

Noonan Syndrome

Sanjeev K. Digra, Deep Aman Singh, Vikram Gupta, Ghanshyam Saini

Abstract

We report a 11 year old boy and his father both Noonan's. Noonan syndrome occurs in 1 out of 2000 live births. Short stature, webbing of neck, pectus carinatum or pectus excavatum, hypertelorism cubitus valgus, epicanthus, downward slanted palpebral fissures, ptosis, microgathia and ear abnormalities are the common features of Noonan syndrome.

Key Words

Noonan syndrome, Congenital heart disease, Short stature.

Introduction

The term Noonan syndrome has been applied to phenotypic males and females who have certain anomalies that occur also in females with Turner syndrome (1, 2). The disorder is usually sporadic but affected siblings of the same and of different gender have been reported. It occurs in 1 in 2000 live births (1). We report a father and son both with Noonan syndrome, suggesting male to male transmission.

Case Report

An 11-year old boy born of non-consanguineous marriage presented with breathlessness, palpitation and chest pain for one month, cough for three days and two episodes of haemoptysis, chest pain during exertion and radiating to the back, which used to get relieved on taking rest. There was no history of fever, sore throat, joint pains or haematuria. In past the child had seizures; first episode at the age of six years for which he took anticonvulsants for one year and then stopped of his own. There was no history of recurrent chest infection in the past. Patient is second in birth order and was born full term at home. Antenatal and perinatal period remained uneventful. His development was delayed. Other sibs, one brother and one sister are normal while his father had short stature and facial dysmorphism. There was no history of

seizures, tuberculosis, hypertension or diabetes in family.

On examination, the child was conscious, cooperative and well oriented to time, place and person. He was pale. He had no icterus, cyanosis, lymphadenopathy, clubbing, splinter hemorrhage, osler nodes and pedal edema. Temperature was 37°C, pulse 100/minute, good in volume, regular synchronous with other side with no radiofemoral delay. All the peripheral pulses were palpable. Respiration rate was 36/minute with intercostal retractions. Blood pressure was 100/60 mmHg. He had short stature, hypertelorism, low posterior hair line, prominently grooved upper lip, low set ears, short neck, widely spaced nipples, pectus carinatum and preadolescent SMR (sexual maturity rate). Examination of external genitalia and hernial sites was normal (Fig.1).

On systemic examination he had ejection systolic murmur best heard in second left intercostal space which radiated to mitral area, aortic area and left axilla. P2 was soft. Investigations revealed dimorphic anaemia, normal coagulogram, and right ventricular hypertrophy in chest skiagram and electrocardiogram. Echocardiography revealed severe valvular pulmonary stenosis. His father also had short stature, low posterior hairline, prominent philtrum, low set ears, short neck, pectus carintum, shield

From the Postgraduate Department of Paediatrics, Govt. Medical College, Jammu (J&K).

Correspondence to : Dr. Sanjeev K. Digra, Postgraduate Department of Paediatrics, SMGS Hospital, Jammu.

chest and cubitus valgus but no cardiac lesion (Fig. 2).

During hospital stay child was given one blood transfusion, antibiotics and decongestive therapy in the form of frusemide and digoxin and was discharged on haematinics after a hospital stay of 20 days. He was advised for a regular follow up.



Fig. 1. :- 11 year old child with Noonan syndrome. Note the short stature, pectus carinatum, widely spaced nipples and preadolescent SMR.

Fig. 2.:- Both father and son with Noonan syndrome.

Discussion

Noonan syndrome is an autosomal dominant condition (3, 4). It resembles Turner syndrome phenotypically but patient has apparently normal sex chromatin. These patients have delayed pubertal development but no primary gonadal failure (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 (1, 2, 4-6). Hernias, clinodactyly and vertebral anomalies occur less frequently. Moderate mental retardation and high frequency sensorineural deafness can be present (1,4). Approximately 50% of these individuals have congenital heart disease (4). Sharland *et al* used cardiosonography in their study and

showed over 80% of individuals with Noonan syndrome to have cardiovascular abnormality (7). Right sided congenital heart disease is commonly present. Most often it is pulmonary valvular stenosis, hypertrophic cardiomyopathy or atrial septal defect (1, 3, 4, 5, 7). 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, 8). Therefore, a full haemolytic workup must be performed in patients with Noonan Syndrome undergoing surgical procedure. Hepatosplenomegaly unrelated to cardiac status is present in approximately 25% of patients (9). Renal anomalies are present in 10% of patients but are not clinically significant (9). More than half of the male patients have undescended testes (9). Female patients have normal pubertal development and fertility. Fertility in males with undescended testes may be decreased. For this reason, the mother is more frequently the transmitting parent in familial cases (9). Joint laxity is present in more than half of patients and talipes equinovarus, radioulnar synostosis, cervical spine fusion and joint contractures are less common (9).Lymphoedema, prominent pads of fingers and toes (67%), follicular keratosis of face and extensor surfaces (14%) and multiple lentiginos (3%) are also seen in these individuals (9). Seizure disorder is present in 13% of these cases (9).

A specific cause for Noonan syndrome is not known. Both sporadic and autosomal dominant cases have been identified (4, 9). A gene for Noonan Syndrome NS-1 is located in the 12q 22-region but there is genetic heterogeneity (4). The differential diagnosis include Williams syndrome, foetal alcohol syndrome, multiple lentiginos syndrome, Watson syndrome, Cardio-facial-cutaneous syndrome, XO/XY mosaicism, Turner syndrome, Costello syndrome and neurofibromatosis-Noonan Syndrome (4, 6, 9).

No confirmatory /diagnostic testing for Noonan Syndrome is available. This entity remains a strictly clinical diagnosis. Karyotyping may be necessary if full phenotypic expression is not apparent (9).

Human growth hormones have resulted in improvement in growth velocity comparable to that seen in patients with Turner syndrome without adverse effects on cardiac ventricular wall thickness atleast in short term. The ultimate efficacy and safety of this treatment in improving final height is yet to be determined (1,9). Certain types of congenital heart lesions can be corrected by surgery. Activity may be limited by cardiac status and the presence of haematologic abnormalities (9). All individuals with Noonan syndrome require detailed and regular follow up for ongoing developmental, audiological, ophthalmologic, cardiac, neurologic and other associated problems.

References

1. DiGeorge AM. Hypofunction of testes. In: Behrman RE, Kliegman RM, Jenson HB (eds). Nelson Textbook of Pediatrics, 16th edn. Philadelphia. WB Saunders Co. 2000; 1746-51.
2. Melmed S. Disorders of anterior pituitary and hypothalamus. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL (eds). Harrison's Principles of Internal Medicine, 16th edn. New York, McGraw-Hill medical publishing division. 2001; 2029-52.
3. Kulkarni ML, Dasari R. Noonan syndrome. *Ind Pediatr* 2003; 40:431-32.
4. Noonan JA. Noonan syndrome revisited. *J Pediatr* 1999; 135: 667-68.
5. DiGeorge AM. Hypofunction of the ovaries In: Behrman RE, Kliegman RM, Jenson HB (eds). Nelson Textbook of Pediatrics, 16th edn. Philadelphia. WB Saunders Co. 2000; 1753-58.
6. Wilson JD. Disorders of sexual differentiation. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL (eds). Harrison's Principles of Internal Medicine, 16th edn. New York, McGraw-Hill medical publishing division. 2001; 2172-76.
7. Sharland M, Burch M, McKenna WM. A clinical study of Noonan Syndrome. *Arch Dis Child* 1992; 67: 178-83.
8. Bader MB, Tchernia G, Mielot F. Occurrence of myeloproliferative disorders in patients with Noonan syndrome. *J Pediatr* 1997; 130: 885-89.
9. Ibrahim J, McGavern M. Noonan syndrome. Available from: URL: <http://www.emedicine.com/PED/topic1616.htm> Accessed October, 30th 2002.