Case Report

Terminal transverse deficiency of fingers, symbrachydactyly with anonychia of toes, and congenital scalp defect: Case report of a subject with Adams-Oliver syndrome

Sajid Malik[1], Hafiza Fizzah Riaz[2]

ABSTRACT

Terminal transverse anomalies of digits and congenital scalp defects can occur as separate entities. Both these malformations may accompany each other in a rare hereditary condition called Adams-Oliver syndrome (AOS; OMIM 117600). AOS is a heterogeneous anomaly which shows occasional involvement of cardio-vascular, pulmonary and frontonasal systems. Additionally, the clinical overlap with other well-characterized malformations like Poland syndrome, cutis marmorata telangiectatica congenita, and aplasia cutis congenita, makes its diagnosis challenging and may compromise accurate genetic counseling and risk estimation. We report a sporadic male child from Southern Punjab, Pakistan in which the phenotypic presentation is consistent with AOS. He had bilateral and asymmetrical terminal deficiency of fingers, symbrachydactyly with anonychia of toes, and aplasia cutis congenita of the scalp. There were no symptoms of any other organ system. We present detailed clinical study with differential diagnosis of AOS.

KEY WORDS: Adams-Oliver syndrome, Transverse limb deficiency, Aplasia cutis congenita, Scalp defect, Symbrachydactyly, Anonychia, Pakistani subject.

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INTRODUCTION

Terminal transverse deficiency of digits is a rare malformation which may affect upper and/or lower autopod. The condition is phenotypically heterogeneous and various grades of digit deficiencies are possible. In adactyly, for instance, a digit is completely missing while in aphalangia, there is an abrupt truncation through certain phalanges of fingers/toes. This anomaly occurs more commonly as isolated and unilateral defect.

Aplasia cutis congenita (ACC) (OMIM 107600) is another rare anomaly with congenital localized absence of skin usually on the scalp.[1] The skin appears as a thin, transparent membrane through which the underlying structures are visible. ACC may occur in isolation or with other congenital malformations. A combination of ACC with various degrees of terminal transverse limb defects and short fingers and/or toes is known as Adams-Oliver syndrome (AOS).[1] AOS is a rare and clinically heterogeneous anomaly. In addition to the classical combination of transverse limb anomalies and ACC, other malformations such as cardio-vascular, pulmonary and orofacial defects have also been reported with AOS.[2,3] Furthermore, there is a phenotypic overlap with other well-characterized malformations like Poland syndrome (OMIM 173800), cutis marmorata

1. Sajid Malik,
Assistant Professor,
2. Hafiza Fizzah Riaz,
1, 2: Human Genetics Program, Department of Animal Sciences,
Quaid-i-Azam University Islamabad,
45320 Islamabad, Pakistan.

Correspondence:

Dr. Sajid Malik,
E-mail: malik@qau.edu.pk

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telangiectatica congenita (OMIM 219250), and aplasia cutis congenita (OMIM 107600), which make its diagnosis challenging and may compromise accurate genetic counseling and risk estimation.[1] Hence, a thorough assessment of clinical presentation is warranted. In this communication, we describe a sporadic male subject with typical features of AOS. To the best of our knowledge this is a first report of AOS from Pakistan.

CASE REPORT

The subject belongs to a remote village of Southern Punjab. He is a six years old boy attending kindergarten. There was no parental consanguinity and he had two phenotypically unaffected younger sisters. At the time of his birth, his mother and father aged 29 and 34 years, respectively. His prenatal events and delivery had been unremarkable. Physical and anthropometric measurements, photographs and radiographs were obtained accordingly. All the information was collected according to the Helsinki II declaration.

The subject had bilateral terminal deficiency of fingers (Fig. 1A, 1B). In the right hand, fingers from second to fourth were short and irregularly amputated through phalanges. In the left hand, the fifth finger was amputated through the proximal inter-phalangeal (PIP) joint (Fig. 1A, 1B). The thumbs were small with tapering ends, bilaterally. Dermatoglyphic analyses demonstrated disorganized triradii in the right hand. In the left hand, weak palmer creases were evident. Additionally, the fingers from second to fourth had three interphalangeal creases each depicting disproportionate phalangeal divisions (Fig. 1B). There were two and one interphalangeal crease in the right and left thumb, respectively.

In the radiographs of the right hand, only two hypoplastic and ill-grown carpals were witnessed (Fig. 1C). Five metacarpals were present in the hand plate and the fifth metacarpal had immature epiphysis. Fourth digital ray was thin and hypoplastic. In the second, fourth and fifth fingers, the middle and distal phalanges were grossly absent/dysplastic. In the third finger, distal phalanx was omitted. The radiographs of the left hand revealed a broad and thick first metacarpal while second metacarpal had hypertrophic proximal end (Fig. 1C). The fifth finger had a short proximal phalanx with absent middle and distal phalanges. Additionally, there was general hypoplasia of terminal phalanges of all fingers.

In the feet, there was symbrachydactyly of toes. The halluces demonstrated varus inclinations, bilaterally (Fig. 1D). In the right foot, there was partial cutaneous webbing between second to fifth toes. In the left foot, second and third toes were involved in partial webbing (Fig. 1D). The syndactylous toes in both feet were short and devoid of nails. Radiographs of the feet revealed severe aplasia/hypoplasia of proximal and distal phalanges, bilaterally (Fig. 1E). Tarsals were hypoplastic and widely spaced. The first digital rays appeared unusually hypertrophic and metatarsals from second to fifth were crowded and overlapping, bilaterally (Fig. 1E).

The subject had additional symptoms of scalp. He had a lesion and absence of hair in the mid-scalp area. Physical examination revealed localized alopecia in antero-posterior and lateral dimensions of 1.2cm and 5cm, respectively. The lesion was a scar tissue with rough and heterogeneous appearance. It had skin atrophy and absence of

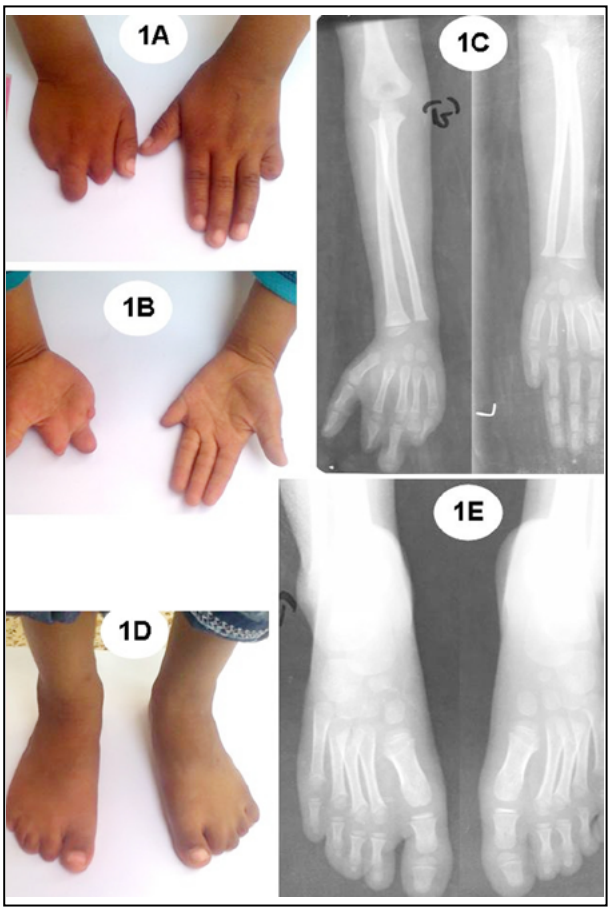

Fig. 1A-B: Dorsal and ventral aspects of hands of subject depicting terminal transverse deficiency of fingers.
1C: Radiographs of forearms showing hypoplastic distal ends of radius/ulna, immature epiphyses, dysplastic carpals, and amputated phalanges, bilaterally.
1D-E: Phenotype in feet. Terminal deficiency, anonychia, and symbrachydactyly with cutaneous webbing of toes are evident.

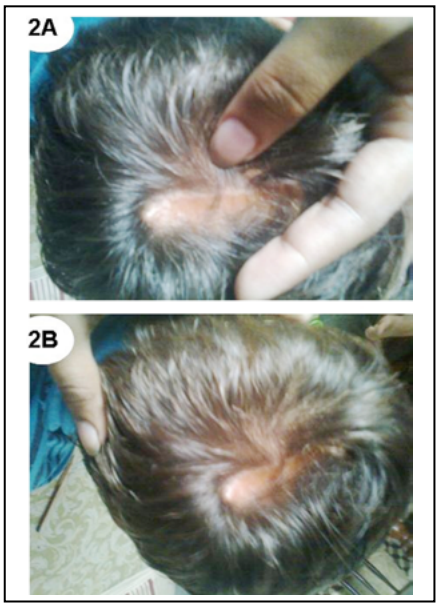

Fig.2: Lesion and alopecia in the skull, a remnant of aplasia cutis congenita.

sweating. Reportedly, the child had a congenital open wound at the lesion/alopecic area. This scar healed gradually leaving behind a lymphoma which had been surgically removed 2-3 years back. Postoperative healing had been normal but there was no hair growth in this area.

There were no other symptoms of orofacial, neurological, skeletal and internal organs. The subject exhibited normal developmental landmarks and there was no family history of any congenital hereditary anomaly. Detail of physical, anthropometric and radiographic measurements of the subject is provided in Table-I.

DISCUSSION

Genetically, AOS is a heterogeneous malformation. For instance, multiple hereditary patterns have been described for AOS and autosomal dominant inheritance has been much emphasized.[4] Most of the reported cases, however, are sporadic without familial inclinations. The molecular bases of at least one type of AOS have been recently elucidated and heterozygous mutations in the *ARHGAP31* gene on chromosome 3q13 have been discovered.[5] However, there is a strong evidence of further genetic heterogeneity as a number of familial and sporadic subjects with AOS revealed no mutation in the *ARHGAP31*.[5] Furthermore, the prevalence and epidemiology of AOS needs to be worked out for better genetic counseling and risk estimation.

The clinical presentation in our subject, i.e., transverse limb defects and aplasia cutis congenita, is consistent with typical AOS without the involvement of other organ systems. Limb defects are considered to be the most common manifestation, present in 84% of AOS patients.[6] The limb defects are usually asymmetrical with a tendency towards bilateral lower limb rather than upper limb involvement. Congenital cutis aplasia is the second most common defect seen in almost 75% of AOS patients and in 64% associated with skull defects.[2,6] Congenital cardiac malformations are present in 20% of all AOS patients.[2] The less common associations with AOS include vascular defects, pulmonary problems, orofacial symptoms, cutis marmorata telangiectatica congenital, and cryptochidism (differential diagnosis of AOS in Table-II).[1] Additionally, the clinical overlap of AOS with well-characterized anomalies makes the diagnosis difficult. For instance, Der Kaloustian et al[3] described two families in which the Adams-Oliver syndrome and the Poland anomaly were coexistent. Therefore, for an accurate diagnosis, a comprehensive clinical ex-

Table-I: Physical, anthropometric and radiological measurements of subject *

Anthropometric parameters	*Measurement (cm)*	
Standing height	103.8	
Sitting height	54.0	
Arm span	99.4	
Head circumference	49.0	
Neck circumference	28.5	
Leg length	53.0	
Clinical and radiological measurements	*Right arm*	*Left arm*
Arm leng th	39.0	42.8
Humerus-distal head circumference	3.4	3.5
Middle arm (Zeugopod)	16.0	16.5
Radius	13.5	13.8
Radius-distal head circumference	1.8 (1.5)	1.9 (1.5)
Ulna	14.8	15.0
Ulna-distal head circumference	0.9	1.0
Radius/Ulna space	0.7	
Hand (Autopod)	9.4	11.7
Palm	6.0	6.5
Wrist (width)	4.2	4.3
Carpal island 1	1.2	1.1
Carpal island 2	0.9	1.0
Metacarpal I	2.7	2.9
Metacarpal II	4.1	4.9
Metacarpal III	3.8	3.9
Metacarpal IV	3.5	3.5
Metacarpal V	3.3	3.2
Finger I	3.8	3.8
Finger II	2.2	5.7
Finger III	3.5	6.4
Finger IV	1.5	6.0
Finger V	2.0	2.5

* Measurements were taken at the age of ~6 years.

Table-II: Differential diagnosis of Adams-Oliver syndrome.

Clinical features	*Malformation (OMIM; Inheritance; Locus/Gene)*					
	Adams-Oliver syndrome	*Scalp defects & postaxial polydactyly*	*Poland syndrome telangiectatica congenita*	*Cutis marmorata congenita with epibulbar dermoids*	*Aplasia cutis congenita*	*Aplasia cutis*
	100300; AD,AR; 3q13; ARHGAP31	181250; AD	173800; AD	219250; AD	600268; AD	107600; AD
Limb defects						
Autopod/digital anomalies	++		++			
Terminal transverse defects	++					
Symbrachydactyly	++		++			
Polydactyly		++				
Skin anomalies						
Aplasia cutis congenita	++				++	++
Scalp defects	++	++				++
Livedo reticularis				++		
Vascular defects						
Cutis marmorata telangiectatica	+					
Telangiectases				++	++	
Other symptoms						
Cardiac malformations	+					
Pulmonary problems	+					
Pectoralis muscle defects			++			
Eye problems/glaucoma				+	++	
Facial problems	+				+	

Legends: ++ cardinal feature; + less common occurrence.

amination of the subjects is essential. In addition to the cardinal feature of transverse limb defects and ACC, the minor associated anomalies should also be documented.

In the case of AOS, the prenatal diagnosis of limb malformations is possible through systematic ultrasound examination. However, there is a poor prognosis that depends on the degree of limb deformity. Limb buds are first seen by ultrasound at about the 8th week of gestation; the femur and humerus are seen from 9 weeks, the tibia/fibula and radius/ulna from 10 weeks, and the digits of the hands/feet from 11 weeks.[7] All long bones are consistently seen from 11 weeks.[7]

Transverse limb defects and the associated syndromes like AOS, are usually not fatal. The impact of the anomaly can be completely evaluated after birth and correct approach and advice could be given. A multidisciplinary approach including obstetricians, geneticists, neonatologists, and pediatric orthopaedists should always discuss the implications of this situation with the parents and counsel thoroughly concerning the management, treatment options, and prognosis.[8]

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