CASE REPORT

Noonan Syndrome

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ABSTRACT A case of Noonan syndrome in an Indonesian baby boy is reported. The diagnosis was based on history, physical examination, and abnormalities on Denver Development Screening Test and Vineland Social Maturity Scale. Treatment consisted of hormonal therapy for cryptorchidism and short stature, physiotherapy, and surgical correction cryptorchidism and cardiac anomaly if necessary. The prognosis for life span was good. **[Paediatr Indones 1994; 34:216-220]**

Introduction

Noonan syndrome refers to short stature female or male children with webbing of the neck, low posterior hairline, characteristic facies of broad forehead, hypertelorism, ptosis of the eyelids, epicanthal folds, downward slanting palpebral fissures, micrognathia, high arched palate, low set and/or malformed ears, shield chest with wide spaced nipples, and congenital heart disease.[1,3,5,7,9,10] Noonan syndrome was first recognized as a clinical entity distinct from Turner syndrome by Noonan and Ehmke in 1963, when they described nine patients with congenital heart disease and other facial anomalies.[2,4,6,8]

Noonan syndrome is known to occur in familial aggregations in several members of the same sibship, and in multiple generations of the same family. A number of reports document the transmission of the Noonan syndrome from mother to son and daughter, and a few indicate its transmission from father to son. It has been described in multiple offspring of apparently unaffected but consanguineous parents. While nosologic-etiologic heterogeneity must be considered, the available evidence seems to favor an autosomal dominant mode of inheritance.[1,3,9,10] It is reported that the incidence is about 1 in 1000 live births and there is a predominance of male cases.[3,9,10]

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Case Report

An Indonesian baby boy, born at term on September 29, 1992 at Sanglah General Hospital in Denpasar showed multiple congenital anomalies including congenital heart disease. The boy was born at 40 weeks of gestation with a body weight of 4300 grams. The delivery was uneventful without evidence of asphyxia. He was the first child in the family. The amniotic membrane ruptured more than 24 hours before delivery, but the pregnancy was normal. The mother had prenatal visits and didn't take either traditional or any other drugs, did not have any X-rays during pregnancy, did not smoke or drink alcohol. The father and mother of the baby were first cousins (his mother's father is the elder brother of his father's mother). The maternal and paternal ages at the time of conception were 23 and 26 years, respectively. There is no family history of a disorder suggestive of Noonan syndrome.

On physical examination, the baby did not look sick and was alert. The body weight was 4300 grams, while the length was 43 cm. The pulse rate and heart rate were 140 beats per minute and regular, the respiratory rate was 36 per minute, and the rectal temperature was 37 C°. There was webbing of the neck, and the patient had a low posterior hairline and characteristic facies with a broad forehead, hypertelorism, ptosis of the eyelids, epicanthal folds, downward slanting palpebral fissures, micrognathia with high arch palate. The ears were normal.

On inspection the chest showed the presence of shield chest and apparently wide spaced nipples; there was no cardiac voussure. The breathing movement was symmetrical, the impulse of the left ventricle was on the left mid clavicular line at the fifth left intercostal space. No abnormal pulsation was palpable, and there were no thrills. On auscultation the first and second heart sounds were normal. There was a pansystolic murmur of grade 3/6, loudest at the 3rd and 4th left sternal border and radiated along the left sternal border, having harsh and not blowing in quality. The liver and spleen were not palpable.

His genital showed that the right testis was not palpable either in the scrotal or inguinal region. The extremities showed downy hirsutism on shoulders, arms, forearms, and forelegs. Pterygium poplitea and bilateral congenital contractures were present at both legs.

Laboratory examination on September 29, 1992 revealed that Hb concentration was 16.4 g/dl, WBC 17 000/µl, hematocrit 47%, blood sugar 72.6 mg/dl, and on gastric lavage 5-7 WBC's were found.

Chest X-ray was taken on September 30, 1992 showing increased pulmonary vascularity without cardiomegaly. Radiological examination of the knee revealed that the bone and joint space were normal, and that there were no abnormal calcifications.

Unfortunately, chromosomal analysis of peripheral blood was not done, because there was no facility in Denpasar. EKG tracing revealed no abnormalities. The working diagnosis was Noonan syn-

drome. Because of the premature rupture of the membrane the patient was treated with ampicillin 200 mg twice daily for 5 consecutive days intravenously.

On October 1, 1992, the patient was consulted to the Department of Orthopedics Denpasar Hospital. The orthopedic diagnosis was multiple congenital anomalies with a bilateral congenital contracture of the knee joints. Skin traction of the feet was done for seven days without any success. Therefore they suggested to correct it surgically when the baby has gained a body weight of about ten pounds. Ophthalmologic evaluation showed that the ptosis was congenital and no treatment was recommended. The patient was also consulted to the surgeon who found a right cryptorchidism, and suggested to see the child every six month to see whether surgical intervention was needed.

The patients was discharged on October 19, 1992. Developmental evaluation was done using Denver Development Screening Test showing abnormal score. The Vineland Social Maturity scale was 70. Cardiologic follow-up showed that the baby had a small ventricular septal defect needed no treatment.

On January 30, 1993, dermatoglyphic picture of the patient's palm and fingers revealed a male type and did not differ from that of the normal population.

Discussion

The clinical features of Noonan syndrome varies greatly from case to case. Approximately 84% of the cases show the classical syndrome (stomata), i.e., webbed neck, low posterior hairline, characteristic facies, high arched palate, shield chest with widely spaced nipples and congenital heart disease. The complete characteristic clinical features of Noonan syndrome[1,3,7,10] compared with the finding in our patient, are listed in Table 1. It is obvious that most of the clinical manifestations of Noonan syndrome were found in our case.

Noonan syndrome must be differentiated with Turner syndrome, Aarskog syndrome, and Leopard syndrome.[1,3,5,7,10] Turner syndrome refers to short female children associated with sexual infantilism, webbing of the neck, low posterior hairline, characteristic facies with ptosis, epicanthal folds, micrognathia, shield chest, congenital heart disease, cubitus valgus, dorsal edema of the hands and feet, primary amenorrhea, sterility, and abnormality of dermatoglyphics. The incidence of Turner syndrome is estimated to be 1 : 2500 to 1 : 6000 live born females. The syndrome is the result of a partial or complete deletion of one X chromosome. Mental retardation is not common.[3,6,7,8,10] Because our case was a boy and no abnormalities of dermatoglyphics were found we may exclude the diagnosis of Turner syndrome.

Aarskog syndrome should be suspected in a male child with a short stature who presents with the major facial features, shawl scrotum, characteristic position of the interphalangeal joints when the fingers are extended.

The characteristic clinical features of Aarskog syndrome include the following features: major facial features include widow's peak, hypertelorism, broad nasal bridge, short nose with anteverted nostrils and long philthrum. Ptosis of the eyelids, opthalmoplegia, strabismus, and astigmatism were reported. The limb manifestations comprise short and broad hands, short 5th finger with or without single flexion crease, mild cutaneous syndactily. Broad feet with bulbous toes have also been found. Genital manifestations consist of a scrotal fold extending dorsally surrounding the base of the penis, and cryptorchidism. Skeletal features include pectus excavatum, metatarsus adductus and joint laxity. Most of the children with the syndrome have normal intelligence. The inheritance of this syndrome is most probably X-linked recessive [3,7,9,10]

Table 1. Clinical features of Noonan syndrome

Features	Frequency	Our case
General :		
Short stature:	72%	+
Mental retardation	61%	+
Craniofacies:		
Broad forehead	84%	+
Hypertelorism	84%	+
Epicanthal folds	51%	+
Ptosis of eyelids	66%	+
Downward slanting palpebral fissures	83%	+
Defective hearing	30%	?
High palatal arch	65%	+
Micrognathia	69%	+
Dental malocclusion	52%	-
Webbed neck	78%	+
Low Posterior hairline	81%	+
Thorax:		
Shield chest with widely spaced nipples	77%	+
Distal pectus excavatus/ proximal pectus carinatum	77%	+
Cardiac/Vascular anomalies	55%	+
Abdomen:		
Urinary tract anomalies	27%	?
Genitalia		
Cryptorchidism	70%	+
Limbs:		
Peripheral lymphedema	37%	-
Cubitus valgus	86%	-
Hypoplastic nails	43%	+
Hirsutism	30%	-
Mental defect:		
Mild (some have IQs < 50%)	60%	+

In our case, we did not find widow's peak, broad nasal bridge short nose, long philtrum, short and broad hands, shawl scrotum and metatarsus adductus and joint laxity, so that we may omit the diagnosis of Aarskog syndrome.

Leopard syndrome is an autosomal dominant entity consisting of a generalized distribution of lentigenes in association with a profound sensori-neural deafness. Other anomalies include retarded growth, a triangular face with biparietal bossing, ocular hypertelorism, congenital heart disease (pulmonary stenosis), abnormalities of the genitalia such as cryptorchidism, and winging of the scapulae.

In our case webbing of the neck, low posterior hairline, facies characteristic with broad forehead, epicanthal folds, downward slanting palpebral fissure, micrognathia, high arched palate, and shield chest with widely spaced nipples were found but there were no lentigenes and winging of the scapulae, so that the diagnosis of Leopard's syndrome can be excluded.[3,7,9,10]

The management of Noonan syndrome consists of:[1,3,10] Primary prevention, i.e., genetic counseling, and secondary prevention, including if indicated repair of cardiac defect, surgical correction of cryptorchidism, hormonal substi-

tution therapy for cryptorchidism and short stature.[3,10] Other therapy should be given as indicated, for example surgery for webbing of the neck, scoliosis, urinary tract anomaly, or orthodontics.

In our case, surgical correction of contracture articulatio genu will be done, if the body weight is around 10 pounds and correction of cryptorchidism if at the age of 2 years cryptorchidism still persists. The life span may be normal except for the presence of a cardiac defect and its complications, and the patients may be infertile.[1,3,5,7,10]

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