Dysphagia as an early presentation of DiGeorge’s syndrome – case report

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Abstract

DiGeorge’s syndrome is a 22q11.2 deletion leading to abnormal embryogenesis of pharyngeal arches and it is manifesting in a variety of clinical signs and symptoms. The spectrum of anomalies varies from minor facial dysmorphism and cleft palate to a broad spectrum of cardiovascular anomalies, thymic dysfunction and immune deficiencies, hypocalcemia due to hypoparathyroidism, growth and developmental delay and speech disturbances. Cardiovascular anomalies might include right sided aortic arch, aberrant vessels and vascular ring. Here we present an atypical case of partial DiGeorge’s syndrome with feeding and swallowing difficulties and laryngeal stridor in the neonatal period. Early presentation in this period is usually due to severe hypocalcemia and cardiac disease. Feeding difficulties in a preterm baby needed clinical assessment skills in order to establish the diagnosis and delineate it from feeding difficulties usually seen in preterm babies. Esophagogram (barium X Ray) showed antero-posterior oblique impression towards the right side, the latero-lateral view showed impression on the rare side, suspected to be esophageal sub stenosis due to vascular anomaly, aberrant right subclavian artery and suspected thymic hypoplasia. We report a 9-year follow up period by a team of subspecialists. The child had two surgeries due to aberrant vessel and velopharyngeal deficiency. Optimal management of patients with DiGeorge’s syndrome requires a multidisciplinary teamwork which should include a cardiologist, immunologist, geneticist, speech/language therapist, endocrinologist and other subspecialists depending on patient’s phenotype.

Дисфагија како рана презентација на DiGeorge Синдром – приказ на случај

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Извадок

Диетодијнот синдром е резултат на делегиција на 22q11.2 која води до пореметена ембриогенеза на фарингеалните лади и се манифестира со различни здравствени проблеми. Спектрот на аномалии во овој период е варијабелен и може да се презентира со минорна лицева дизморфија и расцеп на речната кука, но и со широк спектар на кардиоваскуларни аномалии, дисфункција на тимус и имун дефицитет. Спектрот на кардиоваскуларни аномалии може да се од типот на десен аортен лак, аберантни крвни фаги, хипокалцемија поради хипопаратироидизам, пореметување во растот и развојот и проблеми со говорот. Кардиоваскуларните аномалии може да се од типот на десен аортен лак, аберантни крвни фаги, хипокалцемија поради хипопаратироидизам, пореметување во растот и развојот и проблеми со говорот. Кардиоваскуларните аномалии може да се од типот на десен аортен лак, аберантни крвни фаги, хипокалцемија поради хипопаратироидизам, пореметување во растот и развојот и проблеми со говорот.

Introduction
DiGeorge's syndrome is a 22q11.2 deletion leading to abnormal embryogenesis of pharyngeal arches and it is manifesting in a variety of clinical signs and symptoms. The spectrum of anomalies varies from minor facial dysmorphism and cleft palate to a broad spectrum of cardiovascular anomalies, thymic disfunction and immune deficiencies, hypocalcemia due to hypoparathyroidism, growth and developmental delay and speech disturbances. Cardiovascular anomalies include right sided aortic arch, aberrant vesicles. When the aortic arc, or the associated vessels form a complete or incomplete ring around the trachea and the esophagus the condition is called vascular ring. It is rare congenital malformation that counts less than 1% of all heart anomalies. The symptoms are recognised usually during the period of early infancy or later in life, because of feeding and respiratory difficulties.

We present an atypical case of partial DiGeorge's syndrome with feeding and swallowing difficulties and laryngeal stridor. Vascular ring should be suspected in all neonates with feeding and respiratory problems. Prompt diagnosis and treatment are of great importance for appropriate growth and development. In our case this condition is part of a syndrome, which should be carefully monitored by a multidisciplinary team.

Case report
One-month old infant was admitted to hospital due to feeding difficulties and vomiting. The condition was worsening during feeding. The baby was born premature, 33 weeks gestational age, birth weight 1860 gr, Apgar score 7/8. Polyhydramnios was noticed in the last trimester. She was treated in the nursery for 3 weeks and was tube fed. On admission, neonatal infection was suspected, although the baby had normal values of inflammatory markers. The plain chest X-ray showed displaced mediastinal organs towards the right side, the upper right lobe had lower transparency suspected as consolidation. The tracheal aspirate was positive for Klebsiella aerogenes and antibiotic treatment was started. The baby had intermittent laryngeal stridor and feeding difficulties. Fiberlaryngoscopy was normal. Esophagogram (barium X Ray) showed antero-posterior oblique impression towards the right side, the latero-lateral view showed impression on the rare side, suspected to be esophageal substenosis due to vascular anomaly, aberrant right subclavian artery. Thymic hypoplasia was also suspected. The baby had normal calcium and parathormone levels. Echocardiography showed patent ductus arteriosus. Computer tomography with contrast showed vascular ring with left sided aortic arch with aberrant right subclavian artery and patent ductus arteriosus. Renal ultrasound was normal. FISH (Fluorescence in situ hybridization) was performed showing 22 q11.2 micro deletion (Figure 1).

At the age of 4 months the child had an operation to correct the vascular anomaly. Afterwards she had regular cardiologic assessments, showing normal cardiac structure and function. Following the procedure, swallowing status improved. The
growth remained beneath the third percentile for 9 years follow up. Neurodevelopmental assessment showed developmental delay with delayed speech development, learning delays and disabilities. ERA was normal. At the age of 3 years the child was diagnosed Velopharyngeal deficiency (VPD) by a speech and language pathologist. She was referred to Cleft lip and palate craniofacial clinic where VPD confirmed via nasendoscopy. She was treated surgically with a posterior pharyngeal flap. She continued with speech therapy and was able to produce consonants for the first time and become intelligible to other people at the age of 5 years. Immunological assessment at age of 1 year showed normal function of the humoral immune system and neutrophil dysfunction. She was immunized by inactivated vaccines regularly. Cellular immunity could not be accurately assessed, and immunization with live vaccine (MRP) was not performed. During the 9 year follow up she had mild upper respiratory infections and two episodes of bronchopneumonia that required hospital treatment at her early age.

Discussion
DiGeorge’s syndrome features were first reported by Angelo DiGeorge in 1965 and 1968 although thymic aplasia was noted by Harrington in 1828 and the association with congenital hypoparathyroidism by Lobe in 19591,2,3,4. Additional anomalies were noted to be associated with the syndrome, especially anomalies of the great vessels, esophageal atresia, heart, ear, nose and mouth.
defects. For the first time the cause of the syndrome was suspected to be a deletion in chromosome 22q11 in 1981. This is a 35 mb chromosomal region that contains more than 35 genes that affect the morphogenesis of the pharyngeal arches, heart and brain.

DiGeorge’s syndrome is one of the most common genetic disorders. It occurs in 1:4000 live births but could be higher having in mind the clinical variability. More than 180 different defects have been associated with the syndrome. Typical presentation during infancy usually includes some of the following features: facial dysmorphia, heart defect, hypocalcemia, palatal anomalies and immunodeficiency. The standard method for diagnosis of DiGeorge’s syndrome is the specific FISH test for chromosome 22q11 deletions. Due to the wide availability of these specific probes, clinicians can diagnose affected children, often presenting with cardiac abnormalities, immunodeficiency or hypoplastic calcemic seizures.

This syndrome is rarely diagnosed in the neonatal period. Early presentation in this period is usually due to severe hypocalcemia and cardiac disease.

We present a rare case of early diagnosed patient in the neonatal period with feeding difficulties and swallowing problems. Our patient was a preterm baby, 33 weeks of gestation that stayed in the nursery for 3 weeks and was tube fed. She started having feeding difficulties when she was discharged home and was bottle fed. Feeding difficulties in a preterm baby needed clinical assessment skills in order to establish the diagnosis and delineate it from feeding difficulties usually seen in preterm babies. The patient was admitted to our Clinic with aspiration-based infection as it has been previously reported.

Feeding difficulty is often a symptom of palatal dysfunction, cardiac anomalies and gastrointestinal dysmotility, as a result of the presence of a vascular ring that impairs the esophagus, and hypotonia can lead to feeding difficulty. In some patients, these difficulties likely result from craniofacial dysmorphology including cleft palate and other anomalies that often require surgical intervention. Dysphagia can be seen in different developmental disorders including DiGeorge’s syndrome. As a symptom it may be present during infancy and may last with complications until the age of 4 years and sometimes onwards.

In our case, barium esophagogram showed esophageal sub stenosis due to vascular anomaly, aberrant right subclavian artery. And thymic hypoplasia or agenesis was suspected. The first report of symptomatic aberrant right subclavian artery was published in 1735, and in 1794 the term dysphagia lusoria was used to describe ARSA that has a retroesophageal course.

Association of left sided aortic arch with aberrant right sided aortic arch and ipsilateral patent ductus arteriosus in a patient with DiGeorge’s syndrome as seen in our patient was only described by Taliana et al.

Conclusion
We present a rare case of DiGeorge’s syndrome in a preterm infant with dysphagia due to aberrant right
subclavian artery. This was a case with a challenging diagnosis, in which classical manifestations of DiGeorge's syndrome was initially lacking. We report a 9-year follow up period by a team of subspecialists. The child had two surgeries due to aberrant vessel and velopharyngeal deficiency. Optimal management of patients with DiGeorge's syndrome requires a multidisciplinary team. The team should include a cardiologist, immunologist, geneticist, speech/language therapist, endocrinologist and other subspecialists depending on patient's phenotype, as reported in our case.

References


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