

Johanson-Blizzard Syndrome with Short Stature

Khorasani EN¹, Mansouri F²

Abstract

Johanson-Blizzard syndrome (JBS) is a rare, sometimes fatal autosomal recessive multisystem congenital disorder featuring abnormal development of the pancreas, nose and scalp, with mental retardation, hearing loss and growth failure. It is sometimes described as a form of ectodermal dysplasia. The disorder is especially noted for causing profound developmental errors and exocrine dysfunction of the pancreas, and it is considered to be an inherited pancreatic disease. We report a ten years Iranian child with signs and symptoms suggestive of this syndrome (JBS).

Key words: Johanson-Blizzard, short stature, pancreas insufficiency, Hypothyroidism

Introduction

Johanson-Blizzard syndrome is a rare genetic disorder that characteristic with multisystem involvement particularly: Ectodermal defects, endocrine disorder, pancreatic insufficiency and other disorders. It was named after Ann J Johanson and Robert M Blizzard. The paediatricians who first described the disorder in a 1971^{1,2,3}.

The Case

We introduce a ten years old Iranian boy, product of a non consanguineous marriage, who was referred to us for short stature. His anthropometry were: weight(24 kg), height(130 cm) and head circumference(51cm). According to the natal history he was IUGR at birth and was admitted to NICU because of respiratory distress. Physical examination revealed cleft palate, On auscultation of heart a holosystolic murmur (3/6) was heard at the lower left sternal border. According to the echocardiography he had VSD, and further investigation showed hypothyroidism. (TSH:12.5 IU/ml) and on examination had hypospadias and cryptorchidism noticed since seven years of age. He had constipation from birth and continued till recently despite the use of laxative drugs.

Further investigations after now (malabsorption tests, sweat test, bone age) and a careful examination; we found that he has pancreatic insufficiency and sensory neural hearing loss along

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with visual problems (cornea impairment). He was treated by pancreatic enzymes (lipase:500IU/Kg up to a maximum of 50000IU/day), levothyroxine (50µg/day) and vitamins (VitA:5000IU/day, VitD: 400IU/day and Vit E: 1000IU/day), other supplements (Zinc:20mg/kg/day, Iron:3mg/kg/day, Calcium:1500mg/kg/day) and acid folic (1mg/daily). His cleft palate and hypospadias had been repaired by previous surgery. After follow up for one year of treatment his growth had improved (Wt;29kg, Ht:135cm, HC:54cm) and had no constipation.

Discussion

The most prominent effect of JBS is pancreatic exocrine insufficiency^{1,4,5,6,7}. Varying degrees of decreased secretion of lipases, pancreatic juices such as trypsin, trypsinogen and others, as well



Fig 1: Showing facies of the patient (craniofacial anomalia) permission taken

as malabsorption of fats and disruptions of glucagon secretion and its response to hypoglycemia caused by insulin activity are major concerns when JBS is diagnosed^{1,3,8}. Pancreatic exocrine insufficiency in JBS can additionally stem from congenital replacement of the acini with fatty tissue^{1,3,8,9}. Near total replacement of the entire pancreas with fatty tissue has also been reported. This is a progressive, sometimes fatal consequence of the disorder⁹.

Endocrine insufficiency of the pancreas occurs with JBS, though it is sometimes less common and less pronounced than the more prominent effects on exocrine function¹. Endocrine dysfunction of the pancreas often results in diabetes mellitus. Both insulin resistance and diabetes have been observed with JBS, and it is suggested that diabetes should be considered as a complication of JBS and its course^{5,7,8}.

Endocrine abnormalities in other areas have also been present with the disorder. These include hypothyroidism², growth hormone deficiency^{1,8} and hypopituitarism. Growth failure and associated short stature (dwarfism) in JBS can be attributed to growth hormone deficiency caused by diminished anterior pituitary function, with malabsorption of fats playing a subsequent role^{1,4}.

Other abnormalities, affecting the scalp, head, face, jaw and teeth may be found with JBS. These include: ectodermal mid-line scalp defects with sparse, oddly-patterned hair growth^{2,9}; aplasia cutis (underdeveloped, very thin skin) over the head, an enlarged fontanelle (“soft spot” on the head of young infants), microcephaly (undersized skull), prominent forehead, absence of eyebrows and eyelashes, mongoloidal eye shape, nasolacrimo-cutaneous fistulae (this refers to the formation of an abnormal secondary passageway from either the tear duct or lacrimal sac to the facial skin surface, possibly discharging fluid)⁹,

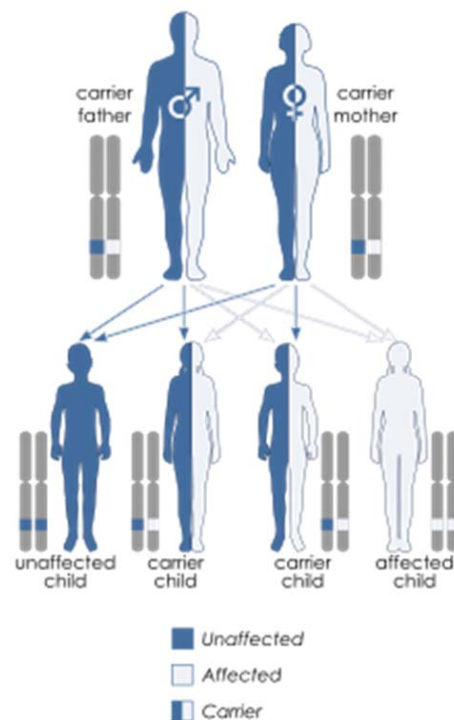
flattened ears, micrognathism of the maxilla and mandible (underdevelopment of the upper and lower jaw, respectively), with the maxilla more prominently affected in some cases; congenital clefting of bones surrounding the optical orbit (eye socket), such as the frontal and lacrimal bone⁸; and maldeveloped deciduous teeth (“baby teeth”), with an absence of permanent teeth⁹.

Findings with the inner ear in JBS give explanation to the presence of bilateral sensorineural hearing loss in most patients affected by the disorder. The formation of cystic tissue in both the cochlea and vestibule, with resulting dilation and malformation of these delicate structures has been implicated^{7,9}. Congenital deformations of the temporal bone and associated adverse anatomical effects on innervation and development of the inner ear also contribute to this type of hearing loss⁸.

Additional congenital anomalies, effects on other organs, and less common features of JBS have included: imperforate anus⁴, vesicoureteral reflux; duplex of the uterus and vagina in female infants, neonatal cholestasis of the liver, with cirrhosis and portal hypertension⁷; dilated cardiomyopathy^{7,8}, dextrocardia¹, atrial and ventricular septal defect¹; low birth-weight⁷, failure to thrive; hypotonia⁸; sacral hiatus (a structural deficiency of the sacral vertebrae), congenital cataracts⁹, and cafe-au-lait spots².

Genetics

Autosomal recessive inheritance



Johanson-Blizzard syndrome has an autosomal recessive pattern of inheritance¹.

Johanson-Blizzard syndrome is caused by mutations in the *UBR1* gene, which encodes one of several *ubiquitin ligase* enzymes of the N-end rule pathway^{1,6}.

The *UBR1* gene is located on human chromosome 15⁶.

Treatment

While there is no cure for JBS, treatment and management of specific symptoms and features of the disorder are applied and can often be successful. Variability in the severity of JBS on a case-by-case basis determines the requirements and effectiveness of any treatment selected.

Pancreatic insufficiency and malabsorption can be managed with pancreatic enzyme replacement therapy, such as pancrelipase supplementation and other related methods^{1,2,3}.

Craniofacial and skeletal deformities may require surgical correction, using techniques including bone grafts and osteotomy procedures. Sensorineural hearing loss can be managed with the use of hearing aids and educational services designated for the hearing impaired^{7,8,9}.

Special education, specialized counseling methods and occupational therapy designed for those with mental retardation have proven to be effective, for both the patient and their families. This, too, is carefully considered for JBS patients^{4,5}.

Conclusion

This case highlights the importance of a careful and thorough physical examination in a neonate especially in SGA and IUGR, and if any congenital anomalies are found then to follow up at a later age and investigate further; in this case short stature, cranio-facial anomalies, malabsorption, malabsorption and bone age.

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