

Yunis-Varón Syndrome: The First Report of Two Iranian Cases

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Abstract- The Yunis-Varón syndrome represents a rare autosomal recessive syndrome of easy recognition characterized by defective growth of the cranial bone along with complete or partial absence of the clavicles (cleidocranial dysplasia), absence of thumbs and halluces, distal aphyalangia, ectodermal anomalies, growth retardation and poor outcome. The molecular genetic basis is unknown. Here, we report an 8 months old girl with Yunis-Varón syndrome, born to a consanguineously married, with normal parents. She had micrognathia, wide fontanel, prominent eyes, poor sucking, congenital heart diseases, asymmetric face, ambiguous genitalia, reduction anomaly in right hand including thumb, and hypoplastic distal phalanges of 3rd fingers, and hypoplastic clavicles. She has glaucoma and lens opacity. There is another similar case in her family. Karyotype is normal. She is the first Iranian known case of Yunis-Varón syndrome.

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Keyword: Congenital heart diseases; Hypoplastic thumb, phalanges and clavicles; Yunis-Varón syndrome

Introduction

Yunis-Varón syndrome (YVS), also called cleidocranial dysplasia with micrognathia, absent thumbs and distal aphyalangia (1,2), is an extremely rare autosomal recessive multisystem congenital disorder which affects the skeletal system, ectodermal tissue, heart and respiratory system (3-5). Features of YVS include growth retardation before and after birth, defective growth of the bones of the skull along with complete or partial absence of the shoulder blades and characteristic facial features (3,6). Additional symptoms may include abnormalities of the fingers and/or toes (6). In most cases, infants with this disorder experience severe feeding problems and respiratory difficulties. In addition, affected infants may have heart defects. This syndrome is inherited in an autosomal recessive manner. YVS has been described relatively recently in the 1980s and since then less than 16 cases have been reported around the world. Many of the infants did not survive beyond one year of age.

Case Report

A 9 day old female child with dysmorphic features referred to our genetic department for counseling. Her mother was 39 years old and healthy woman. She had recurrent abortions in previous pregnancies. Her father

was 46 years old, and also a healthy man. They had two normal daughters. She was born by c/s with Apgar 9/10, and her weight was 3.83 kg and length 52 cm and head circumference was 38 cm. She was born from consanguineous marriage (Figure 1). Her mother's second trimester screening and several fetal sonography was done, but all of these exams were normal. In examination the baby has dysmorphic features, with multiple congenital anomalies. The infant had acrocyanosis, poor sucking, low set ear, high nasal bridge, short palpebral fissure, microcephaly, wide fontanel and micrognathia prominent eyes. In examination of external genitalia, we found very hypoplastic labia major, clitoromegaly, and ambiguous genitalia. She has skeletal anomalies such as hypoplastic distal phalanges of 3rd finger (Figure 2), hypoplastic clavicles (Figure 3), narrow chest (Figure 4), reduction anomaly in right hand including thumb, and. The echocardiography revealed that she has congenital heart diseases (ventral septal defect, patent ductus arteriosus, atrial septal defect, pulmonary hypertension, double outlet right ventricle). Her chest X-ray showed narrow chest and 13 ribs in both sides, and hypoplastic clavicles. Sonography of abdomen, kidneys, and liver are normal. Now she is 8 months old, and appears normally in mental and motor developmental stages. Very interesting features in our case is her lens opacity

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Yunis-varón syndrome

and glaucoma. There is another affected similar case in her pedigree. The second case had the same anomalies, but survived till 10 years old.

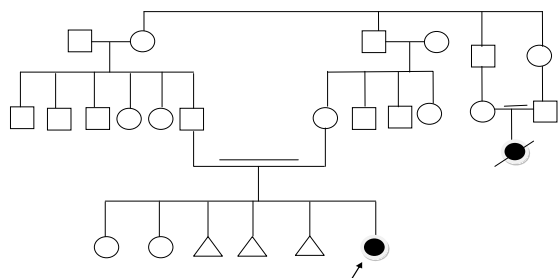


Figure 1. Family Pedigree, The arrow points to the proband.



Figure 2. X-ray of hand. Complete absence of first ray and distal aplasia of finger.



Figure 3. X-ray of chest, skeletal anomalies; hypoplastic clavicles.



Figure 4. X-ray of chest; skeletal anomalies narrow chest.

Discussion

YVS is a rare autosomal recessive condition characterized by limb defects, ossification defects, generalized hypotrichosis and multisystem disorder such as defects affecting the skeletal, ectodermal and cardiorespiratory system, and frequently a severe neonatal course. The characteristics are prenatal and postnatal growth deficiency, defect growth of bones of the skull, craniofacial disproportion, along with complete or partial absence of clavicles, hypoplasia or absence of thumbs and big toes and distal aphalangia. Their death in the first weeks of life is usually occurred. It was first described in 1980 by Emilio Yunis (1) and

Humbuto Varón in five children from three Colombian families. The molecular genetic basis is unknown. Prognosis is uniformly poor, only three of the 13 patients survived the first year of life (2-4,6). Death in the neonatal period has occurred in 8 of 11 live-born infants. Although intellectual performance was normal in one mildly affected 3- year-old boy, the other two children who survived the neonatal period had severe developmental delay at 1 and 4 years of age, respectively (5). There are some reports on newborn infants with previously undescribed findings, including hydrops fetalis, primary pulmonary hypertension and unusually severe abnormalities of toes. The clinical course of most cases of

YVS with severe failure to thrive and marked psychomotor delay dominating the clinical picture.

Clinical recommendations for prenatal and postnatal evaluation of patients and fetuses at risk are discussed. We report on a newborn infant with previously described finding but for first time in Iran.

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