CASE REPORT

YUNIS-VARON SYNDROME

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Yunis-Varon syndrome is a rare autosomal recessive disorder with characteristic facial features and limb anomalies. We report a neonate born to consanguineously married normal parents with typical clinical and radiologic features of Yunis-Varon syndrome along with complete cleft lip and palate: an infrequent association. The family had two previous babies with similar features who died in infancy. This is a first reported case of Yunis-Varon syndrome in Pakistan.

Keywords: Cleidocranial dysplasia; Aplastic thumb and toes; Yunis-Varon syndrome

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INTRODUCTION

Yunis-Varon syndrome is a rare autosomal recessive syndrome with defects involving the skeletal system, nervous system, cardiorespiratory system and ectodermal tissue (hair and teeth). The characteristic features include severe prenatal and postnatal growth retardation, large fontanelles, clavicular hypoplasia, characteristic facial features and abnormalities of fingers and toes. We report the first case of Yunis-Varon syndrome in Pakistan, with complete cleft lip and palate: a feature that has only been reported once in literature.[1]

CASE REPORT

A baby girl was delivered by Lower Segment Caesarean Section at 39 weeks of Gestation in a tertiary care hospital in Lahore with Apgar scores of 5 and 7 at one and five minutes respectively. The order of birth was four with only one alive and healthy sibling. The father aged 35 years and mother 28 years were first cousins and the couple gave history of two previous male babies with similar dysmorphic features who died at 1 month and 3 months of age respectively. The anthropometric data at birth revealed severe growth retardation with weight 1500 g, Fronto-occiptal Circumference 27.5 cm and length 39.5 cm (all below 0.4th centile). The baby had a number of dysmorphic features including microcephaly with prominent eyes, wide open anterior and posterior fontanelle with diastasis of sutures, complete cleft lip and palate, sparse scalp hair, absent eyebrows and eyelashes, hypertelorism, low set malformed ears, thin lower lip and anteverted nares (Figure-1). Skeletal abnormalities included absent clavicles bilaterally with winging of scapulae, agenesis of thumbs and big toes, syndactyly, hypoplasia of distal phalanges of fingers, hypoplastic nails, and bilateral developmental dysplasia of the hip joint. Radiological studies revealed absent clavicles, bilateral hip dislocation, healing fractures of femur bilaterally (Figure-2) and agenesis of thumbs (Figure-3). Ultrasound of cranium revealed dilatation of all ventricles with a large cyst in posterior fossa and a hypoplastic vermis. Fourth ventricle was communicating with the posterior fossa. These features were suggestive of Dandy-Walker malformation. Sonography of abdomen revealed normal liver, spleen and kidneys. Echocardiogram revealed biventricular hypertrophy with good Left Ventricular function and an Ejection Fraction of 60%. The neonate was managed with oxygen support via nasal prongs and feeding was established with Nasogastric tube, but the baby expired on 9th day of life secondary to respiratory complications.

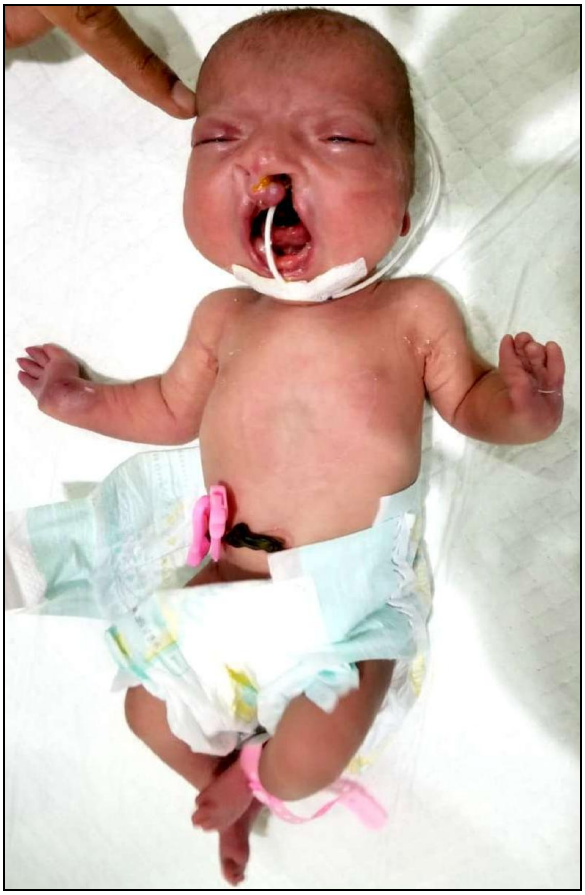

Figure-1: **Microcephaly, cleft lip and palate, absent eye brows and eye lashes with thumb aplasia**

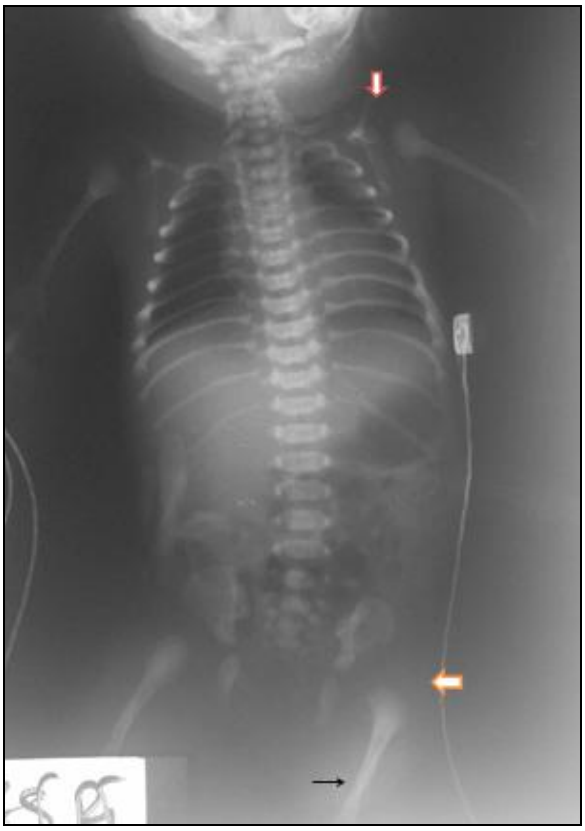

Figure-2: **Bilateral absent clavicles, dislocated hips and healing fracture femur.**

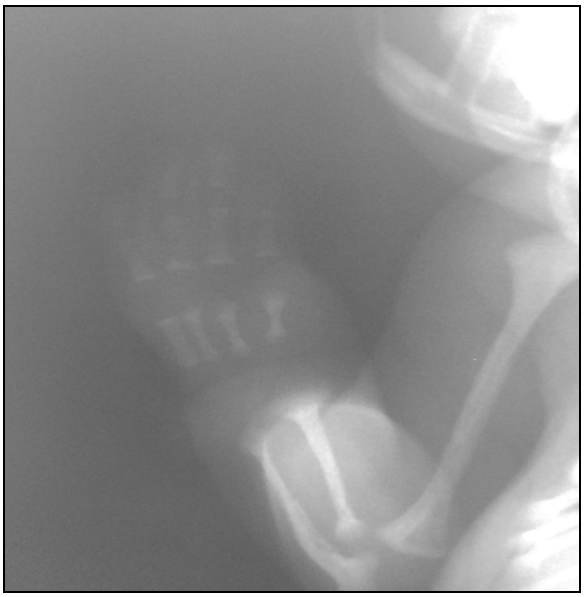

Figure-3: X-ray of hand showing absent thumb

DISCUSSION

Yunis-Varon Syndrome is a rare autosomal recessive disorder involving multiple systems notably the skeletal, ectodermal and cardiorespiratory system with a severe postnatal course secondary to respiratory distress. So far only 25 cases have been reported worldwide and there has not been a single reported case from Pakistan. The condition was first reported by Yunis and Varon in 1980 who observed five children from three families with sparse hair, cleidocranial dysostosis, micrognathia, bilateral absent thumbs and first metatarsal, distal aphalangia and bilateral hip dislocation. None of these children could survive beyond 10 weeks of age. Due to involvement of both male and female gender and consanguity of parents in two families the authors suggested autosomal recessive inheritance pattern.[2] The facial features of our case were similar to those described by Yunis and Varon along with complete cleft lip and palate, a rare association which has only been reported once in a fourteen-month old Japanese boy with typical features of Yunis-Varon syndrome.[1]

The features which were invariably present in all the cases reported in literature to date include severe growth retardation both before and after birth, absent or hypoplastic thumbs and nails, short pointed fingers, abnormal/malformed ears, wide fontanelle with diastasis of cranial sutures, sparse scalp hairs and cleidocranial dysplasia.[3–6] Other frequently reported associations were microcephaly with prominent eyes, anteverted nostrils, ectodermal abnormalities including absent or minimal eyebrows and eyelashes and hypodontia, bilateral dislocation of hips, bone fractures and genital abnormalities including hypospadiasis and undescended testes.[3] Several CNS abnormalities have been reported frequently which include Dandy-Walker malformation, agenesis of corpus callosum, hydrocephalus and hypoplastic vermis.[3,6] Cardiovascular abnormalities are uncommon but biventricular hypertrophy, cardiomyopathy and cardiomegaly have been reported with one reported case having Tetralogy of Fallot.[7] Other unique reported associations include pyloric stenosis with severe hearing impairment[8] and papillo-macular atrophic chorioretinopathy with "salt-and-pepper" appearance in two Mexican sisters with Yunis-Varon syndrome[9].

Yunis-Varon syndrome is suggested to be a lysosomal storage disorder. Campeau *et al*. identified homozygous or compound heterozygous mutations in the FIG4 gene after studying 5 patients from 3 unrelated families with Yunis-Varon syndrome[10] and recently biallelic loss of function variants in VAC14 have also been proposed as the involved genes[11].

Unfortunately, the prognosis of Yunis-Varon syndrome is poor with majority of reported cases having a stormy neonatal course with respiratory problems requiring artificial ventilation and very few surviving beyond neonatal period. So far Only five patients have been reported to survive

beyond infancy who suffered from severe growth restriction hearing abnormalities and mental retardation.[3]

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