Case Report

Double outlet right ventricle and aortopulmonary window in a neonate with Bohring-Opitz (Oberklaid-Danks) syndrome: First case report

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Abstract

Bohring-Opitz syndrome (BOS) is a rare, sporadic genetic disorder, characterized by feeding difficulties, developmental delay, flexion abnormalities, dysmorphic facial features and typical body posture (BOS posture). This syndrome is diagnosed on the basis of distinctive clinical features with or without confirmation by genetic studies. Cardiac abnormalities are seen in almost half of the patients, but are nonspecific. We present a case of a 3-week-old male baby with BOS who was referred to our hospital with congestive heart failure, seizures and failure to thrive. He was diagnosed to have double outlet right ventricle and aortopulmonary window (DORV and APW). To our knowledge, this is the first case of Bohring-Opitz Syndrome ever reported with such clinical presentation.

Keywords: Cardiac abnormalities, congenital heart disease, dysmorphism, flexion abnormalities, trigonocephaly

Introduction

Bohring-Opitz Syndrome (also known as Oberklaid-Danks syndrome), is a sporadic, rare genetic disorder.[1,2] Bohring-Opitz syndrome (BOS) is characterized by growth failure, intellectual disability, variable congenital anomalies, distinctive facial features, and typical posture (BOS posture).[3] This syndrome is diagnosed on the basis of distinctive clinical features with or without confirmation by genetic studies. Almost 50% of cases have de novo mutations in the ASXL1 gene.[1,4] BOS is associated with a high infant mortality rate (40%) mostly due to infections, cardiac arrhythmias and apnea.[3] Cardiac abnormalities are seen in up to 50% of the patients, but are non-specific.[3]

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Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_74_19

Double outlet right ventricle (DORV) associated with aortopulmonary window (APW) is a very rare congenital heart anomaly. Children with DORV and APW usually die due to heart failure and pulmonary hypertension.[5] We present a case of neonate who was referred to our centre with congestive heart failure, seizures and failure to thrive. He had typical features of Bohring-Opitz syndrome associated with double outlet right ventricle and aortopulmonary window. To our knowledge this is first case report of combination of these two very rare disorders.

Case Report

The male baby in this case was born by caesarean section at a different hospital to 24-years- old primigravida at 33 weeks of gestation with a birth weight of 1.6 Kg. The parents were

How to cite this article: Verma B, Abhinay A, Singh A, Kumar M. Double outlet right ventricle and aortopulmonary window in a neonate with Bohring-Opitz (Oberklaid-Danks) syndrome: First case report. J Family Med Prim Care 2019;8:1279-81.

non-consanguineous and there was no significant family history. He did not cry at birth but otherwise seemed to be well except for some "different" facial appearance, as reported by parents. Subsequently, beyond one week of life he started developing respiratory distress, irritability, vomiting, profuse sweating, poor activity, and severe feeding difficulties. Moreover, he had suffered three episodes of generalised seizures. With these complaints he was admitted to our neonatal intensive care unit at 3 weeks of life.

On examination he had jaundice, massive hepatomegaly, signs of poor perfusion and congestive heart failure and failure to thrive. He had striking features of dysmorphism including microcephaly, trigonocephaly, widely set eyes, broad eyebrow, hypertrichosis, low anterior temporal hairline, small mouth, flat and wide nasal bridge, anteverted nares, high arched palate, low set posteriorly rotated ears, prominent and broad antihelix, and deep transverse palmar creases. He had a typical posture (BOS posture) with shoulders externally rotated and adducted, wrists flexed in ulnar deviation, and ulnar deviation of the metacarpophalangeal joints. There was truncal hypotonia with hypertonia of the extremities. The distinctive features are described in [Figure 1].

The echocardiography was done which showed double outlet right ventricle, with pulmonary artery and most of aorta seen arising from right ventricle. There was a large non-restrictive subaortic ventricular septal defect without pulmonary stenosis. Aortomitral continuity was lost. Additionally, he had proximal type of aortopulmonary window, 1.4 cm in size (Type I APW) [Figure 2]. Management on the lines of congestive heart failure was started with explanation of need for corrective surgery. However, the baby died on fifth day of life due to severe congestive heart failure.

Discussion

Bohring-Opitz syndrome (BOS) is characterized by failure to thrive, feeding difficulties, seizures, severe/profound developmental delay, susceptibility to infections, Wilms tumor, nonspecific brain abnormalities, distinctive facial features and BOS posture.[6,7] The distinctive facial features include microcephaly and/or trigonocephaly, nevus flammeus, prominent eyes with high myopia, widely spaced eyes (hypertelorism), upslanting palpebral fissures, flat and wide nasal bridge, anteverted nares, small mouth, palatal anomalies including cleft palate and high arched palate, retrognathia, low-set posteriorly rotated ears, a low anterior/temporal or posterior hairline, and hypertrichosis.[3,4,6-8] The BOS posture is characterized by flexion at the elbows, ulnar deviation, flexion of the wrists and metacarpophalangeal joints and hypertonic extremities with central hypotonia.[3] Currently, the diagnosis of Bohring-Opitz syndrome (BOS) is established in a proband with suggestive clinical features and/or the identification of a constitutional heterozygous pathogenic variant in ASXL1 by molecular genetic testing.[8] Accordingly, the diagnosis in our case was made based of typical clinical features, distinctive facial abnormalities and characteristic BOS posture.

Bohring-Opitz syndrome is a rare, sporadic genetic condition. Literature review till the time of writing revealed 68 cases reported worldwide. Approximately 50% of BOS cases have been attributed to de-novo truncating mutations in the ASXL1 gene.[1,4] BOS is associated with a high rate of infant mortality (40%) and the causes of death include respiratory infections and sepsis (40% of total), cardiovascular/apnoea/bradycardia (33% of total), seizures, severe feeding difficulties and tumours.[7] Our patient presented with congestive heart failure, seizures, feeding difficulties and failure to thrive.

Systemic manifestations have also been described, including neurological, orthopaedic, ophthalmologic, gastrointestinal, and cardiac anomalies. Cardiac abnormalities are seen in almost half of the patients, but are nonspecific. The reported cardiac defects include atrial septal defect, patent ductus arteriosus, ventricular septal defect, patent foramen ovale, septal hypertrophy, biventricular hypertrophy, pulmonary hypertension and valvular abnormalities (most commonly pulmonary stenosis).[3,7,8] Hence, cardiac evaluation by echocardiography is indicated in all such patients. We have

Figure 1: Typical posture (BOS posture) with shoulders externally rotated and adducted, wrists flexed in ulnar deviation, and ulnar deviation of the metacarpophalangeal joints. Additionally, there is truncal hypotonia with hypertonia of the extremities. Also note the generalised hypertrichosis, microcephaly, trigonocephaly, widely set eyes (hypertelorism), flat and wide nasal bridge and small mouth

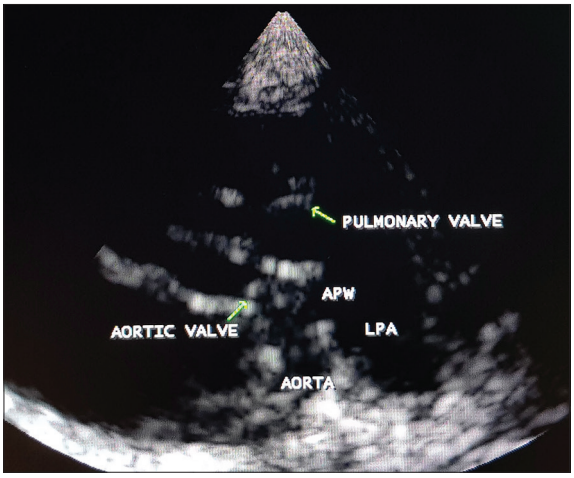

Figure 2: Aortopulmonary window (APW) along with double outlet right ventricle

reported presence of DORV and APW in such a patient. To best of our knowledge, this first case report of this association. Previously, combined presence of APW and DORV has been reported with maternal phenylketonuria and Cornelia de Lange syndrome.[5]

The closest differential to our case is Cornelia de Lange syndrome which also has prenatal and postnatal growth restriction, microcephaly, hypertrichosis and has been reported to be associated with double outlet right ventricle and aortopulmonary window.[9] However, this was easily excluded based on typical cranio-facial abnormalities and characteristic BOS posture in the current case. Recently successful surgical correction of DORV and APW in a neonate has been reported.[10] The neonate in this case too was advised corrective surgery after stabilisation, but had to be discharged against medical advice.

Conclusion

BOS is a rare disorder, and its diagnosis is mainly based on the phenotypic characters. A high degree of clinical suspicion is therefore required. The echocardiographic evaluation is indicated in all patients considering high prevalence of cardiac defects. The presence of complex cardiac anomalies like in this case carries dismal prognosis and would require an urgent multidisciplinary approach.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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