Case report

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 disfunction and immune deficiencies, hypocalcemia due tohypoparathyroidism,growth and developmental delay and speech disturbances. Cardiovascular anomalies might include right sided aortic arch, aberrant vesiclesand 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 arteryand suspectedthymic hypoplasia. We report a 9-year follow up periodbya 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 teamwhichshould include a cardiologist, immunologist, geneticist, speech/language therapist, endocrinologist and other subspecialists depending on patient`s phenotype.

Приказ на случај

ДИСФАГИЈА КАКО РАНА ПРЕЗЕНТАЦИЈА НА DIGEORGE СИНДРОМ - ПРИКАЗ НА СЛУЧАЈ

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Клучни зборови: Синдром на DiGeorge, дисфагија, аберантна артерија субклавија, новородено.

***Кореспонденција:** Наташа Алулоска, Универзитетска клиника за детски болести, Скопје, Република Северна Македонија. E-mail:aluloska@gmail.com.

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Печатарски права: ©2021 Снежана Палчевска, Бети Ѓуркова, Емилија Шукарова, Катарина Ставриќ, Јана Јовановска, Наташа Алулоска. Оваа статија е со отворен пристап дистрибуирана под условите на нелокализирана лиценца, која овозможува неограничена употреба, дистрибуција и репродукција на било кој медиум, доколку се цитираат оригиналниот(ите) автор(и) и изворот.

Конкурентски интереси: Авторот изјавува дека нема конкурентски интереси.

Извадок

DiGeorge Синдромот е резултат на делеција на 22q11.2 која води до пореметена ембриогенеза на фарингеалните лаци и се манифестира со различни знаци и симптоми. Спектарот на аномалии во овој синдром е варијабилен и може да се презентира само со минорна лицева дизморфија и расцеп на непцето но и со широк спектар на кардиоваскуларни аномалии, дисфункција на тимус и имун дефицит, хипокалцемија поради хипопаратироидизам, пореметување во растот и развојот и проблеми во говорот. Кардиоваскуларните аномалии може да се од типот на десен аортен лак, аберантни крвни садови и васкуларен ринг. Во овој приказ на случај прикажуваме атипичен случај на парцијален синдром на DiGeorge кој се презентираше со потешкотии во голтање и ларингеален стридор во неонаталниот период. Раната презентација на овој синдром во неонаталната возраст најчесто се дијагностицира со хипокалцемија и конгенитална кардиопатија. Потребна е добра клиничка проценка за да се разликува проблем при хранење на прематурно новородено од другите проблеми при голтање. Езофагограмот покажа коса импресија на антеро-постериорниот правец со ориентација кон десно суспектна за субстеноза на езофагусот на опишаното ниво од васкуларна етиологија, аберантна десна артерија субклавија и суспектна хипоплазија на тимус. Пациентот беше следен во период од 9 години од тим на субспецијалисти. Во тој период имаше две хируршки интервенции (корекција на аберантен крвен сад и велофарингеален дефицит). Пациентите со синдром на DiGeorge треба да бидат следени од мултидисциплинарен тим кој вклучува кардиолог, имунолог, генетичар, ендокринолог, логопед и други субспецијалисти според фенотипот на пациентот.

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

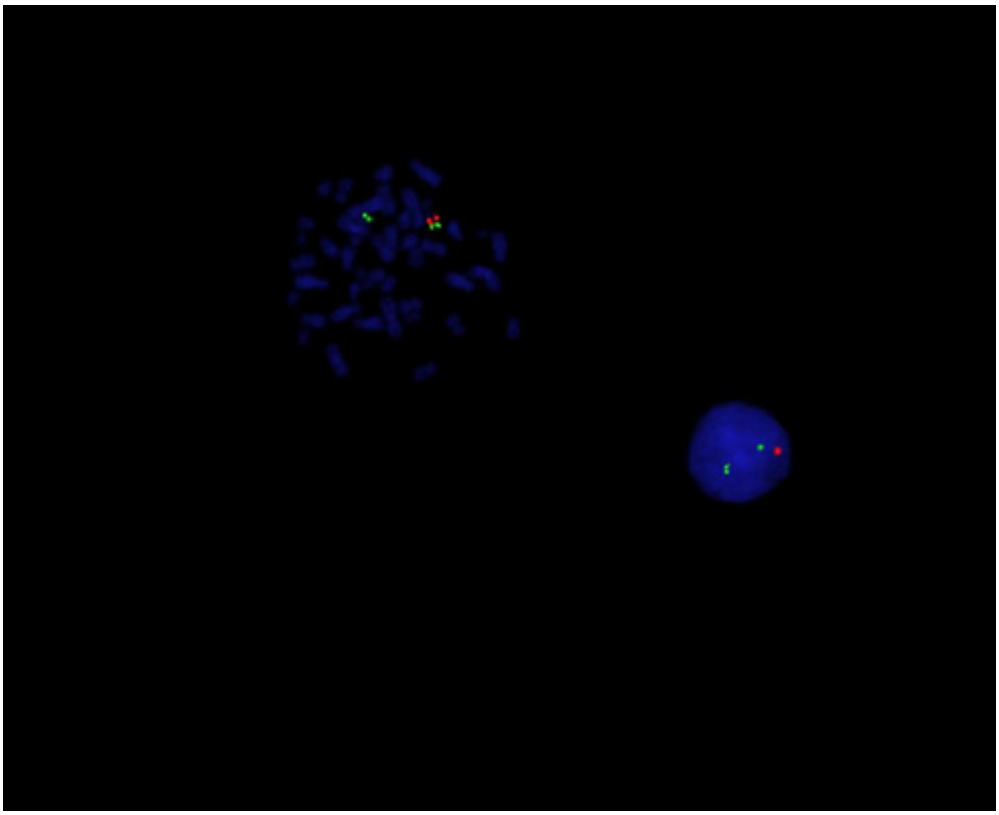

Figure 1. FISH result:46, XX, del(22)(q11.2) FISH probe-Cytocell TUPLE1, green signal-control (22q13.3); red signal-locus-specific -(22q11.2)

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 nasoendoscopy. 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 1959[1,2,3,4]. Additional anomalies were noted to be associated with the syndrome, especially anomalies of the great vessels, esophageal atresia, heart, ear, nose and mouth

defects[5]. For the first time the cause of the syndrome was suspected to be a deletion in chromosome 22q11 in 1981[6]. This is a 35 mb chromosomal region that contains more than 35 genes that affect the morphogenesis of the pharyngeal arches, heart and brain[7,8,9,10].

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[11]. Typical presentation during infancy usually includes some of the following features: facial dysmorphia, heart defect, hypocalcemia, palatalanomalies and immunodeficiency[12]. 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 orhypocalcemicseizures[13].

This syndrome is rarely diagnosed in the neonatal period. Early presentation in this period is usually due to severe hypocalcemia and cardiac disease[14].

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[15,16].

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[7, 17,18]. Dysphagia can be seen in different developmental disorders including DiGeorge'ssyndrome19. 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 agenesia 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[20,21].

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[22].

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.

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