Case Report

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Jacobsen Syndrome: Are We Informative Enough

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Abstract

Jacobsen syndrome is a rare syndrome caused due to deletion of long arm of chromosome 11. Typical clinical manifestations include physical growth retardation, mental retardation, facial dysmorphism, congenital heart disease, thrombocytopenia. The patient admitted with us at one and a half year had facial anomalies including flat occiput, prominent forehead, trigonocephaly, blue sclera, downslanting palpebral fissure, broad nose, hypertelorism, low set ears, high arched palate with bilateral eversion of foot and thrombocytopenia. Karyotyping confirmed deletion of chromosome 11q.

Keywords: Jacobsen Syndrome; Trigonocephaly; Thrombocytopenia; Heart Defects; 11q Deletion.

Introduction

Jacobsen syndrome (JS) is a rare disorder, yet is a clinically recognisable condition with multiple dysmorphic features. The deletion in most cases involves chromosome 11q.[1]. However fryns *et al.* [2] suggested that the deletion of sub band 11q24.1 is crucial for the clinical presentation. The deletion size ranges from ~7 to 20 Mb, with the proximal breakpoint within or telomeric to sub band 11q23.3 and the deletion extending usually to the telomere. The deletion is de novo in 85% of reported cases, and in 15% of cases it results from an unbalanced segregation of a familial balanced translocation or from other chromosome rearrangements. In a minority of cases the breakpoint is at the FRA11B fragile site [3]. More than 200 cases of JS have been so far reported in the literature[4,5]. The estimated occurrence of JS is about 1/100,000 births [3,4,5]. The female/male ratio is 2:1.

It has a varied spectrum of phenotypic variability, the most consistent being mild to moderate psychomotor retardation, trigonocephaly, facial dysmorphism in the form of skull deformities, hypertelorism, ptosis, coloboma, downslanting palpebral fissures, epicanthal folds, broad nasal bridge, short nose, v-shaped mouth, small ears, low set posteriorly rotated ears & thrombocytopenia. A subset of patients have malformations of the heart, kidney, gastrointestinal tract, genitalia, central nervous system and/or skeleton. Ocular, hearing, immunological and hormonal problems may be also present [3,6].

Case Report

The patient is one and a half years old female born out of non-consanguineous marriage to healthy parents. The pregnancy was uneventful and the child was born at term with a birth weight of 1900 grams. The first presentation of the child was at one and a half years of age with complaints of difficulty in hearing and developmental delay. Examination revealed flat occiput, prominent forehead, trigonocephaly, blue sclera, downslanting palpebral fissure, broad nose, hypertelorism , low set ears, high arched palate with bilateral eversion of foot. Anthropometric measurements suggested < -3 Z score

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for weight, -2 z score for length & microcephaly. Developmental delay in all motor, language & social sectors was present. Investigations revealed thrombocytopenia & BERA suggested mild hearing loss. Chromosomal analysis suggested 11q deletion with karyotype designated as 46, xx, del (11q). Thyroid profile, MRI brain, echocardiography, abdominal imaging and opthalmologicevaluations were normal.

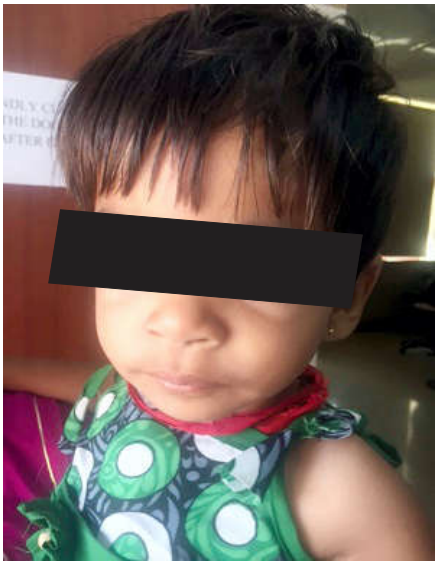

Fig. 1:

Discussion

Jacobsen syndrome is a rare disorder with multiple dysmorphic features. The deletion in most cases involves chromosome 11q. A detailed review of published reports shows that the severity of the observed clinical abnormalities in patients with Jacobsen syndrome is not clearly correlated with the extent of the deletion. The apparent lack of phenotype-karyotype correlation is possibly attributed from undetected mosaicism to redundant gene loci.

There has been an apparent abnormal sex ratio deviating towards the females and ours was also a female patient. Thrombocytopenia observed is usually chronic which was seen in our patient and has to be seen for any association with Paris-Trousseau syndrome in the form of giant platelets and abnormal megakaryocytes in bone marrow. None of these were present in our patient.

On a classical phenotype the diagnosis is suspected on the basis of clinical findings; facial dysmorphism, developmental delay & thrombocytopenia. Cytogenetic analysis is needed for confirmation. Children with JS share some clinical features (short stature, short, wide, sometimes webbed neck, downslanting palpebral fissures, ptosis, aortic or pulmonary stenosis) with Turner and Noonan syndromes. Occasionally, JS children have had a clinical diagnosis of Kabuki syndrome (mental retardation, unusual palpebral fissures, short stature, fingerpads). Thus the differential diagnoses are needed to be kept in mind while assessing.

Dalm *et al.* have recently shown that a subset of JS patients suffer from an impaired adaptive immune response, that is, defects in antibody production. Most patients with JS suffer from combined immunodeficiency in the presence of recurrent infections. Early detection of immunodeficiency may reduce the frequency and severity of infections.[7] There is a wide range of severity of intellectual disability (ID) in JS [8]. Akshoomoff *et al.* had studied 17 JS patients and eight of these patients, including four out of five males and four out of twelve females, fulfilled the diagnostic criteria for Autistic Spectrum Disorder [9].

Management is multi-disciplinary and requires evaluation by a pediatrician, pediatric cardiologist, neurologist and ophthalmologist. Auditory tests, blood tests, endocrine and immunological assessment and follow-up should be offered to all patients. Cardiac malformations can be very severe and require heart surgery in the neonatal period. Newborns with Jacobsen syndrome may have feeding difficulties and tube feeding may be necessary. Special attention should be devoted to hematological problems.About 20% of children die during the first two years of life, most commonly due to complications from congenital heart disease, and less commonly from bleeding. For patients who survive the neonatal period and infancy, the life expectancy remains unknown [10].

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