An additional case of Smith-Lemli-Opitz syndrome in a 46,XY infant with female external genitalia

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SUMMARY Ambiguity of the external genitalia has been frequently documented in male patients classified as the Smith-Lemli-Opitz (SLO) syndrome. Four previous case reports¹⁻³ suggest that in extreme cases of the SLO syndrome there may be complete lack of development of the male external genitalia even in the presence of a normal male 46,XY karyotype. We present an additional case of a phenotypically female infant with dysmorphic features compatible with SLO syndrome and a 46,XY chromosome complement.

Case report

The proband was the 2880 g product of a term pregnancy for a 24 year old gravida 2 mother and 25 year old father. The pregnancy was described as uncomplicated. Drug, tobacco, and ethanol abuse were denied and there was no known exposure to radiation or chemicals. Family histories were unremarkable and there was no parental consanguinity. The parents and an older male sib were of normal intelligence and were in good health.

The infant did poorly after delivery and was placed on ventilatory support. Multiple congenital anomalies were noted including tall, receding forehead; epicanthic folds; broad nasal bridge; apparent hypertelorism and cataracts; triangular, anteverted nares; low set, dysplastic ears; posterior cleft palate; micrognathia; short neck with redundant skin folds; widely spaced nipples; skin dimples over the elbows; and bilateral soft tissue syndactyly of the second and third toes. External genitalia were of normal female appearance. There was hypoplasia of the left heart which resulted in death at approximately 72 hours of age. Permission for necropsy and photography was denied. However, a marked similarity in appearance was noted between this infant and patient LD presented by Greene *et al.*³

CYTOGENETIC STUDIES

Chromosome analysis was performed on cells derived from culture of peripheral leucocytes. GTG banding revealed a normal male 46,XY karyotype. The presence of a Y chromosome was confirmed by fluorescence studies. The above results were confirmed on a separate blood sample.

Discussion

Because of the atypical facies which resembled the 'Greek-warrior' helmet, this 'female' infant was

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TABLE Comparison of phenotypic features in five cases of Smith-Lemli-Opitz syndrome.

	Kretzer <i>et al</i> ¹	Patterson <i>et al</i> ²	Green <i>et al</i> ³		Present case
			1	2	
Term gestation	+	+	+	+	+
Birth weight (g)	2820	2230	2100	2420	2880
Microcephaly	+	+	+	+	+
Broad nasal bridge	+	+	+	+	+
Ptosis	+	+	+	+	+
Epicanthic folds	+	+	+	+	+
Cataracts	+	+	+	+	+
Anteverted nares	+	+	+	+	+
Low set and/or malformed ears	+	+	+	+	+
Short neck with redundant skin folds	+	+	+	+	+
High arched and/or cleft palate	+	+	+	+	+
Downturned mouth	+	+	+	+	+
Micrognathia	+	+	+	+	+
Polydactyly	+	+	+	+	+
Syndactyly	+	+	+	+	+
Simian crease	+	+	+	+	+
Congenital heart disease	+	+	+	+	+
Female phenotype	+	+	+	+	+
Karyotype	46,XY	46,XY	46,XY	46,XY	46,XY

Case reports

initially thought to represent the 4p- syndrome. However, chromosome analysis failed to confirm this diagnosis and instead identified a normal male karyotype.

Review of published reports revealed four case reports¹⁻³ of phenotypically female infants with a 46,XY karyotype and other multiple congenital anomalies consistent with a diagnosis of SLO syndrome. Re-examination and comparison of the dysmorphic features found in our case and the previously reported cases (table) revealed several common features noted in SLO syndrome and substantiated this clinical diagnosis in the proband. Most significant in these cases was the normal female genitalia in the presence of a Y chromosome.

A wide spectrum of genital anomalies has been noted in SLO syndrome. Most commonly seen are cryptorchidism and hypospadias in the male. Cases of normal male phenotype as well as genital ambiguity have also been reported.⁴ However, it appears that in extreme SLO cases there may be complete failure of development of the male external genitalia with resulting normal female appearance. In fact, Lowry *et al*⁵ have suggested that some severe cases of SLO syndrome with male pseudohermaphroditism may have been incorrectly

identified as Meckel syndrome. Therefore, SLO syndrome should be included in the differential diagnosis of male pseudohermaphroditism, especially in the presence of other congenital anomalies.

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Possible Waardenburg syndrome with gastrointestinal anomalies*

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SUMMARY We describe a patient with possible Waardenburg syndrome associated with anal atresia and oesophageal atresia with tracheo-oesophageal fistula. Three other published cases with atretic gastrointestinal anomalies associated with the Waardenburg syndrome are reviewed. We conclude that the association between atretic lesions of the gastrointestinal tract and the Waardenburg syndrome may be a significant one.

Aganglionic megacolon (Hirschsprung disease) is known to be associated with the Waardenburg syndrome.¹ In 1981 we called attention to the fact

that other gastrointestinal anomalies may also be present in this syndrome, namely anal atresia.² Recently we have seen another patient with possible Waardenburg syndrome who had anal atresia and oesophageal atresia with tracheo-oesophageal fistula. The purpose of this report is to present the findings of our patient and to discuss the significance of gastrointestinal anomalies in the Waardenburg syndrome.

Case report

A 1 year old female infant was referred to the Department of Pediatrics because of fever and wheezing bronchitis. The parents were Sephardi Jews originating from Libya and were not consanguineous. The child was born prematurely after 35 weeks' gestation by vertex delivery. Polyhydramnios was noted during pregnancy. Birth

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