

Case Report

Siblings with Imperforate anus and aplastic nasal alae: Johanson-Blizzard syndrome

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Received: 09 June 2021

Accepted: 07 July 2021

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ABSTRACT

Johanson-Blizzard syndrome is a rare genetic entity reported in medical literature resulting from mutations in UBR1 gene, affecting pancreas, craniofacial and urogenital development, causing significant morbidity and mortality. We report a neonate presenting with anorectal malformation requiring surgical intervention at birth, with similar surgeries being performed in two elder siblings. Surviving sibling of the proband neonate also has similar dysmorphic features of absent ala nasi, aplasia cutis of scalp along with pancreatic insufficiency, profound sensorineural hearing loss, phenotype corresponding to Johanson-Blizzard syndrome. Syndromic diagnosis helps in screening for associated potential issues, which can intervene at early stages.

Keywords: Johanson-Blizzard syndrome, Imperforate anus, Aplasia ala nasi, Aplasia cutis of scalp, Pancreatic insufficiency, Sensorineural hearing loss

INTRODUCTION

Johanson-Blizzard syndrome (JBS) is a multisystem congenital disorder, a form of ectodermal dysplasia, featuring abnormal development of pancreas, nose, scalp with mental retardation, hearing loss and growth failure.^{1,2} Incidence is estimated to be 1 in 250000 live births, with around 60 cases described in medical literature. This case report highlights the autosomal recessive inheritance of the disease affecting several family members with variable phenotypic presentation.³

CASE REPORT

A 2 kg term male neonate was born to a third degree consanguineously married couple with multiple congenital malformations - imperforate anus, hypoplastic ala nasi, aplasia cutis of scalp, enlarged fontanelles with midfacial hypoplasia, evident at birth. (Figure) Baby was extracted via caesarean section in view of previous operative

deliveries and severe preeclampsia in the mother. Baby was the fifth born child to the couple. The mother also has similar hypoplastic ala nasi, while other dysmorphic features were not prominent in her.

Mother has had a bad obstetric history. The first born girl child to the mother, delivered prematurely with birth weight of 1.9 kg, is thriving well with no dysmorphism. The second born child, delivered via operative delivery in view of mal-position at labour, also had imperforate anus, underwent colostomy at birth, but succumbed at 3 months age. Third pregnancy unfortunately resulted in intrauterine death at 8 months of gestation, secondary to placental abruption. The fourth child, male, has similar features of the proband newborn, is presently 5 years old. He had anorectal malformation and underwent colostomy in early neonatal period, followed by posterior sagittal anorectoplasty at 8 months age. The child also has similar absent ala nasi with beaked nose, aplasia cutis of scalp with spiky hair, high arched palate along with maldeveloped

dentition, mid face hypoplasia, hypoplastic nipples, prominent forwardly placed ears with short stature, moderate intellectual disability and poor performance in

academics. 2D-ECHO is normal. Child has severe profound bilateral sensorineural hearing loss, confirmed by BERA.



Figure 1-5: Proband neonate with absent ala nasi, beaked nose, midfacial hypoplasia, aplasia cutis of scalp and imperforate anus. Figure 6-9: Elder sibling with spiky hair, midfacial hypoplasia, hypoplastic ala nasi, forwardly placed ears, maldentition, aplasia cutis of scalp and anorectal malformation postoperative scar.

His thyroid hormone levels are within normal limits. Child has low levels of serum amylase and lipase, and is on supplements for pancreatic insufficiency, with presently normal glycaemic levels.

The proband neonate underwent colostomy and is under follow-up. Baby is gaining weight and is thriving well. Ultra-sound abdomen did not reveal any other abnormalities, 2D-ECHO was normal, while BERA done was suggestive of sensorineural hearing loss, similar to his elder sibling. The baby is enrolled for early stimulation and speech therapy, is posted for curative surgery by the end of first year of life. The phenotypes of the children, along with their mother, with the background of consanguinity, corresponds to autosomally inherited Johanson-Blizzard syndrome and needs con-firmation by gene sequencing techniques.

DISCUSSION

JBS phenotype was first described by Johnson and Blizzard in 1971 in 3 girls with aplasia nasal alae, congenital deafness, growth retardation, malabsorption, mental retardation and ectodermal scalp defects and hence the eponym.⁴ Urogenital abnormalities like double uterus and vagina were described by Park et al.⁵ Review by Hurst and Baraister, indicated 11 of 12 children with JBS had anorectal malformations, similar to the presentation in our case.⁶

Zenker et al identified that JBS results from deleterious mutation in Ubiquitin-Protein Ligase E3 Component N-Recognin gene (UBR1) in 15q15.2 chromosomal locus, encoding for ubiquity ligase enzyme involved in protein degradation pathways.⁷ The mutation leads congenital and progressive inflammatory damage, fatty tissue replacement and errors in inner action of acini and islets, resulting in failure of apoptotic destruction of damaged cells, predominantly in pancreas, also in craniofacial area, dentition, musculoskeletal and nervous systems.

Pancreatic exocrine insufficiency is most commonly noted in these individuals presently with fat malabsorption, while endocrine insufficiency resulting in diabetes mellitus with insulin resistance, though rare, is seen in late childhood. Associated endocrine abnormalities in the form of hypothyroidism, growth hormone deficiency and hypopituitarism are also noted.⁸

Hypoplasia of nasal alae resulting in beaked nose is the most apparently noticed malformation along with craniofacial abnormalities affecting scalp, head, face and teeth. Microcephaly, ectodermal midline scalp defects with oddly patterned hair, aplasia cutis of scalp, enlarged fontanelle, nasolacrimocutaneous fistula, micrognathia and maldeveloped dentition designate JBS.^{3,9} Imperforate anus, Neonatal cholestasis, dilated cardiomyopathy, ventricular septal defects, congenital cataracts and cafe-au-lait spots are additional anomalies noted.^{2,10}

As there is no specific cure to JBS, symptomatic management forms the mainstay of treatment with pancreatic enzyme replacement therapy for enzyme insufficiency, hormonal replacement, nutritional therapy with protein hydrolysate diet, surgical corrections of craniofacial and anogenital anomalies, hearing aids for sensorineural hearing loss, special education and occupational therapy for intellectual disability. Multidisciplinary coordinated efforts of paediatricians, surgeons, dentists, endocrinologists, gastroenterologist, cardiologists, speech and occupational therapists greatly benefit the affected individuals.²

CONCLUSION

Anorectal malformations when identified, usually have syndromic associations which need to be actively searched for in the neonate. Hypoplastic ala nasi and aplasia cutis of scalp along with anorectal malformations are characteristic features of Johanson Blizard Syndrome. Pancreatic insufficiency, sensorineural hearing loss and intellectual disability add to the morbidity of the disease and multidisciplinary coordinated efforts are necessary for disease amelioration.

ACKNOWLEDGEMENTS

We would like to thank our colleague, Dr. Harshitha M Swamy for helping us compile the case report. We would like to thank our Paediatric Surgery colleagues for their timely surgical intervention in the child.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Nagarasaiah AH, Gubbari CS, Govindarajan V, Reddy C. Siblings with Imperforate anus and aplastic nasal alae: Johanson-Blizzard syndrome. Int J Contemp Pediatr 2021;8:1439-41.