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Letter to the Editor

Lethal Multiple Pterygium Syndrome in Four Male Fetuses in a Family: Evidence for an X-Linked Recessive Subtype?

To the Editor:

Reports of patients with multiple pterygia date at least to 1902. This syndrome was established as an autosomal recessive disorder comprising limb pterygia, congenital contractures, facial cleft, genital anomalies, and minor facial anomalies.

In 1976, Gillin and Pryse-Davis described three sibling female fetuses with a more severe phenotype than reported previously. This phenotype was designated lethal multiple pterygium syndrome (LMPS). Since their initial report, 43 affected fetuses have been described.

The mother and father described here are in good health with unremarkable family history; they are nonconsanguineous. The couple's first two pregnancies ended in fetal death at 26 weeks of gestation. Both fetuses were male and were hydropic with cleft palate and apparently low-set ears. At autopsy, the second fetus was noted to have rocker-bottom feet and fibrous webs across both antecubital fossae. Fractures of the forearms and the right femur were noted. Neither fetus could be studied cytogenetically because of culture failure. In the third pregnancy, a male fetus with hydrops, decreased fetal movements, and fixed limbs was noted at 16 weeks of gestation. Amniocentesis showed a 46,XY, normal male karyotype. The pregnancy was terminated by dilation and evacuation, which precluded autopsy. In the fourth pregnancy, cystic hygroma and decreased fetal movement was noted in a male fetus at 14 weeks of gestation; the fetus had a 46,XY karyotype. The couple opted to continue the pregnancy and the fetus developed massive hydrops and fixed limbs by 20 weeks of gestation (Fig. 1). Fetal death occurred at 26 weeks of gestation. At autopsy, the macerated hydropic fetus was noted to have a midline cleft of the palate, apparently low-set, small pinnae, small chin, and equinovarus deformity of both feet (Fig. 2). There were no recognizable pterygia, although radiographs demonstrated multiple fractures of the limbs, right scapula, and ribs (Fig. 3).

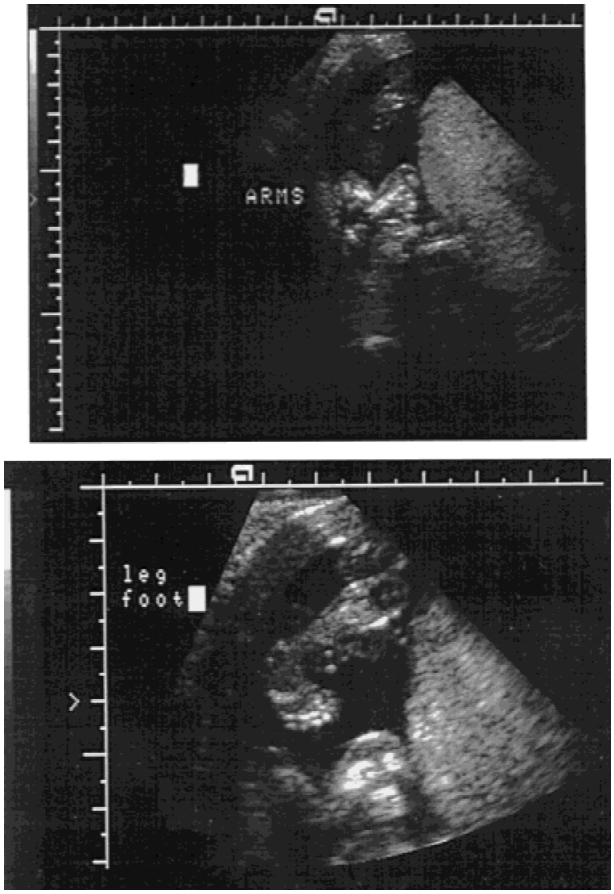

Fig. 1. Ultrasound of fourth affected fetus at 16 weeks of gestation demonstrating arms fixed across chest (**top**) and abnormal positioning of foot (**bottom**).

The couple's most recent pregnancy was noted at 16 weeks of gestation to be female with normal anatomy and movement. This baby was delivered at 37 weeks of gestation and was normal.

To determine whether an X-linked recessive subtype of LMPS could be defined, we reviewed all reported cases of the syndrome found through a search of the Medline database. We included only those in which the sex of the affected fetus(es) was known. Liveborn cases were excluded. One unique case was also excluded be

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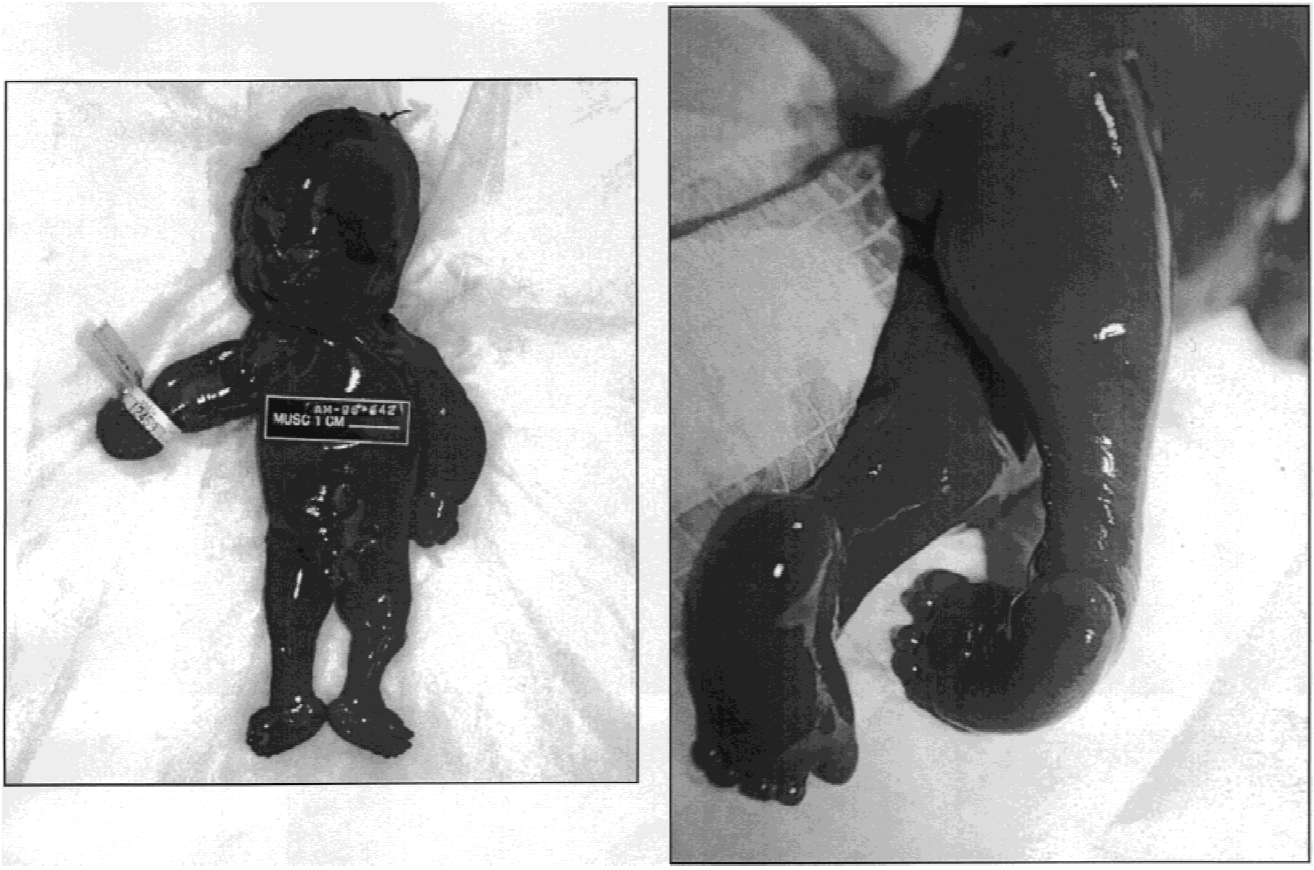

Fig. 2. Frontal (**left**) and lower limbs (**right**) views.

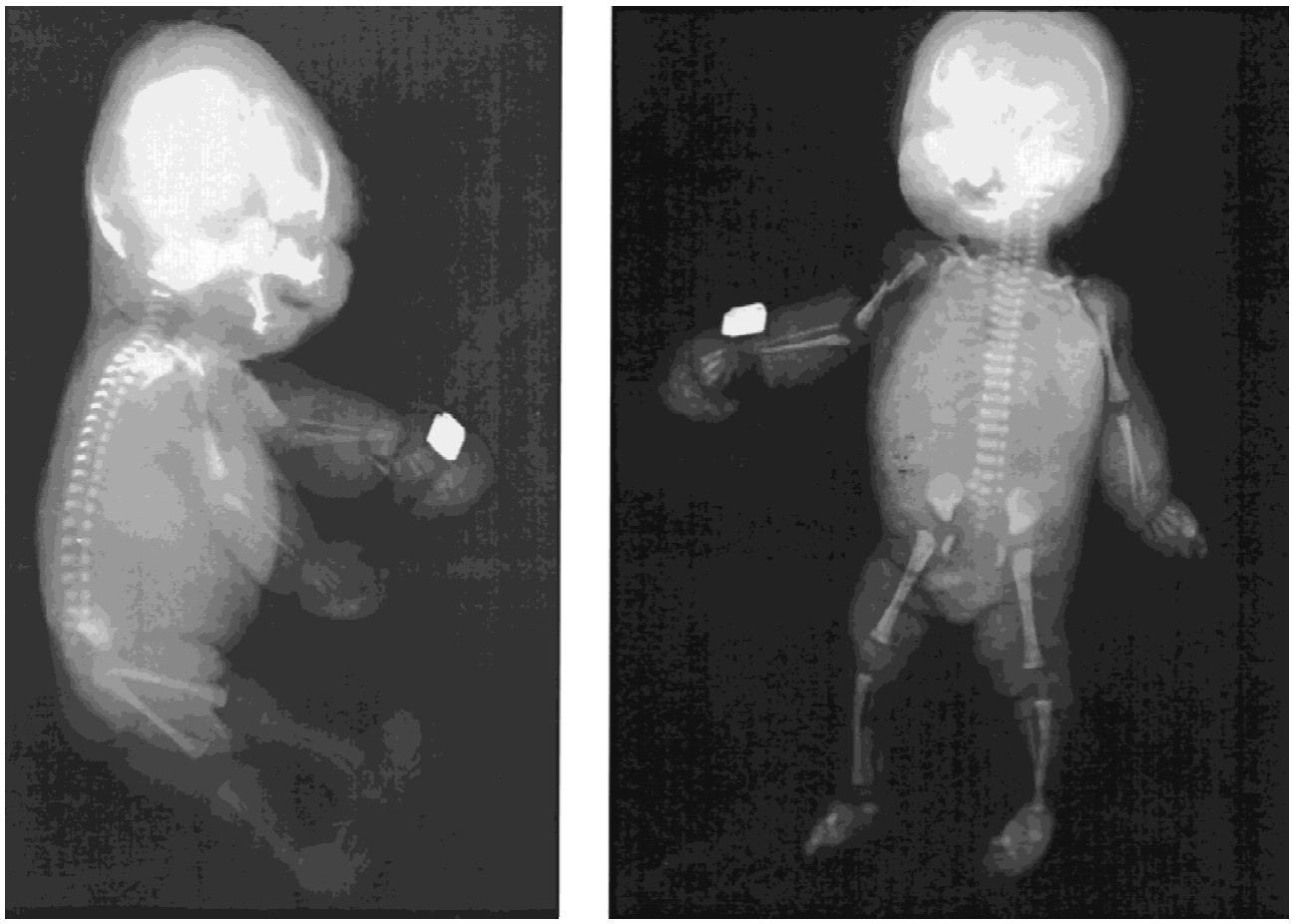

Fig. 3. Anterior–posterior (**left**) and lateral (**right**) X-rays.

TABLE I. Familial Male Cases*

Family	1			2	3		4	5		6		7	8	9	10	11		12	13	14			
Case	a[a]	b[a]	c		a	b		a	b	a	b					a	b			a	b	c	d
Survival	sb	sb	nd	ea	fd	ea	fd	fd	ea	fd	sb	ea	fd	ea	fd	nd	sb	sb	sb	fd	fd	ea	fd
Webbing	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?	?	+	+	?	+	?	–
Contractures	+	+	+	+	?	+	?	+	+	+	+	+	+	+	?	+	+	+	+	?	+	+	+
Hydrops/hygroma	–	–	–	–	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+
Cleft palate	–	–	+	–	–	+	+	?	?	?	–	+	+	+	+	?	?	?	?	+	+	?	+
Facial abn	+	+	+	+	?	+	–	?	?	?	+	+	+	+	+	+?	–	+	+	?	+	?	+
Genital abn	+	+	?	+	–	–	–	–	?	–	+	+	–	–	?	?	?	?	?	?	?	?	–
Other						sa	sa		p		p	sa, p	p, l	sa, p	p, hx	sa	sa	sa, p					sa, l

*sb, still birth; nd, neonatal death; ea, elective abortion; fd, fetal death; sa, skeletal abnormalities by radiography/fractures; p, polyhydramnios; l, lacerations of tissue at joints; hx, history of two prior elective abortions for anomalies.
[a]MZ twins.

cause of atypical anomalies. Since Gillin and Pryse-Davis' [1976] initial report, we found a total of 43 fetuses with LMPS in 27 families. Of these cases, 24 fetuses were male and 19 were female. Thirteen of the 27 families had affected males only including five with multiple affected males (Table I). Our case represents the sixth such family.

In reporting the above cases, many authors alluded to the existance of an X-linked recessive subtype of LMPS, however, only one family was described [Tolmie et al., 1987] in which X-linked recessive inheritance seems certain based on the pedigree. Using our data, we could not find evidence to allow for the diagnosis of an X-linked recessive LMPS subtype without supporting information from a pedigree consistent with this inheritance pattern. Thus, additional cases with multiple generations affected are needed to define the previously proposed heterogeneity in LMPS and to confirm the existence of a distinct X-linked subtype.

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