syndrome and the rare microdeletion of the chromosome 21 is presented.

CASE REPORT

A 12-week-old female infant presented to the children emergency room of a tertiary centre in Nigeria because of recurrent difficulty in breathing since birth, recurrent convulsions of 4 weeks' duration and cough and catarrh of 3 weeks' duration. She had bluish discolouration of the lips and tongue but had no feeding intolerance or easy fatiguability.

The infant, the second child of a monogamous family setting, was born per vaginam at term to a 37–year-old homemaker with uneventful antenatal care. She was not a known diabetic and denied consumption of alcohol during pregnancy. The father was a 50-year-old businessman with tertiary level of education, the same as the mother.

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On examination, she weighed 3.4 kg, her height and occipitofrontal circumference were 59 cm and 37 cm, respectively, which were all not within normal limits. She was febrile (39.4°C), cyanosed and had dysmorphic facies including low set ears, retrognathia, micrognathia and high-arched palate. She had a pulse rate of 184/min that was regular and the apex beat was located at the 4th left intercostal space, in the midclavicular line. The second heart sound was single while a Grade 3/6 pansystolic murmur, loudest at the lower left sternal border was heard. The respiratory rate was 56 cycles/min but was saturating at 65%. She was dyspneic and had widespread crepitations. A soft and tender hepatomegaly was noted. The examination of the other systems was unremarkable. She was assessed to have a congestive heart failure complicating a cyanotic congenital heart disease.

Chest radiography revealed a right-sided aortic arch, increased pulmonary vascular markings, bilateral patchy infiltrates and a cardiothoracic ratio of 60% [Figure 1]. Electrocardiogram showed sinus rhythm and incomplete right bundle branch block. The echocardiogram showed a large subaortic ventricular septal defect (VSD) (8 mm) with bidirectional shunt, a small patent ductus arteriosus (2.5 mm) which was shunting from truncal to pulmonary vessel and a large single truncal vessel which is in keeping with Type I truncus arteriosus [Figure 2]. The haematocrit was 44% and she had hypocalcaemia of 6.2 mg/dl which was considered largely responsible for the recurrent seizures.

The child was managed for bronchopneumonia and heart failure which complicated the persistent truncus arteriosus. DiGeorge syndrome was strongly suspected because of typical dysmorphic features, hypocalcaemia and congenital heart disease. Chromosomal studies using Giemsa C-Banding technique showed microdeletion of chromosome 21.

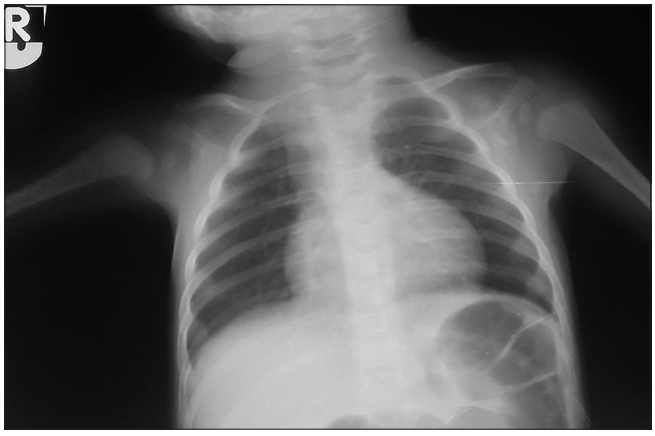

Figure 1: Chest radiograph showing increased pulmonary vascular markings

The infant was admitted and commenced on intravenous antibiotics (cefuroxime and genticin), suspension hydrochlorothiazide, spironolactone, digoxin and captopril. She was also corrected for hypocalcaemia with intravenous calcium gluconate following which seizures abated and calcium level normalised. The child improved and is being prepared for surgical intervention.

DISCUSSION

DiGeorge syndrome is a genetic disorder first described more than four decades ago by a paediatric endocrinologist 'Angelo DiGeorge'[7] and later in 1972 by Lischner.[8] The majority of the cases of DiGeorge syndrome are due to a *de novo* microdeletion of chromosome 22q11.2; about 28% of cases may have an inherited deletion.[4] A few cases of autosomal dominant inheritance have been described. The microdeletion is mostly on long arm of chromosome 22 and less likely on chromosome 10.[3] In the index case, the microdeletion was on chromosome 21, a rare occurrence. The diagnosis of DiGeorge syndrome is confirmed by fluorescent *in situ* hybridisation analysis which shows the microdeletion.[9]

DiGeorge syndrome is synonymous with CATCH 22 syndrome which is used to describe the classic features and phenotype of the syndrome (C - Congenital heart disease, A - Abnormal facies, T - Thymic hypoplasia, C - Cleft palate, H - Hypocalcaemia due to hypoparathyroidism).[4]

Children with DiGeorge syndrome have a variety of congenital heart defects (mainly conotruncal) and these defects are present in about 70% of the patients. The most common cardiac anomalies documented from various literature include interrupted aortic arch, right-sided aortic arch, truncus arteriosus, tetralogy of Fallot, atrial

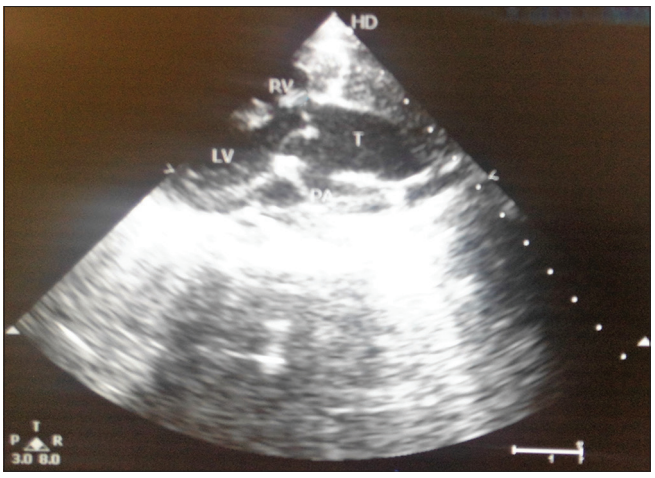

Figure 2: Long-axis parasternal view showing truncal vessel and pulmonary artery

septal defect, VSD, aberrant subclavian artery and right infundibular stenosis.[3,4,10,11] The index case presented with right-sided aortic arch and persistent truncus arteriosus which are key cardiac malformations that are common to this syndrome.

Hypocalcaemia has been reported to occur in about 60% of patients with the syndrome and it is due to hypoplastic parathyroid glands.[12] It commonly manifests in infancy with seizures as was manifested by the index case. Other features include muscle cramps, hypotension, numbness, tetany and prolonged QT interval. These were however absent in the present case.

The immune system is affected in 70%–80% of children with DiGeorge syndrome and this immunodeficiency is due to thymic hypoplasia. Only <1% of these patients present with total thymic aplasia. The patients have reduced T cell numbers although the function is preserved. Children with partial thymic aplasia usually have mild infections while those with complete thymic aplasia have increased susceptibility to fungal, viral and bacterial infections.[13] Seeing the rarity of thymic aplasia, it is therefore no surprise that the patient had no recurrent infections. Autoimmune diseases such as diabetes mellitus and thyroid diseases have been shown to have an increased incidence in children with DiGeorge syndrome.[3] There was however no clinical manifestations of these conditions in the index case.

The characteristic facies of DiGeorge syndrome include bifid uvula, high-arched palate, small mouth, wide set eyes, low set ears, micrognathia and retrognathia and some of which are present in the reported case. However, it has been documented that some patients with DiGeorge syndrome do not present with any facial malformation.[14]

Prenatal testing for DiGeorge Syndrome is widely available and is recommended for foetuses that have been detected through ultrasound as having heart malformation or cleft palate and if at least one parent is confirmed to have a microdeletion on the long arm of chromosome 22.[15] Appropriate and timely diagnosis at any time during the pregnancy might be helpful in planning for the care of the neonate.

Microdeletions of chromosome 21 are extremely rare and may be associated with minimal phenotypic appearance although features such as microcephaly, large ears, low set ears, short philtrum, hypertonia/hypotonia, cleft lip and palate, atrial septal defect and VSD have been described.[16] To the best of the author's knowledge, no one has ever described features of chromosome 21 microdeletion in keeping with the typical phenotypic appearance of DiGeorge syndrome.

In conclusion, a 3-month-old infant with typical features of DiGeorge syndrome and a rare microdeletion of chromosome 21 is presented.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Wilson DI, Cross IE, Burn J. Minimum prevalence of chromosome 22q11 deletion. Am J Hum Genet 1994;55:A169.
2. Devriendt K, Fryns JP, Mortier G, van Thienen MN, Keymolen K. The annual incidence of DiGeorge/velocardiofacial syndrome. J Med Genet 1998;35:789-90.
3. Mølsted K, Boers M, Kjaer I. The morphology of the sella turcica in velocardiofacial syndrome suggests involvement of a neural crest developmental field. Am J Med Genet A 2010;152A: 1450-7.
4. Ryan AK, Goodship JA, Wilson DI, Philip N, Levy A, Seidel H, *et al.* Spectrum of clinical features associated with interstitial chromosome 22q11 deletions: A European collaborative study. J Med Genet 1997;34:798-804.
5. National Population Commission (NPC) [Nigeria] and ICF International 2014. Nigeria Demographic and Health Survey. Abuja, Nigeria, and Rockville Maryland, USA: NPC and ICF International; 2013. Available from: https://www.dhsprogram.com/pubs/pdf/FR293/FR293.pdf. [Last accessed on 2017 Mar 20].
6. Sieberer M, Runte I, Wilkening A, Pabst B, Ziegenbein M, Haltenhof H, *et al.* Spectrum of neuropsychiatric features associated with velocardiofacial syndrome (Deletion 22q11.2). Fortschr Neurol Psychiatr 2006;74:263-74.
7. DiGeorge AM. Discussion of paper by Cooper MD, Peterson RDA and Good RA: A new concept of the cellular base of immunology. J Pediatr 1965;67:907.
8. Lischner HW. DiGeorge syndrome(s). J Pediatr 1972;81:1042-4.
9. Desmaze C, Scambler P, Prieur M, Halford S, Sidi D, Le Deist F, *et al.* Routine diagnosis of DiGeorge syndrome by fluorescent *in situ* hybridization. Hum Genet 1993;90:663-5.
10. Marino B, Digilio MC, Toscano A, Anaclerio S, Giannotti A, Feltri C, *et al.* Anatomic patterns of conotruncal defects associated with deletion 22q11. Genet Med 2001;3:45-8.
11. Kiel EA, Drummond WH, Barrett DJ. Prevalence of T-lymphocyte abnormalities in infants with congenital heart disease. Am J Dis Child 1984;138:143-6.
12. Choi JH, Shin YL, Kim GH, Seo EJ, Kim Y, Park IS, *et al.* Endocrine manifestations of chromosome 22q11.2 microdeletion syndrome.

Horm Res 2005;63:294-9.
13. Piliero LM, Sanford AN, McDonald-McGinn DM, Zackai EH, Sullivan KE. T-cell homeostasis in humans with thymic hypoplasia due to chromosome 22q11.2 deletion syndrome. Blood 2004;103:1020-5.
14. Hirotani A, Morimoto S, Koh E, Ogihara T. Partial DiGeorge syndrome at the age of thirty-four. Intern Med 1994;33:418-21.
15. Perez E, Sullivan KE. Chromosome 22q11.2 deletion syndrome (DiGeorge and velocardiofacial syndromes). Curr Opin Pediatr 2002;14:678-83.
16. Tinkel-Vernon H, Finkernagel S, Desposito F, Pittore C, Reynolds K, Sciorra L, *et al.* Patient with a deletion of chromosome 21q and minimal phenotype. Am J Med Genet A 2003;120A:142-3.