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## Familial Noonan Syndrome

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The Noonan syndrome was first recognized as a distinct clinical entity in 1963 by Noonan and Ehmke(1). The Noonan syndrome is characterized by dysmorphic facies, congenital heart disease and short stature. It may be inherited as an autosomal dominant trait and has a wide range of severity(2). We report on four cases of Noonan syndrome

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from three generations from one family.

### Case Reports

*Case 1:* The index patient, a baby girl was born by lower segment Cesarean section to a 27-year-old mother. Birth weight was 2.7 kg, head circumference 33 cm and length 49 cm. Antimongoloid slant, hypertelorism, epicanthic folds, bilateral ptosis, lowset ears, thick lips and single palmar crease on left hand were noticed at birth. There was no webbing of the neck or limb edema. An ejection systolic murmur was detected on 3rd day of life. There was no cyanosis and the baby was asymptomatic. The neonatal period was uneventful.

In view of the peculiar facial features and the cardiac murmur, the baby was investigated. Two dimensional echocardiography and color doppler revealed supra-valvular pulmonic stenosis with a systolic gradient of 48 mm of Hg across the pulmonary artery. The karyotype was 46, XX. A diagnosis of Noonan syndrome was made because of

dysmorphic faces, pulmonic stenosis and a normal karyotype. Ultrasonography of the abdomen did not reveal any urogenital anomalies. On follow up her physical and mental milestones are normal. At the age of 4 years, her height is 84 cm, and weight 11 kg (both below 3rd percentile). Her IQ is 112 and she is attending normal school.

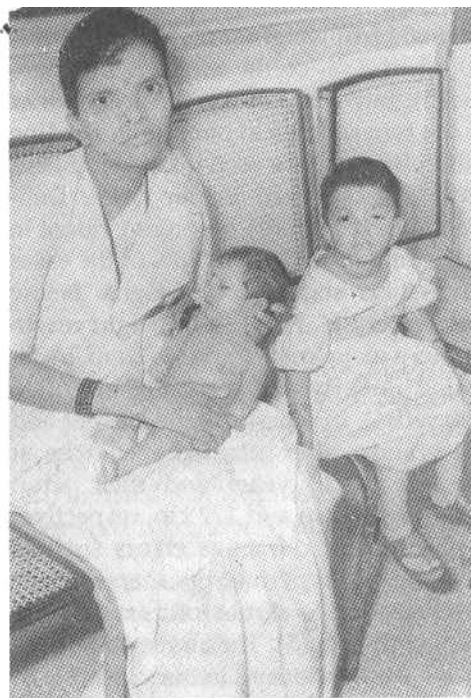
*Case 2:* During postnatal follow up of Case 1, the mother was noticed to have facial features similar to those seen in the baby. A detailed maternal history revealed that she presented to the physician at the age of 25 years with dyspnea on exertion. She was diagnosed to have moderate pulmonic stenosis and pulmonary valvotomy was done. She had a fullterm still birth at her native place three years before the present pregnancy. Details of the still born are not available. Her height is 142 cm and weight is 43 kg. The karyotype of the mother was 46 XX.

In view of the above features the mother was also diagnosed to have Noonan syndrome. Ultrasonography of the abdomen did not reveal any urogenital anomaly.

*Case 3:* The second female child of the mother was born at term by vacuum extraction. Birth weight was 2.3 kg, head circumference 33 cm and length 46 cm. Dysmorphic facial features included antimongoloid slant, lowset ears, thick lips and bilateral single palmar crease. An ejection systolic murmur was also noted at birth but there was no limb edema. Two dimensional echocardiography and color doppler revealed moderate valvular pulmonic stenosis with a systolic gradient of 42 mm Hg

across the pulmonary artery. The karyotype was 46, XX. She had no urogenital anomalies on ultrasonography. In view of the above findings a diagnosis of Noonan syndrome was made in the baby. *Fig. 1* shows the photographs of cases 1-4.

*Case 4:* The 55-year-old maternal grandmother also has antimongoloid slant, hypertelorism, epicanthic folds, lowset ears and thick lips. She has mild exertional dyspnea and cardiovascular examination revealed ejection systolic murmur in pulmonary area and two dimensional echocardiography confirmed valvular pulmonic stenosis. Her karyotype was 46, XX. Her height is 127 cm and weight 34 kg (both below 3rd percentile). In view of the above findings a



*Fig. 1. Photograph of Cases 1-4.*

diagnosis of Noonan syndrome was made in this lady.

### Discussion

The incidence of Noonan syndrome ranges from 1 per 1000 to 1 per 2000(3). The characteristic clinical features of Noonan syndrome are ocular hypertelorism, downward slanting palpebral fissures, ptosis, high arched palate, dental malocclusion, low set ears, webbed neck, low posterior hair line, wool like hair, shield chest, widespaced nipples, sternal deformity, congenital heart disease (most commonly pulmonic stenosis), renal anomalies, delayed menarche, cryptorchidism, cubitus valgus, short stature and impaired intellect(4,5).

Birth weight is usually normal(4,5). Both the children reported here had normal birth weight. Polyhydramnios is noted in 33% of the affected pregnancies(5), but was not seen in the mother of the two siblings in our study. Feeding difficulties may be seen in infancy(5) but were not observed in our cases. Deficient growth usually becomes evident in early infancy and about 80% of the cases have short stature with heights below 3rd percentile. Final adult height reaches 165 cm in males and 152 cm in females. Puberty and menarche are often delayed(4). In our study the mother and the grandmother attained menarche at the age of 13 years and their adult height is 142 cm and 127 cm, respectively. Significant refractive errors such as myopia or hypermetropia and nerve deafness due to serous otitis media are frequently seen(5). The above abnormalities were not noticed in our cases.

Cardiovascular anomalies occur in

about a third of the cases. Valvular pulmonic stenosis is most common although asymmetric septal hypertrophy and pulmonic branch stenosis may also be seen(2). Three of our patients had valvular pulmonic stenosis while one had supra-valvular pulmonic stenosis.

Intelligence of the patients ranges from normal to severe retardation. However when present, the degree of mental retardation is usually mild(4,6). The four cases presented by us had normal intelligence.

In females variable fertility has been reported and a substantial number of females reproduce. Most males are infertile. Cryptorchidism is seen in the males who are infertile(4). Renal anomalies are infrequently seen in Noonan syndrome(5).

There are numerous reports of Noonan syndrome being associated with a wide variety of isolated neurological conditions. These include temporal lobe anomaly, hydrocephalus(2), cerebral abscess and malignant schwannoma. A case of cerebral arteriovenous malformation in association with Noonan syndrome has also been reported(7).

We have made use of the comprehensive scoring system devised by Duncan *et al.* (8) which facilitates accuracy and decreases observer bias in diagnosing Noonan syndrome. The scores of the grandmother, mother, the first child and the 2nd child are 56%, 60%, 62% and 52%, respectively which confirms the diagnosis of Noonan syndrome.

Varying modes of inheritance of

Noonan syndrome have been suggested by Levy and associates, who reported the first case of male to male transmission of this condition and postulated that in some families it may be transmitted in an autosomal dominant manner with variable expressivity(9). Baird and DeJong have subsequently reported a family in which the syndrome was transmitted through three generations in a dominant manner(10). The four cases reported by us, in three, generations from one family, also follow the dominant mode of transmission.

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## Conjoined Twins with Jugular Lymphatic Obstruction Sequence

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Antenatal ultrasonographic diagno-

sis of conjoined twins and associated anomalies have been well documented in the past few years. We are reporting an unusual combination of conjoined twins with jugular lymphatic obstruc-

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