INTRODUCTION

Johanson-Blizzard syndrome (JBS) was named after AJ Johanson and RM Blizzard, who first described the disorder in 1971. It is a rare autosomal recessive multisystem disorder; important characteristic features being exocrine pancreatic insufficiency, small beak like nose, long and narrow upper lip, small pointed chin, sparse coarse up-sweep hair, sensori-neural hearing loss, hypothyroidism, congenital heart defects, varying degree of mental retardation, growth failure, and café-au-lait spots. The majority of the reported cases include children with significant pancreatic insufficiency, markedly abnormal facial features and moderate to severe mental retardation. Other related anomalies with characteristic facial appearance are short stature in more than 80%, hypothyroidism in 40%, sensorineural hearing loss in more than 80%, mental retardation in 77%, imperforate anus in 39% and genitourinary abnormalities in 38%. Growth hormone deficiency, hypopituitarism and impaired glucagon secretion response to insulin induced hypoglycemia has been reported.

In 2005, disease associated locus in individual with this syndrome was mapped to chromosome 15q15-21 with identified mutations in gene UBR1 encoding a ubiquitin ligase of the N-end rule pathway. In the pancreas, there is selective defect of acinar cells, whereas the islets of Langerhans and ducts are preserved. Apart from trypsinogen deficiency Diabetes has been reported in older children, suggesting the progressive nature of pancreatic disease.

This report describes a new association with JBS namely Diamond-Blackfan anemia, which has not been reported in literature previously.

CASE REPORT

We report a sporadic case of JBS in a 3 months male infant diagnosed at Children Hospital and the Institute of Child's Health, Lahore. The diagnosis was based on typical clinical features, pancreatic insufficiency, hypothyroidism, atrial septal defect, and Diamond-Blackfan anemia (congenital pure red cell aplasia). The patient was hospitalized with history of five to eight large, bulky, loose stools per day since birth, progressive pallor for last one month and he was not thriving well. He was born at term to non-consanguineous parents with birth weight of 2.90 kg and was breastfed initially, then at the age of 2 months shifted to formula feeding. His weight and height at the time of admission were 3.5 kg and 53 cm respectively (both were below 3rd percentile). There was no significant family history. His general physical examination was remarkable for aplastic alae nasi giving beak-like appearance to his nose, upsweep frontal hair with midline scalp hair defect, umbilical hernia, protuberant tongue, low set ears, triangular upper lip with flat philtrum (Figure 1), micrognathia and multiple café-au-lait spots predominantly distributed over the trunk, lower limbs and genitalia, 12 in numbers, varying in size from 4-3 cm (Figure 2).

His initial laboratory evaluation showed haemoglobin (Hb) of 3.2 gm%, haematocrit (Hct) of 9.6%, reticulocytes of 0.2%, total red cell count of 0.8 million/mm³, mean corpuscular volume (MCV) of 106 fl, mean corpuscular haemoglobin (MCH) of 30.6 gm, mean corpuscular...
Haemoglobin concentration (MCHC) of 33% and red cell distribution width of 18.5%. Total white cell count was 5200/mm³, with 59% polymorphs, 33% lymphocytes, 5% monocytes and 3% eosinophils. Platelets count was 343,000 /mm³, and blood peripheral morphology was unremarkable. Bone marrow aspiration revealed erythroid hypoplasia with normal myeloid and megakaryocytes series. A diagnosis of primary red cell aplasia was made, (Diamond-Blackfan anemia). His serum T₃ and T₄ levels were 35 ng/dl (normal range 70-200) and 1.90 ug/dl (normal range 0.3-6.0) respectively while TSH level was 12 u IU/ml (normal range 0.3-6.0). Serum amylase was less than 30 u/l (normal range 30-100) and serum lipase 8 u/l (normal range 3-32 u/l). Total serum albumin was 4.0 gm/dl (normal range 4.9-7.4). Blood sugar was normal.

His echocardiography result revealed atrial septal defect. CT scan of abdomen was unremarkable and on audiometry, there was no evidence of sensorineural deafness. Serum folic acid, B₁₂ and erythrocyte adenosine deaminase (ADA) level could not be performed because of non-availability of the facility. Based on presumed diagnosis of pancreatic insufficiency, he was given pancreatic enzyme replacement and fat soluble vitamins supplements. After confirmation of Diamond-Blackfan anemia, corticosteroids were given, at the dose of 2 mg/kg/day in divided doses which he tolerated well. A repeat bone marrow aspiration was done after one month of starting steroids that showed normal cellularity.

**DISCUSSION**

JBS is a rare autosomal recessive multisystem disorder and primary and the most prominent feature is exocrine pancreatic insufficiency. Pancreatic hypoplasia resulting in exocrine insufficiency and malabsorption is thought to be responsible for growth failure. Since the initial description of JBS in 1971, more than 60 cases have been reported. Endocrine dysfunction of the pancreas has been observed in JBS and it is suggested that Diabetes should be considered as a complications of JBS.\(^8\)

Pure red cell aplasia is a condition characterized by an isolated depletion of marrow erythroblasts and blood reticulocytes.\(^8\) Diamond-Blackfan anemia has not been reported previously with JBS in literature. Once the diagnosis of JBS is established, patients with this condition need to be screened for renal anomalies, referral for dental evaluation, monitoring for the development of hypothyroidism and Diabetes.\(^9,^{10}\) Early detection of a constellation of features suggestive of JBS is essential for establishing accurate diagnosis and early management. Variability in the severity of JBS on a case to case basis determines the requirements and effectiveness of any treatment. There is no curative treatment for this disorder except genetic counseling and supportive care or symptomatic care along with a multidisciplinary approach. Involving coordinated efforts of a team of general practitioners, gastroenterologists, cardiologists, endocrinologists, geneticists, neurologists and physical therapists to ensure a systemic and comprehensive approach to treatment.

**REFERENCES**


