

10p deletion in a Sri Lankan infant with partial DiGeorge syndrome

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Introduction

DiGeorge syndrome (DGS) is a diagnosis usually made early in life with the classical triad of congenital heart defect (conotruncal abnormalities in the majority) hypocalcaemia and thymic aplasia / hypoplasia¹. Defective morphogenesis of the third and fourth branchial arches from where the thymus, parathyroid glands and the outflow tract of the heart originate explains this clinical syndrome². Heterozygous chromosomal deletion at 22q11.2 is the well-known underlying cause for this relatively common and easily recognized chromosomal disorder^{1,2}. Feeding difficulties, palatal abnormalities, including cleft palate and the velo-cardio-facial syndrome, are other entities included in the chromosome 22q11.2 deletion syndrome.

We report an infant whose phenotype resembled chromosome 22q11 deletion syndrome but whose genotype showed 10p deletion syndrome with no abnormality of chromosome 22. This clinical presentation is explained by the deletion of the DiGeorge critical region 2 (DGCR2) identified on the short arm of chromosome 10. This rare syndrome highlights the need for genetic studies for accurate phenotype-genotype correlation in patients with DGS.

Case report

A girl with failure to thrive, difficulty in swallowing, congenital heart defects and recurrent respiratory tract infections developed hypocalcaemia and seizures at sixteen weeks of age. She was the first child of healthy, unrelated parents (mother 22 years, father 26 years) and was growth retarded at birth, weighing 1.86 kg at 38 weeks gestation. At age four

months physical examination found her poorly grown (2.7 kg). Weight, length and head circumference were all at -3SD. There was dysmorphism, which included hypertelorism, small hooded eyes, epicanthic folds, flat nasal bridge, prominent nostrils, receding chin, low set malformed ears, thin upper lip and bifid uvula (Figure 1).



Figure 1: Characteristic facies resembling DiGeorge syndrome

There was a systolic murmur but no features of heart failure. Motor development was delayed with head lag. Bilateral sensori-neuronal hearing loss was present but she was alert and able to follow objects visually.

Laboratory investigations showed hypocalcaemia, normal serum sodium, potassium and magnesium. T cell activity was present. A narrow superior mediastinum was seen on chest radiography. Ultrasonography identified a small hypoplastic thymus in the anterior mediastinum. Echocardiography revealed a perimembranous ventricular septal defect, atrial septal defect and small patent ductus arteriosus. Kidney and brain ultrasound were normal.

Chromosome culture and karyotyping showed a karyotype of 46,XX,del(10)(p12.3 →15).(Figure 2) Parental karyotypes were normal.

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Figure 2: karyotype showing 46,XX,del(10)(p12.3→15)

Discussion

DGS is a common chromosomal disorder with an incidence of 1 in 4000 to 6000³. Some patients do not show all the features of classical DGS and therefore cause delay in diagnosis⁴. Palatal and speech problems together with congenital heart defect are the main issues in such patients who may be detected by speech pathologists or through ENT services⁵. Due to phenotypic overlap with other disorders the 22q11 deletion syndrome has expanded and velo-cardio-facial syndrome is the best known condition included in this syndrome⁶.

This child had the cardinal features of DGS (hypocalcaemia, hypoplastic thymus and congenital heart defects) as well as the characteristic facial features, cleft palate and feeding difficulties. The presence of thymic tissue (hypoplastic rather than an absent thymus) and circulating T cells lead to the diagnosis of partial DGS which is commoner than the complete DGS⁷. Despite the clinical, radiological, biochemical and immunological features being compatible with the diagnosis of partial DGS, chromosome analysis did not show chromosome 22q11 deletion. Instead the much rarer condition of chromosome 10p deletion was found.

10p deletion is a very rare chromosomal abnormality⁸. Clinical entities reported are attributed to haploinsufficiency caused by deletion of genes located in close proximity to each other. Therefore 10p deletion is a contiguous gene deletion syndrome⁹ and clinical descriptions vary from deafness which occurs with deletion of the distal most region of the short arm of chromosome (10p15) to wider array of symptoms and signs when deletion of more proximal regions (10p12, p13,p14) occurs.

A specific region identified on the short arm of chromosome 10 (10 p) is the DiGeorge critical region 2 (DGCR2) and deletion of 10p13 causes haploinsufficiency of DGCR2¹⁰. In our patient karyotyping with high resolution banding showed deletion from 10p12 to 15¹⁰ and loss of DGCR2 explained the phenotype.

10p deletion syndrome is also known to cause the HDR syndrome (hypoparathyroidism, deafness and renal abnormalities) when genes in p14, which is located very close to the DGCR2 region, is deleted¹¹. We did not find any renal abnormality. However, sensori-neuronal hearing loss was found. In a review of 36 patients with 10p deletion and partial DGS, sensori-neuronal deafness was highly associated with 10p deletion. Deafness is absent in DGS caused by 22q11 deletion and may help in differentiating which has been suggested in previous case reports¹¹. This case supports this. In view of the genetic heterogeneity, we recommend karyotyping even when classical phenotype of DGS is present for accurate genotype-phenotype correlation.

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