Case reports

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A case of Fryns syndrome

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SUMMARY A case of Fryns syndrome is presented. Characteristic features of this lethal autosomal recessive disorder include corneal clouding, camptodactyly with hypoplastic nails, and abnormalities of the diaphragm.

Fryns *et al*[1] have recently described female sibs with a lethal multiple congenital abnormality syndrome. Two subsequent reports describing three similar babies have helped delineate this new lethal syndrome which is likely to be autosomal recessive in inheritance.[2 3] All of these cases have been stillborn or died within a few hours of birth. We now report a sixth case who survived for 12 days.

Case report

The proband was the third child of a healthy and unrelated 36 year old father and 34 year old mother who already had two normal sons. He was born at 31 weeks by breech delivery after an uneventful drug free pregnancy and spontaneous onset of labour. Apgar scores were 3 at one minute and 9 at five minutes after active resuscitation. Growth parameters at birth were weight 1·75 kg (50th centile), length 40·5 cm (10th centile), and head circumference 28·5 cm (50th centile).

The baby died at the age of 12 days despite intensive care and ventilatory support throughout life, with persistent acidosis, bradycardia, and apnoea when encouraged to breathe spontaneously. Abnormalities noted during life included an unusual facies (fig 1) with prominent glabella, anteverted nares, low set ears with folded helices, and micrognathia. Both eyes showed generalised stromal corneal clouding with attenuation of the retinal arteries. His neck was short with prominent folds posteriorly (fig 2). Both hands showed camptodactyly involving primarily the proximal interphalangeal joints (fig 3). The nails on all digits were small. There were no other obvious external abnormalities.

Chest *x*-ray showed an abnormal anterior shadow which was found at necropsy to be a diaphragmatic

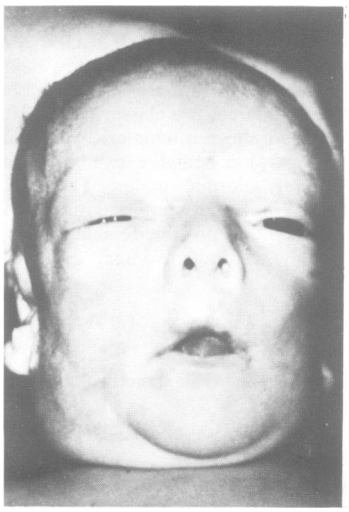

FIG 1 *Anterior view of the face (post mortem).*

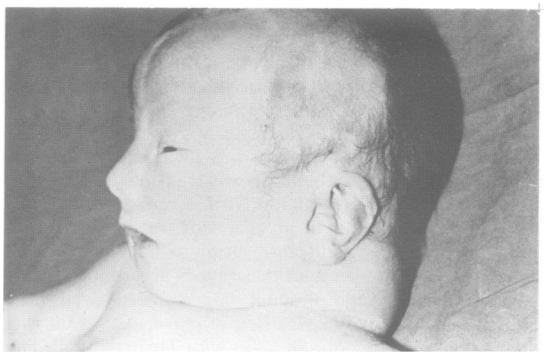

FIG 2 *Left lateral view of the face (post mortem).*

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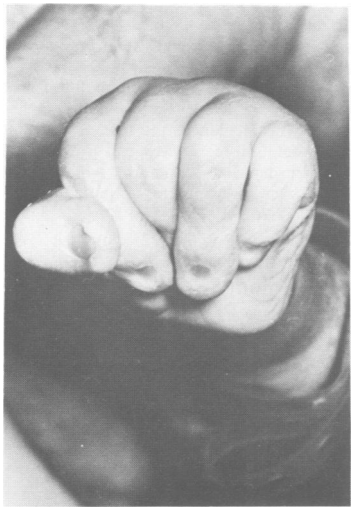

FIG 3 *The right hand. Note the overlapping fingers, camptodactyly, and hypoplastic nails.*

eventration with ballooning of the anterior membranous parts of the diaphragm. This was associated with enlargement of the liver which weighed 100 g and extended well into the left side of the abdomen. Additional findings at necropsy included congested, poorly aerated lungs, normal kidneys, heart, and gastrointestinal tract, and extensive cerebral destruction consistent with anoxic damage.

Investigations giving normal results included a congenital infection screen and G banded karyotype. Serum iron was normal and no excess urinary pipecolic acid was detected. Skeletal survey revealed no evidence of stippling.

Discussion

The abnormalities in this case are very similar to those in the female sibs reported by Fryns *et al.*[1] The table summarises the relevant findings in published cases of this disorder. Features common to all cases include early death, diaphragmatic defects with pulmonary hypoplasia, and craniofacial dysmorphism. It is the pulmonary hypoplasia which precipitates early death in those infants who are liveborn.

The differential diagnosis of corneal clouding, camptodactyly, and diaphragmatic defects or hepatomegaly or both includes trisomy 18 and the cerebro-hepato-renal syndrome.[4] Trisomy 18 can be readily excluded by chromosome studies, while a high forehead, hypotonia, and epiphyseal stippling are characteristic of the cerebro-hepato-renal syndrome in which the basic defect may lie in pipecolic acid metabolism[5] or mitochondrial oxidation.[6]

It is concluded that the case presented here helps further establish Fryns syndrome as a distinct entity. The description of this disorder in two sib pairs

TABLE *Summary of clinical features in published cases of Fryns syndrome.*

	Fryns et al[1]		*Goddeeris et al*[2]	*Lubinsky et al*[3]		*Present case*
	1	*2*		*1*	*2*	
Sex	F	F	F	F	M	M
Gestation (weeks)	28	29	31	41	39	31
Birth weight (kg)	1·20	1·60	1·36	4·78	4·03	1·75
Birth length (cm)	39		43		53·3	40·5
Head circumference (cm)			27·5	36·5	36·8	28·5
Survival	Stillborn	Stillborn	Stillborn	15 hours	<1 hour	12 days
Corneal clouding	+	+	−	−		+
Anteverted nares	+		+			+
Abnormal helices/lobules	+			+	+	+
Micrognathia	+		+	+	+	+
Short/thick neck	+		−	+		+
Camptodactyly	+					+
Small nails	+		+	+	+	+
Hypoplastic lungs	+	+	+	+	+	+
Diaphragmatic defects	+	+	+	+	+	+
Hepatomegaly				+		+
Renal abnormalities	−			+	+	−
Genital abnormalities	+		+	+	+	−
CNS abnormality				+	+	+/−
Cleft palate	+	+	+	+	+	−

indicates that autosomal recessive inheritance is probable.

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Umbilical cord hernia in a child with autosomal recessive chondrodysplasia punctata

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SUMMARY An infant with congenital chondrodysplasia punctata with a secondary deformation of umbilical cord hernia is reported. The paper discusses deformation syndromes as anomalies due to unusual mechanical or intrinsic factors.

Deformations resulting from in utero compression are relatively common problems, first described by Hippocrates.[1] Little attention had been paid to their pathophysiology until Smith[2] reported several varieties of deformation and deformation sequences due to extrinsic mechanical forces causing in utero fetal constraint, especially during the rapid growth period in the last trimester. Deformations are defined as anomalies that represent the normal response of a tissue to unusual mechanical forces, in contrast to malformations which arise as the result of a primary problem in the morphogenesis of a tissue. Disruption represents the breakdown of previously normal tissue, as produced, for example, by an amniotic band, and has been implicated in the causation of some types of cleft lip and palate. Deformations have been classified into two types: (1) primary deformations being produced by extrinsic mechanical forces to a normal fetus; and (2) secondary deformations occurring as a result of an intrinsic problem of the fetus, such as a malformed fetus or a malpositioned fetus. Rarely, these can also occur together.

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We report a case of an unusual umbilical cord hernia arising as a secondary deformation in a malformed infant with congenital chondrodysplasia punctata.

Case report

The male proband, the product of an uncomplicated term pregnancy, was delivered by caesarian section because of cephalopelvic disproportion and clinical evidence of fetal distress to a 25 year old primigravida with blood group AB, Rh positive, and VDRL negative. The pregnancy was uneventful except for one episode of maternal urinary tract infection which was successfully treated with ampicillin. An ultrasound at 30 weeks' gestation was normal, and the fetus was said to be compatible in size for the date. The parents are first cousins.

At birth, the baby was deeply cyanotic and in shock and was noted to have multiple congenital anomalies including a large umbilical cord hernia (fig 1). He required immediate resuscitation; Apgar score was 9 at 5 minutes. After stabilisation, the patient was transferred to the Intensive Care Nursery (ICN) at the Jersey City Medical Center. Physical examination in the ICN revealed a term male newborn, weighing 3050 g, length 42 cm, and head circumference 34·5 cm. Multiple anomalies were noted including small skin tags on the lips, short thorax, and widely spaced nipples. Scrotal folds were normal but the testes bilaterally were