SHORT REPORTS

The newly recognised limb/pelvis-hypoplasia/aplasia syndrome: report of a Bedouin patient and review

T I Farag, S A Al-Awadi, M J Marafie, L Bastaki, S A Al-Othman, F M Mohammed, I S AlSuliman, D S Krishna Murthy

Abstract

A Bedouin infant born to consanguineous parents and grandparents is reported. She had Müllerian aplasia and the phenotypic features of the limb/pelvis-hypoplasia/aplasia syndrome (MIM 276820). Phenotypic variability of this newly recognised syndrome is briefly discussed. (*J Med Genet* 1993;30:62-4)

In 1985 Al-Awadi *et al*¹ reported two sibs in a Jordanian family with a non-lethal profound limb deficiency malformation with unusual facies, thoracic dystrophy, and normal intelligence. Autosomal recessive inheritance was suggested. In 1987 Richieri-Costa² reported a 12 year old Brazilian girl with a similar phenotype. In 1988 Raas-Rothschild *et al*³ reported a consanguineous family from the Oriental Jew-

ish community of Mashad in Iran with three affected offspring (the proband and two aborted fetuses). They showed most of the phenotypic findings of the previously reported cases. They called this condition limb/pelvis-hypoplasia/aplasia syndrome (LPHAS) and speculated whether or not this rare gene is confined to the Middle East gene pool.

Here we report Müllerian aplasia in the first Bedouin patient with this newly recognised syndrome and briefly discuss the phenotypic variability of the pleiotropic gene.

Case report

A healthy, young, first cousin Bedouin couple was referred with their first baby to the Jahra Regional Liaison-Community Genetics Programme from an area near the Iraq-Kuwait border. The proband, born on 23.1.1990, was

Kuwait Medical Genetics Centre, Maternity Hospital, and Jahra Regional Liaison-Community Genetics Programme, Kuwait.

T I Farag
S A Al-Awadi
M J Marafie
L Bastaki
S A Al-Othman
F M Mohammed
I S AlSuliman
D S Krishna Murthy

Correspondence to
Dr Farag, PO Box 31145,
Sulibikhat, 90802 Kuwait.

Received 21 January 1992.
Revised version accepted
10 April 1992.

Figure 1 Proband showing disproportionate short stature.

Figure 2 X ray showing multiple contracture deformities.

Figure 3 X ray of pelvis showing gross skeletal deformities.

a female born at term by assisted breech delivery after an uneventful pregnancy. Her parents were 19 and 17 years old and came from a tribal community with a multigenerational practice of consanguineous marriage. There was no history of maternal exposure to teratogens. Birth weight was 2900 g (mean), length was 35 cm (-3 SD), head to pubis measurement was 27 cm (mean), and OFC was 36 cm (mean). Apgar scores were 7 and 9 at one and five minutes. The disproportionate short stature was characterised by profound limb hypoplasia and aplasia, especially in the lower limbs (fig 1). The upper limbs showed contracture deformities of the elbow joints, brachymesomelia, absent ulnae, angulated radii, mobile wrist joints, and postaxial oligodactyly (fig 2). Her rudimentary lower extremities showed 'flask shaped' thighs, phocomelia, hypoplastic feet, and mono/didactyly. Anonychia was seen

in the 10 fingers and toes present in the four limbs. The external genitalia were displaced anteriorly. Karyotyping of peripheral blood with trypsin G banding showed a normal 46,XX karyotype.

In July 1990 reassessment of the baby confirmed the previous findings and showed no developmental retardation.

RADIOLOGICAL FINDINGS

Radiographs showed a normal skull with no signs of increased intracranial pressure and normal ribs with three lumbar hemivertebrae. The upper limbs showed normal humeri, short ulnae, angulated radii (90° deformity noted at the junction of the proximal quarter), oligodactyly with absent rays 1 and 2 of the left hand and ray 1 of the right hand. The lower limbs showed proximal hip dislocation (the femora reached the level of the iliac crest), bifurcated femora with absence of both the tibiae and fibulae and of rays 3 to 5 of the right foot and rays 2 to 5 of the left foot. The pelvis showed gross malformations (fig 3).

Ultrasonography showed no central nervous system or abdominal malformations. Pelvic ultrasonography showed an absent uterus.

Discussion

Profound limb deficiency involving the upper and lower limbs has been described as part of a number of heterogeneous syndromes.⁴⁻⁸ The main characteristic findings in this Bedouin infant are symmetrical hypoplasia/aplasia of the upper and lower extremities with fibulo-tibial agenesis and malformed pelvis, which are different from the complex femur-fibula-ulna cases with asymmetrical limb defects.⁹⁻¹² Her phenotype resembles the recently delineated

Table 1 The biological and phenotypic variables compared with the Al-Awadi-Richieri-Costa-Raas-Rothschild syndrome.

	Proband	Al-Awadi <i>et al</i> ¹		Richieri-Costa ²	Raas-Rothschild <i>et al</i> ³		
		1	2		1	2	3
Age	Neonate	12 y	10 y	12 y	Neonate	Fetus	Fetus
Sex	F	F	M	F	M	F	M
Parental consanguinity	FC	FC	FC	NC	DFC	DFC	DFC
Religion	Muslim	Muslim	Muslim	Christian	Jewish	Jewish	Jewish
Craniofacial							
Elongated face (4/7)	+	+	+	+	-	?	?
Broad nasal bridge (3/7)	-	+	+	+	-	?	?
Epicanthic folds (1/7)	-	+	-	-	-	?	?
Long ears (1/7)	-	-	-	-	+	?	?
Pointed chin (1/7)	-	-	-	-	+	?	?
Occipital meningocele (1/7)	-	-	-	-	-	+	-
Thorax							
Barrel shaped chest (3/7)	+	+	+	-	-	?	?
Prominent sternum (3/7)	-	+	+	+	-	?	?
Upper limbs							
Flexion contracture of elbow joint (6/7)	+	+	+	+	+	+	?
Shortened forearms (7/7)	+	+	+	+	+	+	+
Mobile wrist (2/7)	+	-	-	-	+	?	?
Ectrodactyly (7/7)	+	+	+	+	+	+	+
Pelvis							
Severely malformed (7/7)	+	+	+	+	+	+	+
Lower limbs							
Stick-like projections (7/7)	+	+	+	+	+	+	+
Hypoplastic feet (7/7)	+	+	+	+	+	+	+
Oligodactyly (7/7)	+	+	+	+	+	+	+
Genitalia							
Displaced external genitalia (5/7)	+	-	+	-	+	+	+
Absent uterus (1/4)	+	-	-	-	-	-	-

Table 2 Radiological findings compared with the Al-Awadi-Richieri-Costa-Raas-Rothschild syndrome.

	Present report	Al-Awadi <i>et al</i> ¹		Richieri-Costa ²	Raas-Rothschild <i>et al</i> ³		
		1	2		1	2	3
<i>Skull</i>	—	—	—	—	—	—	—
<i>Upper limbs</i>							
Humeroradial synostosis	+	+	+	+	+	?	?
Short bowed radii	+	+	+	+	+	?	?
Angulated radii	+	—	—	—	—	?	?
Aplasia of ulnae	+	+	+	+	+	+	+
Aplasia of carpal bones	+	—	—	?	+	+	+
Hypoplasia/aplasia of metacarpals and phalanges	+	+	+	+	+	+	+
<i>Thorax</i>							
Broad clavicles	—	—	—	?	+	+	+
Broad ribs	—	—	—	?	+	+	+
<i>Pelvis</i>							
Severe malformation	+	+	+	+	+	?	?
<i>Lower limbs</i>							
Short bowed hypoplastic femora	+	+	+	+	+	+	+
Bifurcated femora	+	+	+	—	—	?	?
Aplasia of fibulae	+	+	+	+	+	+	+
Aplasia of tibiae	+	+	+	—	+	—	—
Hypoplasia/aplasia of tarsals, metatarsals, and phalanges	+	+	+	+	+	+	+

autosomal recessive Al-Awadi-Richieri-Costa-Raas-Rothschild limb/pelvis-hypoplasia/aplasia syndrome.¹⁻³

It is apparent from tables 1 and 2 that the LPHAS phenotype is characterised by 'mild' intra- and interfamilial variability of expression; it seems that the pleiotropic gene causing the condition affects both the skeletal and genital systems since displaced genitalia occur in most published cases (5/7) and Müllerian aplasia in one quarter. This Bedouin baby cannot be considered as a variant of the LPHAS on the basis of the presence of one additional sign (Müllerian aplasia), since the number of reported cases with LPHAS is still small (four females and three males). The apparently high degree of concordance of the type of cardinal anomalies in both the limbs and pelvis argues against different alleles and supports variability of expression of the LPHAS gene.

The consanguineous parents of the Bedouin infant are obligatory carriers, as both of them received the autosomal recessive gene for LPHAS from their common founder ancestors in this tribal community characterised by the multigenerational practice of consanguineous marriages and a plethora of autosomal recessive disorders. It seems that the speculation of Raas-Rothschild *et al*³ that the rare LPHAS gene is confined to the Middle East is not true since the Brazilian case has Latin American ancestors.²

According to a recent hypothesis of Lewin and Opitz¹³ and Opitz¹⁴ on the growth process of the lower limbs, there exist at least two distinct developmental field defects: (1) the 'fibular' defect including the proximal femur and postaxial ray and (2) the 'tibial' defect

including the distal femur and tibia. This Bedouin infant with LPHAS has tibiofibular aplasia. Studying future patients together with world wide reporting of similar cases will help a better understanding of this newly delineated rare autosomal recessive syndrome, which seems to be commoner among Middle East populations.

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