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Case Report

Bohring opitz syndrome: a rare case report

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ABSTRACT

Bohring- Opitz syndrome (BOS) first described by Bohring et al in 1999, is a rare congenital disorder of unknown etiology. He described 4 cases with characteristic features. This syndrome is characterized by distinctive facial features and posture, growth failure, variable intellectual disability, and variable anomalies. The diagnosis of BOS is established in a proband with suggestive clinical features and/or Identification of constitutional heterozygous pathogenic variant in ASXL1 by molecular genetic testing. We presented a case which phenotypically and genetically matches the findings of this syndrome.

Keywords: Bohring opitz syndrome, ASXL1, BOS posture, Glabellar nevus sim

INTRODUCTION

Bohring-opitz syndrome is a sporadic, rare genetic disorder with an unknown etiology.[1] Cardinal symptoms include feeding difficulties, Intrauterine growth retardation, microcephaly, trigonocephaly, micro/retrognathia, flammeus nevus, prominent eyes, cleft palate, and BOS posture (posture with shoulders externally rotated and adducted, elbows and wrists flexed in ulnar deviation, and ulnar deviation of the metacarpophalangeal joints).[2] The disease is often fatal in early childhood, due to obstructive apnea and unexplained bradycardia.

CASE REPORT

A female neonate delivered at our hospital Presented with complaints of respiratory distress at birth. She was full term, birth weight 2.380kg, small for gestational age, born to a 23 year old primi gravida mother, non-consanguineous marriage delivered via lower segment caesarean section. She had history of delayed cry at birth. On admission vitals: temperature 37.4°C, respiratory rate 68/min, pulse rate 146/min, CRT <3 sec, SPO2 97% with oxygen. On general examinations, there had phenotypically abnormal features which include hypertrichosis, depressed nasal bridge with anteverted nares, glabellar nevus simplex, long philtrum, cleft palate, low set ear, overriding fingers, low frontal and temporal hair line, prominent eyes, hypertelorism, club foot.

We gave oxygen via nasal prong, IV fluid and manage symptomatically. We started gavage feeding on day 3. Investigation findings were (a) X-ray pelvis with both hips and lower extremities revealed acetabulum is incompletely formed; acute angle seen between tibia and forefoot suggestive of bilateral clubfoot; (b) USG small part (hip) revealed abnormal position of bilateral femoral head is noted and acetabulum appears dysplastic. Alpha angle measure 41 degree on right side and 45 degree on left side suggestive of bilateral DDH; (c) USG whole abdomen revealed lower poles of both kidneys are fused at mid line suggest horseshoe kidney, (d) MRI brain findings revealed subtle focal abnormal areas of restricted water diffusion are noted involving the bilateral centrum semiovale, posterior limb of internal capsule and midline vermis appearing hyper intense on DW and low on ADC map, suggesting area of cytotoxic edema. Underlying sequelae of hypoxic ischemic injury is of concern; and (e) genetic

analysis showed ASXL1 genetic mutation. Baby's vitals were stable on day 5, wean off oxygen and shifted on spoon feeding. She was discharged successfully on day 12.

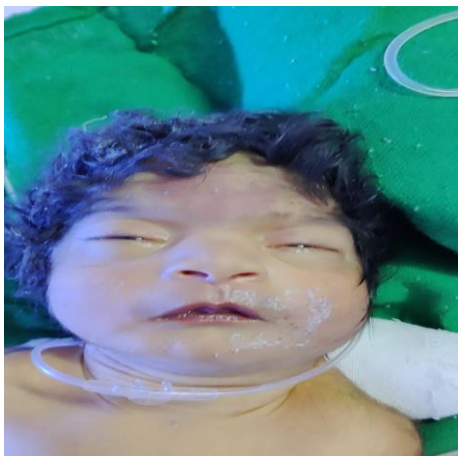

Figure 1: Glabellar nevus simplex, long philtrum, excessive hair growth.

Figure 2: 'BOS posture', which consists of the external rotation and/or adduction of shoulders, with flexion at the elbows and wrists and ulnar deviation of the wrists and/or fingers at the level of the metacarpophalangeal (MCP) joint and club foot.

DISCUSSION

BOS has a 40% infant mortality rate and many patients die before 5 years of age.[2] Mortality is usually due to recurrent infections, bradycardia or respiratory distress/failure.[2,3] Hasting et al proposed a set of diagnostic criteria in which 7 out of 10 features must be present: typical facial appearance (trigonocephaly/prominent metopic ridge, retrognathia, prominent eyes with hypoplastic supraorbital ridges, up-slanting palpebral fissure, depressed nasal bridge, anteverted nares, low-set and posteriorly rotated ears, palatal abnormalities and broad alveolar ridges, flammeus nevus, low anterior hairline), microcephaly, IUGR and short stature, joint abnormalities, abnormal tone, severe/profound developmental delay, susceptibility to infections, feeding difficulties and high infant mortality.[2] Other characteristics described in other reports include hirsutism, exophthalmos, and low frontal and temporal hairline. Systemic manifestations have also been described, including gastrointestinal, ophthalmologic, cerebral and cardiac anomalies. Of the latter, the cardiac defects specifically described in the literature include: pulmonary hypertension, biventricular hypertrophy, patent ductus arteriosus (PDA), patent foramen ovale (PFO), dysplastic pulmonary valve with mild stenosis, atrial septal defect (ASD) and perimembranous ventricular septal defect (VSD).[2-5] Given the small number of reported cases of BOS, it is difficult to establish the significance of other abnormalities as unique to BOS or as manifestations of concomitant conditions. The mechanism and inheritance pattern of BOS remain unclear, however de novo heterozygous frame shift or nonsense mutations in ASXL1 gene have been identified in ten of cases of BOS by different authors.[3,6,7] The ASXL1 gene has been associated with both activation and silencing of HOX genes, which are involved in body segment formation, chromatin remodeling, as well as having oncogene properties.[8,9] Interestingly, not all patients with BOS have abnormalities in their ASXL1 gene, suggesting the possibility of multiple etiologies.[2,3] Mutations of the ASXL3 gene, which is part of the same gene family as ASXL1, have been described in five distinct cases.[10,11] While these patients had similar characteristics as those found in patients with BOS, they did not fully exhibit the specific characteristics defined for BOS.[4] Treatment of BOS is supportive and often includes a gastrostomy tube (G-tube) for feedings and mechanical ventilation in the neonatal period. As patients survive through early childhood, problems such as feeding difficulties and recurrent infections become less significant. Despite early intervention, profound intellectual delay tends to persist, although there is case by case variability in severity.[2] Children who survive into their teenage years and adulthood still face significant morbidity despite decreased mortality.

CONCLUSION

Next generation chromosomal analysis technology and sharing evidence based knowledge on the condition will

enable clinicians to overcome the diagnostic challenge of Bohring-Opitz syndrome and offer expert therapy to patients.

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REFERENCES

1. Bohring A, Silengo M, Lerone M, Superneau DW, Spaich C, Braddock SR, et al. Severe end of Opitz trigonocephaly (C) syndrome or new syndrome? Am J Med Genet. 1999;85(5):438-46.
2. Hastings R, Cobben JM, Gillessen-Kaesbach G, Goodship J, Hove H, Kjaergaard S, et al. Bohring-Opitz (Oberklaid-Danks) syndrome: clinical study, review of the literature, and discussion of possible pathogenesis. Eur J Hum Genet. 2011;19(5):513-9.
3. Hoischen A, Bon BW, Rodríguez-Santiago B, Gilissen C, Vissers LE, Vries P, et al. De novo nonsense mutations in ASXL1 cause Bohring-Opitz syndrome. Nat Genet. 2011;43(8):729-31.
4. Russell B, Johnston JJ, Biesecker LG, Kramer N, Pickart A, Rhead W, et al. Clinical management of patients with ASXL1 mutations and Bohring-Opitz syndrome, emphasizing the need for Wilms tumor surveillance. Am J Med Genet A. 2015;167A(9):2122-31.
5. Bohring A, Oudesluijs GG, Grange DK, Zampino G, Thierry P. New cases of Bohring-Opitz syndrome, update, and critical review of the literature. Am J Med Genet A. 2006;140(12):1257-63.
6. Dangiolo SB, Wilson A, Jobanputra V, Anyane-Yeboa K. Bohring-Opitz syndrome (BOS) with a new ASXL1 pathogenic variant: Review of the most prevalent molecular and phenotypic features of the syndrome. Am J Med Genet A. 2015;167A(12):3161-6.
7. Magini P, Della Monica M, Uzielli ML, Mongelli P, Scarselli G, Gambineri E, et al. Two novel patients with Bohring-Opitz syndrome caused by de novo ASXL1 mutations. Am J Med Genet A. 2012;158A(4):917-21.
8. Avila M, Kirchhoff M, Marle N, Hove HD, Chouchane M, Thauvin-Robinet C, et al. Delineation of a new chromosome 20q11.2 duplication syndrome including the ASXL1 gene. Am J Med Genet A. 2013;161A(7):1594-8.
9. Guo YB, Shao YM, Chen J, Xu SB, Zhang XD, Wang MR, et al. Effect of overexpression of HOX genes on its invasive tendency in cerebral glioma. Oncol Lett. 2016;11(1):75-80.
10. Dinwiddie DL, Soden SE, Saunders CJ, Miller NA, Farrow EG, Smith LD, et al. De novo frameshift mutation in ASXL3 in a patient with global developmental delay, microcephaly, and craniofacial anomalies. BMC Med Genomics. 2013;6:32.
11. Dinwiddie DL, Soden SE, Saunders CJ, Miller NA, Farrow EG, Smith LD, et al. De novo frameshift mutation in ASXL3 in a patient with global developmental delay, microcephaly, and craniofacial anomalies. BMC Med Genomics. 2013;6:32.

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