Smith's Recognizable Patterns of Human Malformation

5th Edition

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NOONAN SYNDROME

(Turner-like Syndrome)

Webbing of the Neck, Pectus Excavatum, Cryptorchidism, Pulmonic Stenosis

Kobilinsky reported in 1883 a 20-year-old male with webbing of the neck, incomplete folding of the ears, and low posterior hairline, but no mention was made of other physical findings. The first complete description appears to be that of Weissenberg in 1928. In 1963, Noonan and Ehmke further delineated the clinical phenotype and documented its association with valvular pulmonic stenosis. Recently, Mendez and Opitz have set forth the entire phenotype based on a review of 63 publications since 1883.

ABNORMALITIES

Growth. Short stature of postnatal onset in 50 per cent.

Performance. Mental retardation (25 per cent).

Facies. Epicanthal folds, ptosis of eyelids, hypertelorism, low nasal bridge, downslanting palpebral fissures, myopia, keratoconus, strabismus, nystagmus. Low-set and/or abnormal auricles. Anterior dental malocclusion. Increased width of mouth. Prominent, protruding upper lip; moderate retrognathia.

Neck. Low posterior hairline, short or webbed neck.

Thorax. Shield chest and pectus excavatum or pectus carinatum or both.

Other Skeletal. Cubitus valgus. Abnormalities of vertebral column.*

Heart. Pulmonary valve stenosis due to a dysplastic or thickened valve, left ventricular hypertrophy most frequently due to localized anterior septal hypertrophy and less often diffuse hypertrophy involving entire septum and free wall, septal defects, patent ductus arteriosus, branch stenosis of pulmonary arteries.

Genitalia. Small penis, cryptorchidism.

Bleeding Diathesis. A variety of defects in the coagulation and platelet systems including abnormalities in the intrinsic pathway (partial factor XI:C, XII:C, and VIII:C deficiencies), von Willebrand disease, and thrombocytopenia in approximately one third of cases.

OCCASIONAL ABNORMALITIES. High arched palate; large or asymmetric head; cerebral arteriovenous malformation, nerve deafness, hypoplastic nipples; kyphoscoliosis; winging of scapula, cervical ribs, edema of the dorsum of the hands and feet; lymphatic vessel dysplasia; chylothorax; simian creases; unusual wool-like consistency of the hair (curly); skin nevi, keloids, hyperelastic skin. Hypogonadism. Malignant hyperthermia.

NATURAL HISTORY. There is no apparent propensity to any special type of illness. The degree of mental retardation is seldom severe, and the social performance is usually better than anticipated from the intelligence quotient. Although impairment in fertility is present in some males, the major contributing factor is bilateral cryptorchidism. Fertility is normal in males with normally descended testes and in females.

Allanson et al. have documented changes in the clinical phenotype from birth through adulthood. In teenagers and in young adults, the face becomes more triangular and facial features are sharper. There is a tendency toward normalization.

ETIOLOGY. Usually a sporadic occurrence within families. Apparent autosomal dominant inheritance has been documented. A gene for this disorder has been mapped to 12q22-qter. However, nonlinkage has been documented in at least one family, indicating genetic heterogeneity for this disorder. Because of the wide variability in expression, careful evaluation of both parents must be undertaken prior to recurrence risk counseling.

COMMENT. The differential diagnosis for patients with the Noonan syndrome is extensive. XO/XY mosaicism, fetal hydantoin syndrome, fetal mysoline syndrome, and fetal alcohol syndrome have all been considered in patients with this phenotype. A number of patients have been described with features of both neurofibromatosis and Noonan syndrome. It is unclear if this is a distinct entity.

*Abnormal curvature of abnormal vertebrae (e.g., spina bifida occulta, hemivertebrae).

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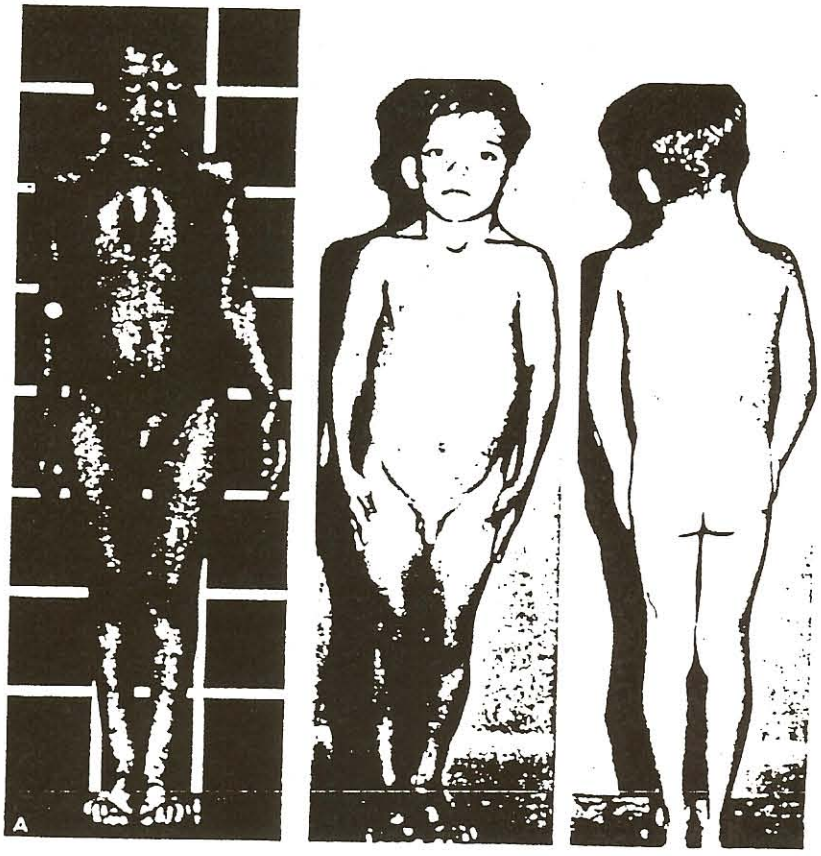

FIGURE 1. Noonan syndrome. *A*, A 12-year-old with height age of 7 years. Mental deficiency but a very affable personality. Cardiac defect. Cryptorchidism. (From Smith, D. W.: J. Pediatr., 70:473, 1967, with permission.) *B*, A 9-year-old, height age at 10 6/12 years was 5 6/12 years. (From Ferrier, P. E.: Pediatrics, 40:575, 1967, with permission.)