Cardiology in the Young

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Interstitial 5p15.2-p13.3 deletion in association with situs inversus, dextrocardia, L-loop of the ventricles, and transposition of great arteries in a newborn infant

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Brief Report

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Abstract

We report a rare association of interstitial deletion of 5p15.2-p13.3 with situs inversus, dextrocardia, L-loop of the ventricles, and transposition of great arteries: [I, L, L] Transposition of Great Arteries. We did not find such an association reported in the medical literature.

Case

A female infant is born at 35 3/7 weeks of pregnancy to a 36-year-old G4P0131 mother. The duration of rupture of membrane was 6 hours. All maternal prenatal laboratory results including rapid plasma reagin, human immunodeficiency virus, hepatitis B, chlamydia and gonorrhea were negative. Maternal past medical history was positive for Human simplex virus (last outbreak 1 year ago), systemic lupus erythematosus, deep vein thrombosis, and seizure disorder for which she was treated with levetiracetam.

At delivery, the infant required resuscitation with positive pressure ventilation. Apgar scores were 2, 7, and 9 at 1, 5, and 10 minutes, respectively. Cord gas showed a pH of 7.31, PCO_2 of 41, PO_2 of 55, and HCO_3 of 19.7. Infant's measurements were appropriate for gestational age, with weight 2.13 kg (4 lb 11.1 oz), length 47 cm (1′ 6.5″), and head circumference 29.5 cm (11.61″). Admission vital signs were stable: temperature, 99.1°F (37.3°C); heart rate, 196; respiration, 32; blood pressure, 67/35 mmHg with a mean of 44; SpO_2, 93%.

Physical examination showed flat anterior fontanelle. No facial dysmorphic features were noted with normal appearing cranium and face. No hypertelorism was noted with normal nose. Back and neck were normal. Cardiovascular exam showed regular rhythm, S1 normal and S2 normal, and no murmur heard. Pulses were palpable in all limbs. Point of maximum impulse was displaced to the right chest. Chest exam showed retraction and tachypnea. Abdomen was soft with no distension or hernia. Musculoskeletal exam showed talipes equinovarus. Ortolani and Barlow test was negative. Genital exam showed normal female. She was noted to be lethargic with low muscle tone. Skin was warm and dry. Capillary refill was less than 3 seconds and normal turgor. No rash or jaundice was noted with visible cyanosis.

After stabilisation in the delivery room, the infant was taken to the neonatal ICU and was placed on ventilator. Chest x-ray showed dextrocardia with situs inversus (Figure 1). Infant continued to have low oxygen saturations despite ventilatory support with 100% oxygen. Serial blood gases showed persistent hypoxaemia. An urgent echocardiogram (Figure 2) was obtained, which showed a rare association of dextrocardia with transposition of the great vessels (I, L, L-Atrial Inversus/L-loop/L-transposition; mirror image with transposition of the great vessels): [I, L, L] Transposition of Great Arteries. Infant was transferred to level IV neonatal ICU cardiology centre in stable condition for surgical intervention. Genetic testing (CombiSNP Array Analysis) showed interstitial deletion of 22 Mb (megabases) on 5p15.2-p13.3. We did not have further details about the results of single-nucleotide polymorphism array including the extension of the deletion and molecular breakpoints. It will be interesting to map the genes involved in cardiac and laterality development.

Discussion

Velo-cardio-facial syndrome and conotruncal heart defects have been reported in association with 22q11.2 deletion. Recently, Lejeune et al[1] reported isolated heart disease with the same deletion. However, an extensive literature search did not show any reports of association of 5p deletion with dextrocardia and L-transposition of great arteries.

Disorders resulting from 5p deletions (5p–) were first recognised in 1963 by Lejeune et al.[1] The most recognisable phenotype is characterised by a high-pitched cry, dysmorphic features, poor growth, and developmental delay also named as Cri du Chat syndrome.[2] The incidence of

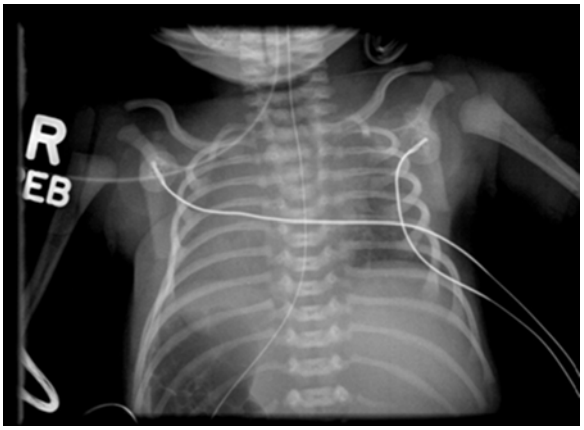

Figure 1. Chest x-ray obtained soon after birth.

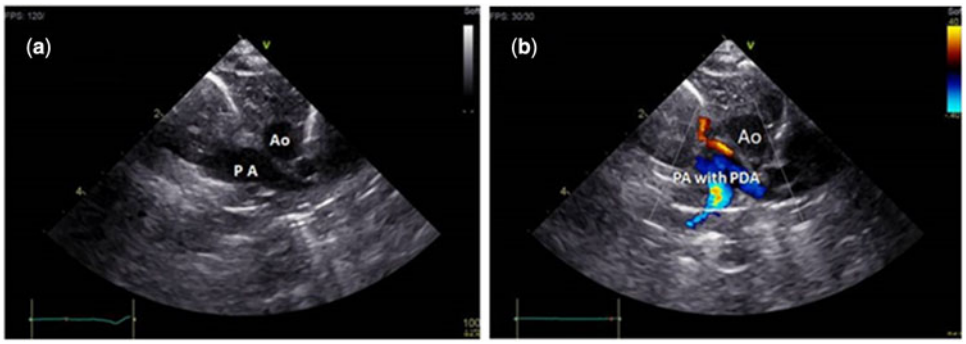

Figure 2. Echocardiogram. (***a***) Transposition and (***b***) Doppler study. Ao=aorta; PA=pulmonary artery; PDA=patent ductus arteriosus.

Cri du Chat syndrome is between 1/15,000 and 1/50,000 live birth. 5p deletions are most commonly de novo occurrences, which are paternal in origin in 80–90% of cases.[3] Terminal deletions comprise 80–90% of cases and interstitial deletions account for 3–5%.[4] In the case presented, we noted a significant interstitial deletion of 5p involving a big area from p15.2-p13.3, which includes the CTNND2 gene that has been implicated in the intellectual disability phenotype of Cri du Chat syndrome. Recently, Balta et al[5] have reported a case of multiple congenital abnormalities with hypoplastic left heart in association with interstitial deletion of 5p involving an area from p15.2-p14.2.

The critical regions in cases of Cri du Chat syndrome have been mapped to certain symptoms as described in the review by Nguyen et al.[2] As far as the association of cardiac defect is concerned, Kondoh et al[6] reported six patients with 5p deletion out of which two had CHD. They did not mention the type of CHD in their article; however, the region deleted in CHD was p13.2–p14.1, which is seen in our case as well. Also one of their patients with CHD had talipes that was also noted in our case. Earlier Hills et al,[7] in a study of 21 patients with Cri du Chat syndrome, reported 6 patients with ventricular septal defect, 6 with patent ductus arteriosus, 5 with tetralogy of Fallot, 2 with pulmonary valve atresia with ventricular septal defect, and 1 each with pulmonary valve stenosis and double-outlet right ventricle. No association with transposition of great arteries was reported. Transposition of great arteries is the most mysterious cyanotic heart disease because it has no precedent in phylogenetic and ontogenetic development and its aetiology and morphogenesis are still largely unknown but was recently related to lateralisation defects.[8] While reporting this association, we are not undermining the fact that this could be a coincidental finding but in view of previously described cardiac defect with 5p deletion, further evaluation is warranted.

Not all deletions result in phenotypic manifestations. For example, terminal deletions of 5p in some cases were found to have no phenotypic effects.[9] Similarly, life expectancy varies with presentation and complications. The reported ranges are 36% of deaths in the first month of life and 64% in the first year of life with CHD being one of the most common causes of death.[5] In view of complex heart with known 5p deletion, comfort care was offered to our patient with no escalation in therapy.

In conclusion, interstitial 5p deletion is a rare genetic disease. Our report of association of this with dextrocardia and L-transposition of great arteries is not presented in literature that needs further evaluation.

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Conflicts of Interest. None.

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References

1. Lejeune J, Lafourcade J, Berger R, et al. 3 cases of partial deletion of the short arm of a 5 chromosome. C R Hebd Seances Acad Sci 1963; 257: 3098–3102.
2. Nguyen JM, Qualmann KJ, Okashah R, Reilly A, Alexeyev MF, Campbell DJ. 5p deletions: current knowledge and future directions. Am J Med Genet C Semin Med Genet 2015; 169: 224–238. doi: 10.1002/ajmg.c.31444
3. Mainardi PC, Perfumo C, Cali A, et al. Clinical and molecular characterisation of 80 patients with 5p deletion: genotype-phenotype correlation. J Med Genet 2001; 38: 151–158.
4. Mainardi PC, Pastore G, Castronovo C, et al. The natural history of cri du chat syndrome. A report from the italian register. Eur J Med Genet 2006; 49: 363–383.
5. Balta B, Erdogan M. Ergul AB, Sahin Y, Ozcan A. Interstitial deletion 5p14.1-p15.2 and 5q14.3-q23.2 in a patient with clubfoot, blepharophimosis, arthrogryposis, and multiple congenital abnormalities. Am J Med Genet A 2017; 173: 2787–2802. doi: 10.1002/ajmg.a.38386
6. Kondoh T, Shimokawa O, Harada N, et al. Genotype-phenotype correlation of 5p–syndrome: pitfall of diagnosis. J Hum Genet 2005; 50: 26–29.
7. Hills C, Moller JH, Finkelstein M, Lohr J, Schimmenti L.Cri du chat syndrome and congenital heart disease: a review of previously reported cases and presentation of an additional 21 cases from the Pediatric Cardiac Care Consortium. Pediatrics 2006; 117: e924–e927
8. Unolt M, Putotto C, Silvestri LM, et al. Transposition of great arteries: new insights into the pathogenesis. Front Pediatr 2013; 1: 11. doi: 10.3389/fped.2013.00011
9. Bengtsson U, Mcmahon J, Quarrell O, et al. Phenotypically normal carriers of unbalanced terminal deletions of 5p transmit the deletions to offspring who display growth and developmental delay. Am J Hum Genet 1990; 47: A818.