

## Case Reports

### Yunis-Varon Syndrome

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*Yunis-Varon syndrome is a rare, autosomal recessive syndrome characterized by growth retardation, defective growth of the cranial bones along with complete or partial absence of the clavicles (cleidocranial dysplasia), characteristic facial features, and/or abnormalities of the fingers and/or toes.*

**Key words:** *Cleidocranial dysplasia, Yunis-Varon syndrome.*

The diagnosis of a syndrome in a neonate with multiple congenital malformations is very important from the point of view of short and long-term management and genetic counseling. We report a male neonate with Yunis-Varon syndrome, with some features not earlier reported such as recurrence in successive offspring, polyhydramnios, large testes and periosteal reaction and widening of ends of long bones.

#### Case Report

Male neonate weighing 2.6 kg was born at 36 weeks of gestation of a non-consanguineous

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marriage by spontaneous vaginal delivery to a 22-year-old gravida 2 mother. The mother gave history of having given birth to an earlier baby with dysmorphic features who had died on day 1 of life. Apart from polyhydramnios, the antenatal period was unremarkable. The neonate required resuscitation at birth and developed respiratory distress soon after.

Anthropometric data were in the 50th centile for gestational age and upper: lower segment ratio was 1.9 : 1. The skull bones were membranous, with wide, confluent fontanels and sutures. There was sparse hair, absent eyebrows and eyelashes, high forehead, anteverted nostrils, malformed ears, proptosis, hypertelorism, corneal haziness and micrognathia. The thoracic cage was narrow and the nipples were absent. Limbs were short with hypoplastic thumbs, absent terminal phalanges and absent great toes. The scrotum was large and well formed with a testicular volume of 6 mL bilaterally (*Fig 1*). The parents confirmed that their previous offspring had similar malformations.

Radiological study revealed a poorly developed calvarium, absent clavicles bilaterally, small thorax, hypoplastic thumbs and great toes and terminal aphyalangia of both hands and feet. Other findings included periosteal reaction of mid-shaft of the humeri and femurs, narrow diaphysis and widened ends of tibiae and femurs. The neonate was diagnosed as a case of Yunis-Varon syndrome.

The neonate was managed with ventilation and supportive therapy, but expired at 10 hours of age. Autopsy ruled out any additional malformations.



Fig. 1 Absent nipples and toes, hypoplastic fingers and thumbs and large scrotum.

### Discussion

Yunis-Varon syndrome is an extremely rare inherited multisystem disorder with defects affecting the skeletal, ectodermal tissue and cardio-respiratory systems. Less than sixteen cases have been reported in the world literature. It is characterized by growth retardation prior to and after birth; defective growth of the cranial bones along with complete or partial absence of the clavicles (cleidocranial dysplasia); characteristic facial features; and/or abnormalities of the fingers and/or toes.

The first report of this condition appeared in 1980 when Yunis and Varon described 5 children from 3 families with cleidocranial dysplasia associated with certain other dysmorphic features including micrognathia, absent thumbs, distal phalanges of fingers, and distal phalanx of the big toes, pelvic dysplasia, bilateral hip dislocation, and retracted and poorly delineated lips(1). Two of the three sets of parents were consanguinous, suggesting an autosomal recessive disorder. Subsequently, there have been isolated case reports numbering a total of approximately fifteen cases with absent or hypoplastic thumbs, short pointed fingers and toes and nail hypoplasia or agenesis, being the invariable feature in addition to cleidocranial dysplasia, macrocrania and diastasis of cranial sutures(3,4). Anteverted nostrils and short upper lip, microcephaly, dislocated hips, hypoplastic great toes, syndactyly, dolicocephaly, micropenis, absent eyebrows and mental retardation have been frequently described. Other associations reported have been tetralogy of Fallot(5), severe hearing impairment, pyloric stenosis(6), Dandy-Walker malformation, hydrocephalus, and hypertension(7). The possibility of the syndrome resulting from disordered lysosomal storage was suggested by Dworzak, *et al.* based on the finding of vacuolar myopathy on muscle biopsy(8). Qualitatively abnormal bands for oligo saccharides and neuraminic acid on urinalysis by thin-layer chromatography and prominent intraneuronal inclusions with vacuolar degeneration, mainly in the thalamic nuclei, dentate nuclei, cerebellar cortex, and inferior olivary nuclei, suggesting a defect of lysosomal storage were reported by Walch, *et al.*(7).

Our patient, born of a non-consanguinous marriage was the second offspring of the parents having similar physical features. Although, our patient had no gross mal-

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formations of the organ systems, polyhydramnios, large testes and radiological features of widened ends of tibiae and femurs and periosteal reaction in the long bones were seen, which have not been reported earlier. Microscopic examination of the internal organs did not show characteristic features suggesting a storage disorder.

The prognosis of this syndrome is poor. Only three of the 13 patients from the literature reviewed by Ades, *et al.*(5) survived the first year of life, Two of the three survivors developed severe physical and mental retardation(9), and one patient showed growth retardation with normal intelligence.

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