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Syndrome of the month

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The Schinzel-Giedion syndrome

L I Al-Gazali, P Farndon, J Burn, D B Flannery, C Davison, R F Mueller

In 1978 Schinzel and Giedion[1] reported male and female sibs with a syndrome characterised by midface retraction, hypertrichosis, multiple skeletal anomalies, and cardiac and renal malformations.

Three other cases have subsequently been reported.[2–4] We review the features in these five published cases with five previously unreported cases.

Department of Clinical Genetics, The Clarendon Wing, Leeds General Infirmary, Belmont Grove, Leeds LS2 9NS.
L I Al-Gazali, R F Mueller

Clinical Genetics Unit, Birmingham Maternity Hospital, Birmingham.
P Farndon

Regional Genetics Advisory Service, 19 Claremont Place, Newcastle upon Tyne.
J Burn

Regional Genetics Service, Addenbrooke's Hospital, Cambridge.
C Davison

Department of Paediatrics, Division of Medical Genetics, Medical College of Georgia, Augusta, Georgia, USA.
D B Flannery

Correspondence to Dr Al-Gazali.

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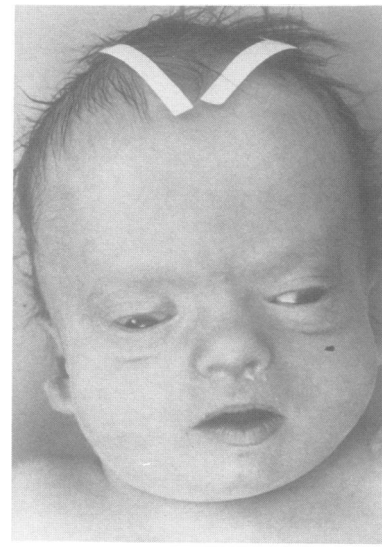
Clinical features

CRANIOFACIAL DYSMORPHIC FEATURES (TABLE 1)

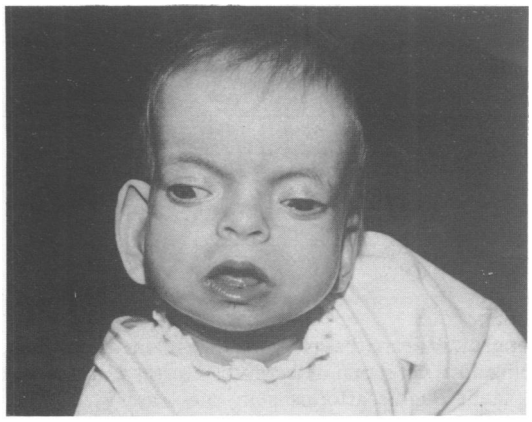
Children with this syndrome have a distinctive facial appearance with coarse features (fig 1). The most



(a)

Table 1 Craniofacial dysmorphic features.

	Schinzel and Giedion[1]		Donnai and Harris[2]	Kelly et al[3]	Burck[4]	Present cases				
	1	2	3	4	5	6	7	8	9	10
Widely open sutures/ anterior fontanelle	+	+	+	+	+	+	+	+	+	+
Frontal bossing	+	+	+	+	+	+	+	?	+	+
Midface hypoplasia	+	+	+	+	+	+	+	+	+	+
Orbital hypertelorism	+	+	+	+	+	?	+	+	+	+
Short, upturned nose	+	+	+	+	+	+	+	−	+	−
Low set ears	+	+	+	+	?	+	+	−	+	+
Facial haemangiomata	−	−	+	+	−	−	−	−	−	−



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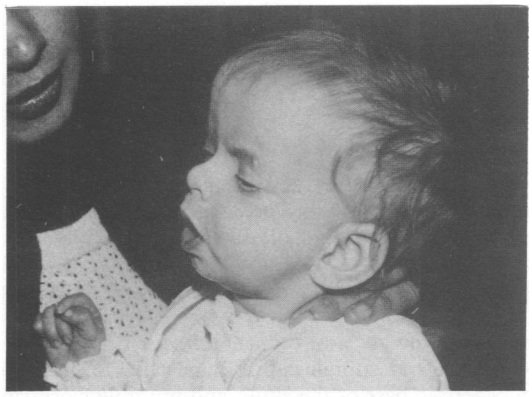

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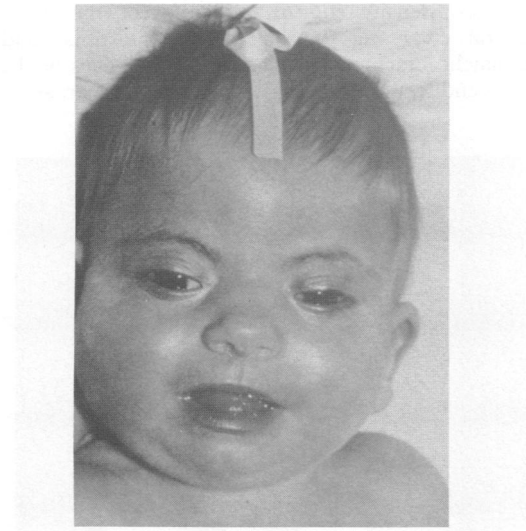

(d)

Figure 1 The distinctive facial appearance in a child with the Schinzel-Giedion syndrome: (a) case 6, (b, c) case 7, and (d) case 8.

consistent feature is the midface hypoplasia, which was present in all cases. Other features include frontal bossing, which was present in nine cases, orbital hypertelorism, and abnormal, low set ears, present in eight cases. All 10 cases had widely open sutures and anterior fontanelle and eight had a short, upturned nose. Two cases had a facial haemangioma.

MAJOR STRUCTURAL ABNORMALITIES (TABLE 2)

Genital

Genital abnormalities are an important feature of this syndrome, being present in all cases. These abnormalities include hypospadias, hypoplastic scrotum, and short penis in males (fig 2), and a deep interlabial sulcus, hypoplasia of the labia majora or minora, hymenal atresia, and a short perineum in females (fig 3).

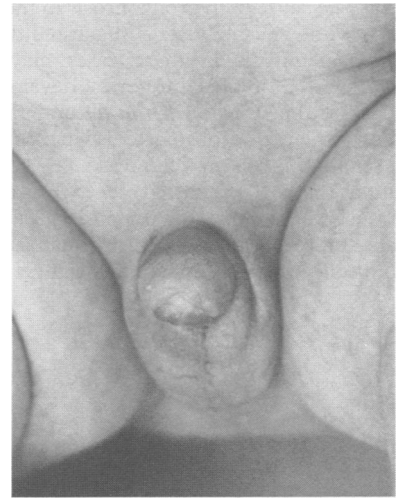

Figure 2 Hypospadias in case 2.

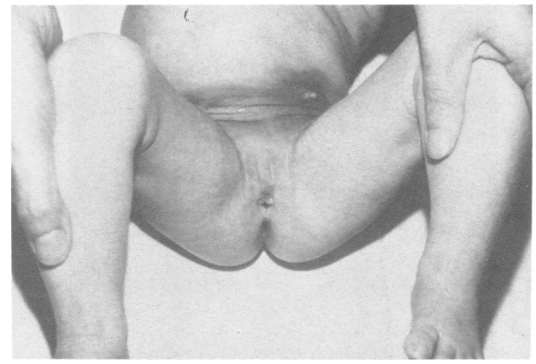

Figure 3 Hypoplasia of the labia majora in case 8.

Table 2 Major structural abnormalities.

	Schinzel and Giedion[1]		Donnai and Harris[2]	Kelly et al[3]	Burck[4]	Present cases				
	1	2	3	4	5	6	7	8	9	10
Genital abnormalities	+	+	+	+	+	+	+	+	+	+
Hydronephrosis	+	+	(+)	+	+	+	+	+	+	−
Congenital heart defect	+	+	−	?	−	−	+	−	−	−
Choanal stenosis	+	+	+/−	−	+	+	−	−	−	−

Renal

Another important clinical feature in these children is renal involvement; eight cases had hydronephrosis, bilateral in six cases (fig 4). One child (case 3) had palpable kidneys on both sides but no radiological investigations were performed. Another child (case 7) had radiological evidence of vesicoureteric junction dysplasia, while in another (case 9) ureteric stenosis was present. The cause of hydronephrosis in the other children is not known. Kelly *et al*[3] suggested that the bilateral hydronephrosis in these cases may be a primary anomaly of pelviureteric development because, despite the severity of the hydronephrosis, there was no evidence of obstructed urinary flow or abnormal renal function in their case.

In a child (case 2) reported by Schinzel and Giedion,[1] the kidneys were low in position and had short, dilated ureters. One child (case 5) had a duplex kidney and collecting system on the right.

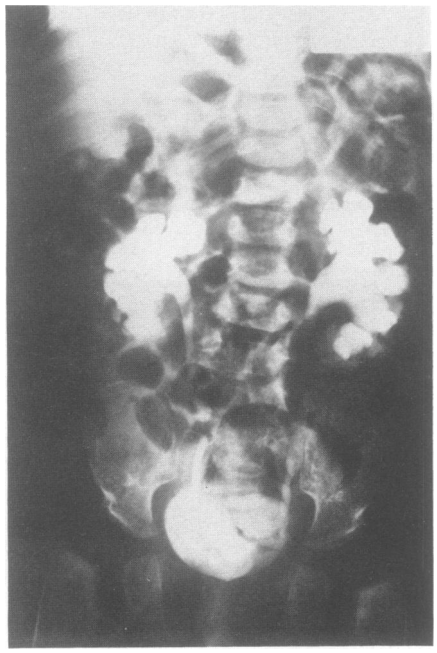

Figure 4 IVP of case 6 showing bilateral hydronephrosis.

Cardiac

Congenital heart disease was present in three cases, being an atrial septal defect in two (cases 1 and 2) and a patent ductus arteriosus in one (case 7).

ENT

Four children had choanal stenosis, being bilateral in two (cases 1 and 6). One child (case 3) was reported to be snuffly and difficult to feed.

SKELETAL ABNORMALITIES (TABLE 3)

Talipes equinovarus was present in seven children, being bilateral in five. Postaxial polydactyly was present in one child and another child had a small forefoot with syndactyly of the second and third toes and overriding toes (case 8). Skeletal radiographs typically show a wide synchondrosis between the exoccipital and supraoccipital bones (fig 5), a steep and sclerotic base of the skull, and multiple wormian bones. The long bones show a broad cortex and increased density (fig 6), widening of the distal femoral ends (fig 7), bowing of the tibia, and mesomelic brachymelia. The distal phalanges of the hands and feet are hypoplastic and the metacarpals of

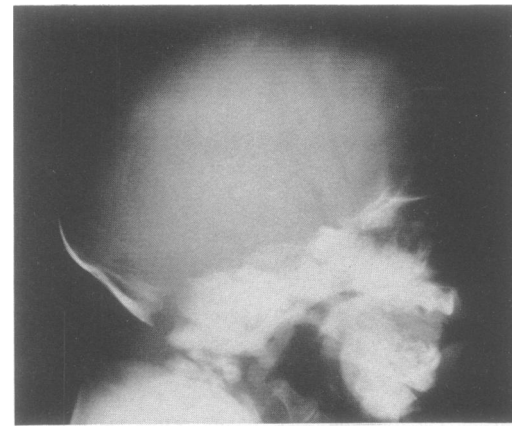

Figure 5 X ray of the lateral skull of case 6 showing sclerotic base of the skull and wide occipital synchondrosis.

Table 3 Craniofacial dysmorphic features.

	Schinzel and Giedion[1]		Donnai and Harris[2]	Kelly et al[3]	Burck[4]	Present cases				
	1	2	3	4	5	6	7	8	9	10
Clinical										
Talipes	+	+	+	+	+	+	+	−	+	−
Postaxial polydactyly	+	−	−	−	−	−	−	−	−	−
Radiological										
Skull										
Short sclerotic base	+	+	−	+	+	+	+	−	+	?
Steep base	+	+	+	+	+	−	−	−	−	?
Wide occipital synchondrosis	+	+	+	+	+	+	−	−	−	?
Multiple wormian bones	+	+	+	+	?	−	−	−	?	?
Long bones										
Broad cortex, increased density	+	+	+	?	−	+	−	+	?	+
Widening of distal femora	−	−	+	−	−	+	+	?	?	+
Tibial bowing	+	?	+	−	−	−	+	−	?	+
Mesomelic brachymelia	−	+	+	+	+	−	+	−	?	+
Hands and feet										
Short thumb metacarpal	+	+	−	−	+	−	+	−	?	?
Hypoplasia of distal phalanges	+	+	+	+	+	−	+?	−	?	?
Chest and abdomen										
Broad ribs	?	+	+	+	+	+	+	+	−	+
Long clavicles	−	+	+	?	?	+	+	+	?	+
Hypoplasia/aplasia of pubic bones	−	+	−	+	−	−	−	+	−	+

the thumbs are short. The ribs are broad with long clavicles (fig 8) and there can be hypo/aplasia of the pubic bones.

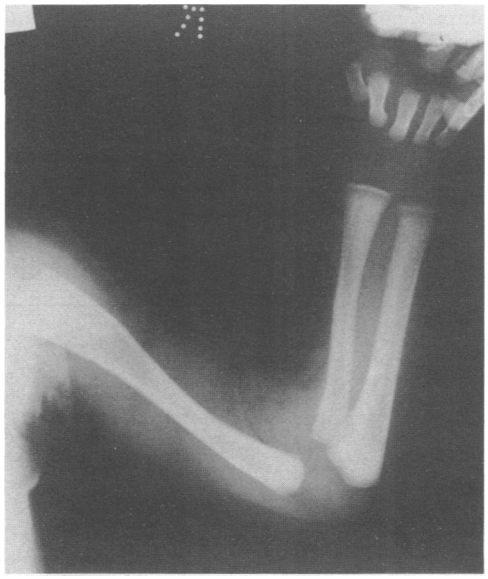

Figure 6 Radiograph of the right arm of case 6 showing a broad cortex and increased density of the bone.

MINOR FEATURES (TABLE 4)

Hypertrichosis at birth was present in nine children. Other frequent minor features include single palmar creases, hypoplastic dermal ridges, hyperconvex nails, redundant neck skin, and hypoplastic nipples.

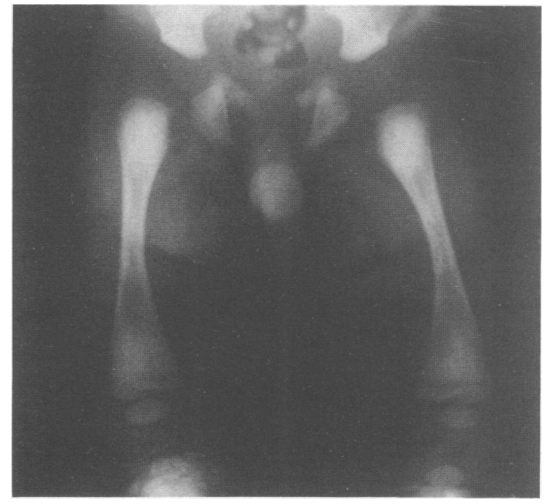

Figure 7 Radiograph of both femora in case 6 showing widening of the distal metaphyses.

Table 4 Minor features.

	Schinzel and Giedion[1]		Donnai and Harris[2]	Kelly et al[3]	Burck[4]	Present cases				
	1	2	3	4	5	6	7	8	9	10
Hypertrichosis	+	+	+	+	+	+	+	+	+	–
Hypoplastic dermal ridges	+	+	+	?	+	?	+	+	+	?
Single palmar crease	–	+	+	+	?	+	–	+	+	?
Hyperconvex nails	–	+	+	+	+	+	?	?	+	?

Natural history and prognosis (table 5)

Four out of the 10 children died, one child at the age of 24 hours and the other three before the age of 2 years. Necropsy was done in only one of these children (case 2). This confirmed the suspected renal and cardiac malformations and in addition showed abnormal gyration of the cerebral cortex.

Eight of the nine children who survived beyond the neonatal period had severe developmental delay and seizures. Seven of these children also had severe spasticity. One child (case 5) had less severe developmental delay, walking at 16 months, but with no words at 2½ years.

CT scan was performed in four of the children (cases 4, 6, 7, and 9). It was completely normal in one child (case 6), and showed moderate ventricular enlargement in one child (case 4), generalised cerebral atrophy including brain stem atrophy in another (case 7), and multiple small areas of atrophy in the last (case 9).

One child (case 5) developed a hepatoblastoma at 2 years of age.

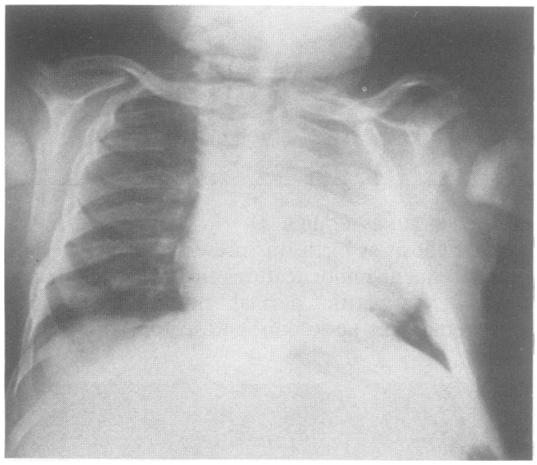

Figure 8 Chest x ray of case 6 showing broad ribs and long clavicles.

Differential diagnosis

The facial appearance of these children resembles the facial appearance of patients with hypothyroidism, one of the mucopolysaccharidoses, or gangliosidosis. These various disorders were excluded by the appropriate screening tests and the absence of characteristic skeletal abnormalities. Children with Rudiger's syndrome have a similar facial appearance, hydronephrosis, and shortening of the long bones, but they lack the other skull and long bone abnormalities found in children with the Schinzel-Giedion syndrome.

Genetics

Although consanguinity has yet to be reported, the

Table 5 Natural history and general features.

	Schinzel and Giedion[1]		Donnai and Harris[2]	Kelly et al[3]	Burck[4]	Present cases				
	1	2	3	4	5	6	7	8	9	10
Sex	F	M	M	F	M	M	F	F	M	M
Birthweight (g)	2900	3880	3500	2870	3550	3710	3970	1530	?	?
Gestation (wk)	41	41	41	36	38	40	40	32	41	?
Growth retardation	+	?	+	+	+	+	+	?	+	+
Developmental delay	+	?	+	+	+	+	+	+	+	+
Convulsions	+	?	+	+	+	+	+	+	+	+
Spasticity	+	?	+	+	+	+	?	+	?	+
Mortality	16·5 mth	1 d	Alive at 10 mth	19 mth	Alive at at 2½ y	Alive at 2y	Alive at 3y	20 mth	Alive at 18 mth	Alive at 27 mth
Chromosomes	46,XX	46,XY	46,XY	46,XX	46,XY	46,XY	46,XX	46,XX	46,XY	—

observation of two unlike sex sibs with this disorder[1] born to healthy, normal parents suggests autosomal recessive inheritance. Alternative possibilities, such as gonadal mosaicism for a dominant gene in one of the parents or an unbalanced structural chromosomal abnormality not detectable with presently available banding techniques, must also be considered.

Prenatal diagnosis could be offered by means of ultrasound at 18 weeks' gestation looking for renal abnormalities and the more severe skeletal abnormalities. It is difficult, however, to know how reliable this might be in practice.

We would like to thank Dr A Schinzel for his help in putting us in touch with colleagues who have children with this disorder.

1 Schinzel A, Giedion A. A syndrome of severe midface retraction, multiple skull anomalies, clubfeet and cardiac and renal malformation in sibs. *Am J Med Genet* 1978;**1**:361–75.
2 Donnai D, Harris R. A further case of a new syndrome including midface retraction, hypertrichosis, and skeletal anomalies. *J Med Genet* 1979;**16**:483–6.
3 Kelly R, Zackai E, Charney E. Congenital hypertrichosis, skeletal dysplasia and severe developmental retardation: the Schinzel-Giedion syndrome. *J Pediatr* 1982;**100**:943–6.
4 Burck U. Mittelgesichtshypoplasie, Skelettanomalien, Apnoen, Retardierung-eine weitere Beobachtung. In: Tolksdorf M, Spranger J, eds. *Wissenschaftliche Information. Klinische Genetik in der Padiatrie*. 3 Symposium in Kiel, Jahrgang 8, Heft 5, 1982.