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Jacobsen Syndrome - A Case Report

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ABSTRACT

We report a case of Jacobsen Syndrome in a 7 month old male child with multiple facial abnormalities including trigonocephaly, psychomotor retardation, compromised visual and auditory functions, thrombocytopenia, heart defects including atrial septal aneurysm, mild tricuspid regurgitation and mildly dilated right atrium and right ventricle and deletion of chromosome 11q ter on karyotyping.

Keywords : Jacobsen Syndrome, trigonocephaly, psychomotor retardation, thrombocytopenia, heart defects, 11q ter deletion

Introduction:
Jacobsen syndrome (JBS) is a rare inherited disorder with variable phenotypic expression and partial deletion of chromosome 11q. To date more than 200 cases were reported, with an estimated prevalence of 1/100,000 births [1]. The most common clinical features of JS include: pre- and postnatal physical growth retardation, psychomotor retardation, characteristic facial dysmorphism, thrombocytopenia or pancytopenia. A subset of patients has malformations of the heart, kidney, gastrointestinal tract, genitalia, central nervous system and/or skeleton. Ocular, hearing, immunological and hormonal problems may be also present [2, 3]. The female/male ratio is 2:1. In most cases, de novo isolated terminal deletions of 11q have been found, while in the remainder, one of the parents has been a carrier of a balanced chromosome translocation involving 11q [4]. About 20% of children die during the first two years of life, most commonly related to complications from congenital heart disease, and less commonly from bleeding. For patients who survive the neonatal period and infancy, the life expectancy is unknown [5].

Case report:
The patient, 8 month old boy, is the first child of unrelated healthy parents. He was born by vaginal delivery after a full term pregnancy weighing 2.5 kg at birth. His perinatal period was uneventful. His first medical interaction occurred at the age of 2 months due to facial dysmorphism and increasing pallor.

On physical examination he appeared as a healthy child with mild dysmorphic facial features such as ocular hypertelorism, downward slanting palpebral fissures, epicanthal folds, flat nasal bridge, short nose with flat philtrum, and thin upper lip. He also had short neck, simian crease in hand, icthyosis of the skin of lower legs, hypopigmented patch over trunk (Fig.2), and chronic constipation. His weight was 6.6kg (25th percentile), length 67 cm (50th percentile) and head circumference 46 cm (25th percentile).

His motor development was delayed and had difficulty in sitting with support. Assessment on DASII corresponded with chronological age of 6.2 months. On neurological examination he was slightly hypotonic but without asymmetry. Heart auscultation revealed a mild systolic murmur. His visual as well as auditory functions were compromised. Hematological tests revealed anemia with Hb of 8.5 g/dl, ANC of 1220/ µl, with normocytic normochromic RBC and platelet counts 75,000/µl. Bleeding time was prolonged. Serum iron was 43 µg/dl and transferrin saturation 7%. Hemoglobin HPLC was normal. Bone marrow aspiration showed 8-10% atypical cells and absent megakaryocytes. USG abdomen was normal. ECHO revealed atrial septal aneurysm, mild tricuspid regurgitation, and mildly dilated right atrium and right ventricle. NCCT Head showed trigonocephaly9 (Fig.1). Karyotype was 46,XY,del(11q ter).

Fig.1 Trigonocephaly

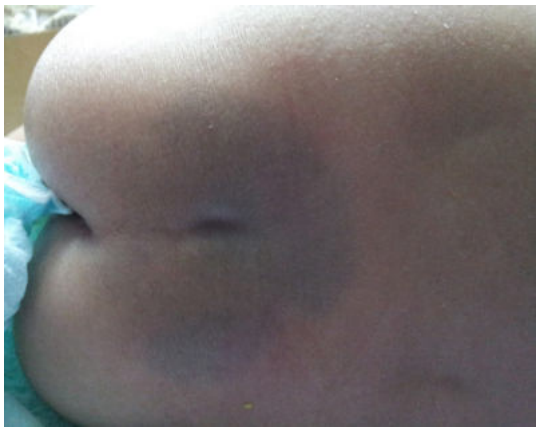

Fig.2 Hypopigmented patch in trunk

Discussion:

Jacobsen syndrome (JS) is a rare cytogenetic disorder that has a well-characterized phenotype. The deletions are variable in size, ranging from as small as 7 Mb to greater than 20 Mb [2]. A review of published reports shows that the severity of the observed clinical abnormalities in patients with JS is not clearly correlated with the extent of the deletion. Thus, there is no clear phenotype-karyotype correlation in patients with JS [5]. However, Penny et al.[2] suggested that there was a general relationship between the degree of psychomotor impairment and extent of deletion. Patients with larger deletions extending into 11q23 or q24.1 tended to have moderate psychomotor retardation with significant speech impairment, while the patients with small terminal deletions had mild or no psychomotor retardation. Many possible explanations have been suggested for the apparent lack of phenotype-karyotype correlation in JS patients. These explanations range from undetected mosaicism to redundant gene loci [6].

There has been an apparent abnormal sex ratio deviating towards females in patients with JS. Approximately 70% of the patients with 11q deletion were female [7]. Ours was a male patient

Thrombocytopenia in JBS is usually chronic. Abnormal platelets are detected with giant granules and the bone marrow shows many micromegakaryocytes. Moreover, electron microscopy reveals granule fusion within blood platelets [8]. Paris-Trousseau syndrome is characterized by thrombocytopenia, abnormal platelet function, abnormal megakaryocytes (from bone marrow), and abnormally appearing giant platelets in the peripheral blood. This phenotype is highly penetrant, affecting at least 92% of patients with JS [9]. Our patient was found to have none of the features of Paris-Trousseau.

In patients with the classical phenotype, the diagnosis is suspected on the basis of clinical findings: intellectual disability, facial dysmorphic features and thrombocytopenia. The diagnosis must be confirmed by cytogenetic analysis.Prenatal diagnosis is possible by amniocentesis or chorionic villus sampling and cytogenetic analysis. Management is multi-disciplinary and requires evaluation by a general pediatrician, pediatric cardiologist, neurologist, and ophthalmologist.

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