



CASE REPORT

Johanson-blizzard syndrome: the importance of differential diagnostic in pediatrics

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Abstract

Objective: to promote a clinical entity that could be part of differential diagnosis of most disorders that affect the pediatric age group.

Description: we describe a Brazilian girl affected by Johanson-blizzard syndrome and review the literature.

Comments: Johanson-Blizzard syndrome is an autosomal recessive condition characterized by hypoplastic alae nasi, scalp defect, deafness and pancreatic insufficiency with malabsorption. Looking at the major signs, this disorder should be considered as differential diagnosis in several pediatric diseases.

J Pediatr (Rio J) 2002; 78(5):433-6: abnormalities; craniofacial abnormalities; pancreatic insufficiency.

Introduction

In 1971, Johanson and Blizzard described three patients carrying a clinical entity characterized by aplasia of the ala nasi, ectodermic scalp defects and varying degrees of mental retardation.¹ A literature review found other cases, such as that of two siblings who presented exocrine pancreatic insufficiency,¹⁻³ reported by Lumb and Beautyman; and three girls, two of them with trypsinogen deficiency, reported

by Morris and Fisher, and the other one reported by Townes.^{2,3} In 1966, Grand et al. described a new case, which presented 47, XXY syndrome in addition to low stature, microcephaly, deafness, pancreatic insufficiency and chronic lung disease.⁴

Approximately 38 patients have been reported (Table 1). In these descriptions, pancreatic insufficiency was a constant finding with only one exception, the patient reported by Krisjansson et al., who had hypopituitarism.⁵ Other frequent signs are hypoplasia or aplasia of the ala nasi; ectodermal scalp lesions; growth retardation and deafness.^{1,5-8}

Among the unusual findings, microcephaly, ophthalmic disorders, lacrimal duct anomalies, dental anomalies; hypothyroidism; genitourinary and anorectal anomalies; heart defects; and café-au-lait spots have been described.^{1,5,8-10}

Neuropsychomotor retardation is extremely variable and may not be present.¹⁵ Central nervous system disorders,

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Table 1 - Reported cases according to literature review

	Total n. of reported patients (n=38)	Articles with reference to the characteristic
Microcephaly	5/38	1, 2, 7, 14
Scalp lesions	18/38	1, 6, 7, 8, 9, 10, 11, 15
hypoplasia of the ala nasi	21/38	1, 5, 6, 7, 8, 9, 10, 11, 13,14,15
Malabsorption syndrome	23/38	1, 6, 7, 8, 9, 10, 11,13,14,15
Growth retardation	17/38	1, 6, 7, 8, 9, 10, 11, 13,14,15
Deafness	20/38	1, 5, 6, 7, 8, 9, 10, 11,13,14,15
Café-au-lait spots	2/38	7, 10
Lacrimal duct anomalies	8/38	1, 5, 7, 14
hypothyroidism	8/38	1, 5, 7, 9, 10
Dental anomalies	13/38	1, 8, 13
Genitourinary anomalies	10/38	1, 8, 9, 13, 15
anorectal anomalies	12/38	
Neuropsychomotor retardation	12/38	1, 7, 9, 10, 11
Consanguinity	9/38	7, 8, 10, 13, 15

malnutrition, deafness and hypothyroidism are potential coexisting factors.

The malabsorption syndrome, of pancreatic origin, which is characterized by chronic diarrhea and the inability to absorb fat, can begin immediately after birth or shortly thereafter, requiring strict medical follow-up in order to avoid complications, such as hypoproteinemia, infections and edema, all of which could lead to death during childhood.

This autosomal recessive disorder often occurs among siblings and in the presence of consanguinity, as described in some cases.^{7,8,13,15}

The present report presents a clinical status typical of this condition and appears to be the first Brazilian case described in the literature. Since this is a rare syndrome, whose differential diagnosis includes many pediatric conditions, we regard the case reported herein as highly relevant.

Case report

One year and one month old patient, daughter of consanguineous parents (F-1/8), of African descent. Gestational and family histories are not noteworthy. (Figure 1). A C-section was necessary due to dystocia; the birthweight was 3.2 kg (50<P<75); with height of 50 cm (50<P<75); head circumference of 33 cm (25<P<50) and Apgar score of 8 and 9. In the neonatal period, interatrial communication was detected, but the problem resolved spontaneously.

In the first year of life, the patient presented malabsorption syndrome and malnutrition, and had to be hospitalized many times during this period.

On physical examination, the following aspects were observed: weight of 7 kg (P<3); height of 99 cm (P=3); head circumference of 43.5 cm (P<25); inner intercanthal distance

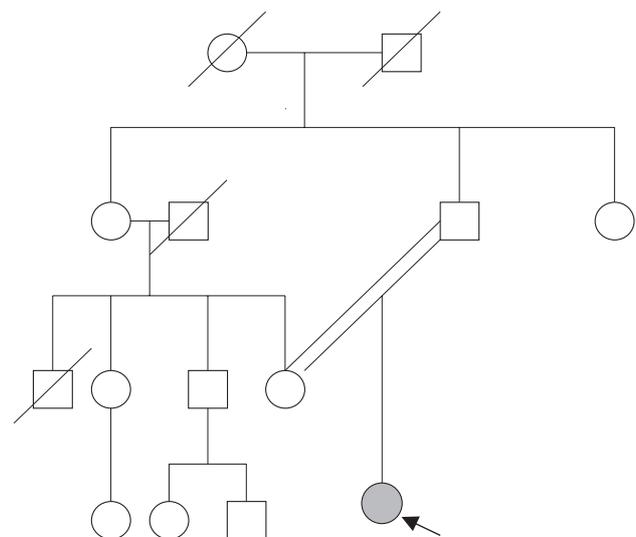


Figure 1 - Hereditary diagram

of 2.2 cm ($3 < P < 25$); outer intercanthal distance of 7.5 cm ($75 < P < 97$); ear measuring 4.5 cm ($25 < P < 50$), craniofacial disproportion; aplasia of the alae nasi; scalp agenesis in the occipital region; wide and high forehead; malnutrition; generalized hypotonia; normal genitals (Figures 2,3)

Complementary exams

Ophthalmic evaluation revealed epiphora. Hearing assessment showed total neurosensory hearing loss in the left ear and partial hearing loss in the right ear. Abdominal and urinary tract ultrasounds were normal, and so was the thyroid function.



Figure 2 - Scalp aplasia



Figure 3 - Aplasia of the alae nasi

Discussion

Our patient presents signs which are consistent and compatible with Johanson-Blizzard Syndrome, the most important of which are aplasia of the alae nasi, scalp agenesis in the occipital region and the malabsorption syndrome, often associated with the condition.

The first cases described by Johanson and Blizzard consisted of three girls, although the syndrome appears to affect both sexes equally. Consanguinity appears to be frequently reported; this is reinforced by the case report described herein, suggesting that this syndrome may be transmitted by an autosomal recessive gene.¹

Our patient presented severe hypotonia at birth and in the first months of life, which is a frequently described sign in most of the cases (Table 1). However, after the implementation of the treatment, there was a progressive improvement in her neuromotor development. The patients reported by Moeschler and Lubinsky clearly demonstrated that people with Johanson-Blizzard Syndrome can be intellectually normal. Microcephaly, hypothyroidism, deafness and malnutrition can be associated with mental retardation.⁹

Deafness was reported in 17 patients (Table 1); the case described by Sismanis et al. was investigated in detail, showing severe neurosensory hearing loss in association with the lack of vestibular function, although the inner ear was structurally normal at computerized tomography.¹¹

Hypothyroidism was studied in nearly 17 patients, but only seven presented thyroid disorders, whose etiology is unclear.⁵ The patient described by Daentl et al. (1979) showed atrophy of the thyroid gland and follicles distended with colloid at autopsy.⁷

The malabsorption syndrome, caused by pancreatic insufficiency, seems to be a universal complication of Johanson-Blizzard Syndrome. The pancreatic disorder presented here differs from the other two primary pancreatic deficiencies found in childhood. The defect found in cystic fibrosis has been described as a defect in the electrolyte transport protein in the cell membrane, which makes the pancreatic juice abnormally thick, causing its retention and immobility in the pancreatic canalicular system and promoting the formation of cysts and fibrosis. In contrast, in patients with Shwachman Syndrome, the secretion of fluid and electrolytes is preserved and there is a hypoplasia of the exocrine tissue of the pancreas. In Johanson-Blizzard Syndrome there is no evidence of a ductular defect, the secretion of fluids and electrolytes is preserved, and what appears to happen in this case is a primary failure in the development of acinar pancreas, similar to what occurs in Shwachman Syndrome. The autopsy showed ductular complexes with multiple clusters of Islets of Langerhans separated from each other by connective tissue.² No acinus was identified with certainty.² The pancreatic insufficiency seen in patients with Johanson-Blizzard Syndrome and Shwachman syndrome seems to be caused by the same physiopathological mechanism. However, we observe an

improvement of the pancreatic function as the child grows, in the former one, and a slight improvement in the latter one. In some cases, hypoplasia of the exocrine parenchyma gives way to steatorrhea.

Our patient tolerated only a casein protein hydrolysate. The patient has been maintained on this formula, associated with medium-chain triglycerides and pancreatin, up to the moment.

If the problems associated with the malabsorption syndrome are overcome, the child could survive childhood, but a long-term medical follow-up is necessary. Sometimes, even under medical care, these children can develop serious problems associated with hypoproteinemia, infection and edema, which can lead to childhood death. In addition, it is not possible, as in other heterogeneous conditions, to predict neurological damage in each case.

Currently, prenatal diagnosis has changed the approach to congenital defects, allowing for an early diagnosis. In

1999, Auslander et al. described the first case of Johanson-Blizzard Syndrome diagnosed in the prenatal period.¹³

Given the mechanism of transmission, it is important to refer the couple for genetic counseling, because the risk of recurrence after the birth of one affected individual is 25% in each pregnancy.

Thus, we emphasize the importance of recognizing the syndrome associated with malabsorption so that adequate treatment is provided to the patient.

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