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Noonan's Syndrome

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Abstract

Noonan's syndrome is a complex familial syndrome with a large phenotypic overlap with the Turner syndrome. Individuals with this syndrome have small stature, broad or webbed neck, lymphedema, facial dysmorphism, mental retardation, skeletal abnormalities, and thrombocytopenia. In males there is undescended testes and sexual infantilism. Diagnosis is currently based on clinical presentation and a normal karyotype. Here we report a case of Noonan's syndrome.

Keywords: *Noonan syndrome; Pseudo Turner syndrome; Pulmonary stenosis.*

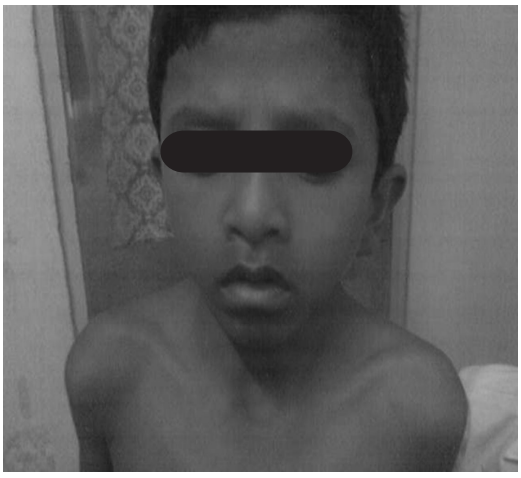
Introduction

Noonan Syndrome (NS) is complex familial Turner like syndrome without chromosomal defect. Commonest abnormalities seen in NS are skeletal and cardiac. There may be developmental delay.[1] The cardinal features are unusual facies (ie, hypertelorism, down-slanting eyes, and webbed neck), congenital heart disease (50%), short stature, and chest deformity. Approximately 25% of individuals with Noonan syndrome have mental retardation. Here we report a case of NS who has normal development for age and congenital heart disease.

Case Report

A 7-year-old male child presented with complaints of breathlessness and short stature. There was no history of fever, sore throat, joint pains or hematuria. There was no history of recurrent chest infection in the past. In the mother, there was no history of perinatal exposure to any known teratogens, like drugs or radiation. The age of mother during conception was 22 years and that of father was 25 years. There was no history of fetal loss. There was no family history of malformations. On external examination most obvious features were short stature (<5 percentile), dysmorphic face and webbing of the neck (Figure 1). The chest was broad, shield like and there was cubitus valgus. Mild

Figure 1



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hypertelorism and epicanthal folds was presnt. Depressed nasal bridge, low posterior hairline, posteriorly angulated and low ear set was present. External genitalia were normal. Development was normal for age. Pallor was present but icterus, cyanosis, lymphadenopathy, clubbing, splinter hemorrhage, osler nodes and pedal edema were absent. All the peripheral pulses were palpable. Respiration rate was 30/minute with intercostal retractions. Blood pressure was 90/60 mmHg. Cardiovascular examination revealed grade III ejection systolic murmur best heard over the pulmonary area. Detailed examination of other systems was normal. Karyotyping showed XY-46 with G-banding. Skeletal survey and abdominal ultrasonography (USG) were normal. Echocardiography revealed severe valvular pulmonary stenosis (gr.60mmHg) with small size ostium secundum atrial septal defect. Hematological work-up was normal. Patient was advised human growth hormone therapy but could not be given due to economic constraints.

Dicussion

Jacqueline A. Noonan in 1968, described 19 cases of a syndrome having a large phenotypic overlap with Turner syndrome along with other anomalies. The eponym "Noonan's syndrome" (NS) was first used in the same issue of the Journal where Noonan's article appeared.[2] Since then different synonyms used for NS include Pseudo Turner syndrome, Turner syndrome with normal XX and Male Turner syndrome.[2] Incidence of NS is 1:1000 to 1:1250 per live births.[3] Inheritance is autosomal dominant with variable expression but half of the cases are sporadic new mutations. This syndrome occurs in both genders.[2,3] There is no chromosomal defect though recently the gene has been mapped on chromosome 12q in the 12q24.2-q24.31 region.[1,2]

The most common abnormalities in Noonan syndrome are short stature, webbing of the neck, pectus carinatum or pectus excavatum, cubitus valgus, hypertelorism, downward slanted palpebral fissures, ptosis, micrognathia and ear abnormalities.[4,5] Hernias, clinodactyly and vertebral anomalies occur less frequently. Moderate mental retardation and high frequency sensorineural deafness can be present.[1,4] Right sided congenital heart disease is commonly present. Most often it is pulmonary valvular stenosis, hypertrophic cardiomyopathy or atrial septal defect.[5-6] Several haemolytic diseases such as low clotting factors XI and XII, acute lymphoblastic leukemia and chronic myelomonocytic leukemia have been described in patients with Noonan Syndrome.[1,7] Therefore, a full haemolytic workup must be performed in patients with Noonan Syndrome undergoing surgical procedure. Males have cryptorchidism and infertility. Females have normal genitalia and usually normal fertility. [3,8] There is mild developmental delay in cognitive and motor fields. Many children have normal development and the reported IQ ranges from 53% to 127%. Neurological manifestations reported are seizures, hearing deficit, peripheral neuropathy and Schwannomas. Skin may have nevi, freckles or café au lait spots. Diagnosis of NS is currently based on clinical presentation and normal karyotype. In antenatal ultrasound initial anomaly most likely to be observed is a posterior nuchal cystic hygroma which may regress later in the gestation into a nuchal fold redundancy and/or pterygium colli. Some fetuses are suspected and identified because of congenital heart disease, pleural effusions, and hydrops and by triple marker screening. During prenatal counseling, management costs, poor results of treatment, potential complications and psychological trauma to the family and the child, should be brought to parent's attention. Standard prenatal care is not altered when continuation the pregnancy is opted for. Most patients with NS should be managed conservatively.[1,2] Growth hormone therapy may be offered for treatment of short stature. Noonan syndrome is second

only to Downs syndrome as one of the most common syndromes hence clinically it is important to recognize this condition. Prognosis depends on associated anomalies. Normal life expectancy is seen in those without major complications of heart disease.

The differential diagnosis include Williams syndrome, foetal alcohol syndrome, multiple lentigines syndrome, Watson syndrome, Cardio-facialcutaneous syndrome, XO/XY mosaicism, Turner syndrome, Costello syndrome and neurofibromatosis- Noonan Syndrome.[1,4] Early identification of the condition is important for anticipation of problems, their early diagnosis that is required for a timely intervention and for genetic counseling.[2,4] Certain types of congenital heart lesions can be corrected by surgery. Activity may be limited by cardiac status and the presence of haematologic abnormalities (7). All individuals with Noonan syndrome require detailed and regular follow up for ongoing developmental, audiologic, ophthalmologic, cardiac, neurologic and other associated problems.

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