J Med Genet 1992; 29: 434–436

Two sibs with Wiedemann-Rautenstrauch syndrome: possibilities of prenatal diagnosis by ultrasound

Graciela Castiñeyra, Marcelo Panal, Hector Lopez Presas, Ernesto Goldschmidt, José María Sánchez

Abstract

A girl with Wiedemann-Rautenstrauch syndrome was born to a non-consanguineous couple. During the pregnancy, growth retardation particularly in the biparietal and abdominal diameters but not the femoral length was detected through serial ultrasound scans. When the woman became pregnant again, in spite of having been assessed as having a 25% risk of recurrence, the prenatal findings seen in her previous pregnancy led us to suggest sequential echography and a similar pattern of growth retardation was shown. After termination, the male fetus was found to be affected by Wiedemann-Rautenstrauch syndrome. This case shows that ultrasound examination can be a useful tool in the prenatal diagnosis of this rare, autosomal recessive syndrome.

In 1979, Wiedemann[1] delineated a new progeroid syndrome, based on two personal observations and on two sisters reported by Rautenstrauch and Snigula.[2] Devos *et al*[3] reported another case born to consanguineous parents and proposed the names of Wiedemann-Rautenstrauch or neonatal progeroid syndrome. We report another family with two affected sibs, providing evidence for an autosomal recessive pattern of inheritance of this syndrome, and draw attention to the unusual prenatal findings in both cases found on ultrasound scanning.

Fundación de Genética Humana, Salta 661, 1074 Buenos Aires, Argentina.
G Castiñeyra

GENOS, Genética Periconcepcional y Pediátrica, Fco Acuña de Figueroa 731, 1180 Buenos Aires, Argentina.
M Panal
E Goldschmidt
J M Sánchez

Hospital Zonal de Agudos Narciso Lopez, Lanús, Argentina.
H L Presas

Correspondence to Dr Sánchez.

Received 25 February 1991.
Revised version accepted 6 September 1991.

Case reports

CASE 1

A non-consanguineous couple requested prenatal diagnosis because the woman's brother had Down's syndrome. Paternal and maternal ages were 32 and 30, respectively. They already had a normal daughter.

Amniocentesis was performed during the 16th week of gestation; only mild oligohydramnios was noted.

During the 20th week, the cytogenetic results were received (46,XX) but ultrasound showed that both biparietal and abdominal diameters were on the 5th centile, while the femoral length was on the 50th centile. Three weeks later another ultrasound scan showed that both the abdominal and biparietal diameters were below the 3rd centile; the femoral length was normal. This intrauterine growth retardation pattern was confirmed in each subsequent study until the 36th week of gestation (fig 1). A girl was born at 38 weeks by elective caesarian section. At birth her weight was 1450 g, her length was 47 cm, and her head circumference was 31 cm. She had two neonatal teeth. In spite of the microcephaly, her cranial size seemed to be large in relation to her face and body size. The baby had feeding difficulties, which continued until her death.

At 2½ months of age her weight was 2000 g and her length 49 cm. Her head circumference was 37 cm, showing very rapid growth since birth, making the disproportion between her cranium and face more evident. Her features were strikingly progeroid (fig 2), the hair was sparse, fine, and depigmented, and the cranium showed biparietal bulging, prominent scalp veins, frontal bossing, and a wide open anterior fontanelle. The face was asymmetrical with sunken eyes, low nasal bridge, thin, beaked nose, very high palate, and retrognathia. The neck was short. The limbs were

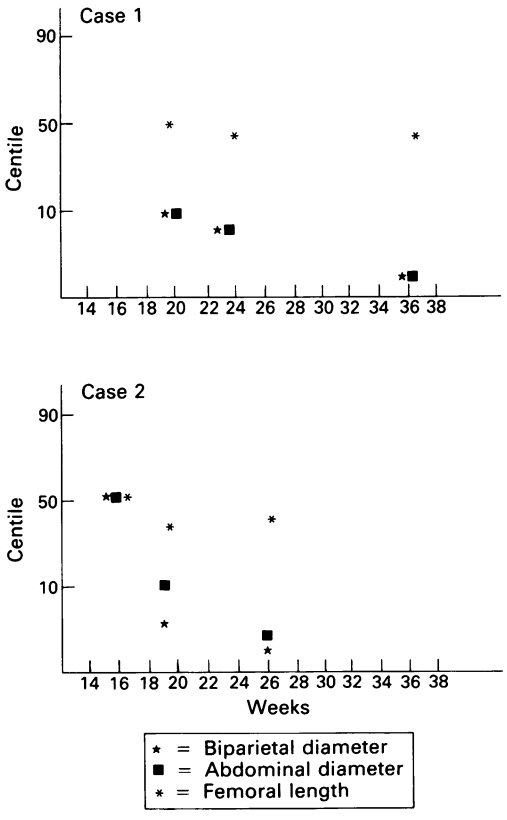

Figure 1 Prenatal development of biparietal diameters, abdominal circumferences, and femoral lengths of cases 1 and 2, assessed through ultrasound scans.

slender and relatively long. In spite of intensive medical care, she became more dystrophic with an almost total absence of subcutaneous fat but with patches of fat in the buttocks. She died at the age of 7 months from a respiratory infection.

The results of laboratory studies were as follows: karyotype 46,XX (G banding), negative TORCH, normal ECG, normal neurometabolic screening (Dr Nester Chamoles), normal blood cholesterol and triglycerides, and normal renal ultrasound. Urine analysis showed bacteriuria. CT scan showed dilatation of all the ventricles with cortical atrophy. There were no densitometric abnormalities. Necropsy (Dr Guillermo Gallo, Buenos Aires Children's Hospital) showed severe growth retardation (weight 4500 g, height 50 cm), relative macrocephaly, and widely open sutures. The brain weighed 525 g (normal 715 g) and had smooth circumvolutions, a subcerebellar cyst, marked dilatation of all the ventricles including the aqueduct of Silvius, very thin corpus callosum, occluded orifices of Lushka and Magendie, and atrophy of the inferior cerebellar vermis. The liver weighed 228 g (normal 254 g) and showed lipid degeneration, the spleen weighed 13 g (normal 20 g) and showed hypertrophy of the white matter, and the thymus was atrophic.

The couple was informed that the diagnosis of the baby was Wiedemann-Rautenstrauch syndrome with a recurrence risk of 25% in each subsequent pregnancy.

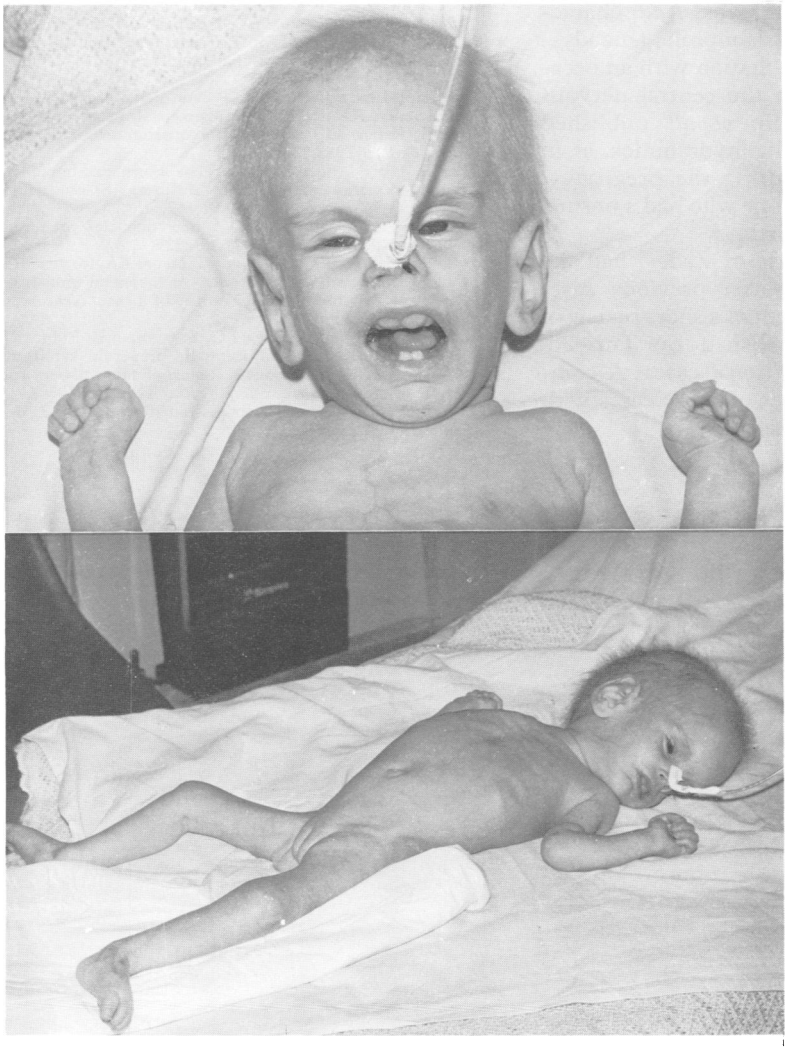

Figure 2 Case 1 at the age of 6 months.

CASE 2

The mother became pregnant 1½ years later and enquired about prenatal diagnosis. She was told that there was no specific prenatal test for the disease. However, as the first affected baby had shown a growth retardation pattern that affected the biparietal and abdominal diameters but spared the femoral length, we intended to find out through serial ultrasound if this fetus showed a similar growth pattern. The scans performed at 12 and 16 weeks gave normal results, but in the 19th week the biparietal diameter was on the 5th centile, the abdominal diameter on the 25th, the femoral length on the 50th, and there was a mild oligohydramnios. In the 25th week of pregnancy the biparietal diameter fell below the 3rd centile, the abdominal between the 3rd and 5th centiles, and the femoral length was on the 50th (fig 1). The oligohydramnios had become more severe. The couple elected to terminate the pregnancy in the 28th week. The fetus was a male with a strikingly similar phenotype to the previous dead girl, including one erupted tooth.

Necropsy (Dr Lopez Presas) showed identical pathological findings, apart from the Dandy-Walker malformation and the ventriculomegaly; however, cerebral cortical atrophy was present.

Discussion

There have been few cases of this syndrome reported. We diagnosed Wiedemann-Rautenstrauch syndrome in the first child because, as can be seen in the table, the proband shared all the signs with the previously reported patients. Particularly significant findings were: senile appearance, neonatal teeth, hydrocephalus, and fat accumulation in the buttocks. In the fetus distinctive features were: one erupted tooth, a similar intrauterine growth retardation pattern, and the accumulation of subcutaneous fat in the buttocks.

In 1977, Rautenstrauch and Snigula[2] reported two sisters with neonatal progeroid syndrome, although they believed that they had Hutchinson-Gilford syndrome; they emphasised the unusual neonatal symptoms along with the presence of neonatal teeth, while in Hutchinson-Gilford syndrome the dentition is usually delayed. In addition, they compared their patient with a previous patient reported in 1940,[4] who shared the same phenotype to the extent that ". . . it would be easy to take them for one and the same child".[2]

In 1979, Wiedemann[1] reported two unrelated male patients seen by him in 1966 and 1977, both with neonatal incisors; he grouped them with those reported by Rautenstrauch

Comparison of features of our patients with previously reported cases.

	Wiedemann[1]		Rautenstrauch and Snigula[2]		Devos *et al*[3]	Rudin *et al*[7]	Present report	
	1	2	1	2			1	2
Birth weight (g)	2200	2550	2380	2110	2100	2500	1450	–
Birth length (cm)	45	49	48	47	48	45	47	–
Head circumference (cm)	NR	NR	32·5	32	33	34	31	–
Sex	M	M	F	F	F	M	F	M
Senile aspect	+	+	+	+	+	+	+	+
Dry skin and hair	+	+	+	+	+	+	+	+
Hydrocephalus	+	+	+	+	+	+	+	+
Prominence of scalp veins	+	+	+	+	+	+	+	+
Large fontanelles	+	+	+	+	+	+	+	+
Parietal bulging	NR	NR	+	+	+	NR	+	+
Triangular face	+	+	+	+	+	+	+	+
Sunken eyes	+	+	+	+	+	+	+	+
Beaked nose	+	+	+	+	+	+	+	–
Low set ears	+	+	+	+	+	+	+	+
Natal teeth	+	+	+	+	+	+	+	+
Long and slender limbs	+	+	+	+	+	+	+	+
Long fingers	+	+	+	+	+	+	+	+
Fat accumulation in buttocks	+	+	NR	NR	+	+	+	–

NR = not reported.

and Snigula[2] as a new syndrome of neonatal progeria. In 1981, Snigula and Rautenstrauch[5] reported a follow up study of their surviving younger patient, adding a personal communication from Curry on another case. In 1981, Devos *et al*[3] reported another patient born to consanguineous parents, providing evidence for autosomal recessive inheritance, and proposed the names by which this syndrome is now known. In 1984, Martin *et al*[6] reported the neuropathological signs of the case published previously by Devos *et al*[3]: characteristic lesions of pure sudanophilic leucodystrophy (extensive demyelination with an occasional tigroid pattern in the central nervous system). In 1988, Rudin *et al*[7] published another case in which oligohydramnios, as in our cases, was noted during the pregnancy; this patient was the only one who had a normal head circumference at birth.

Accepting that the case of Zeder[4] had the same syndrome, only seven previous cases have been reported. Recently, a short review of this syndrome was published by Toriello[8] without adding any additional cases. A comparison of the phenotypes of these cases with ours is shown in the table.

The main differences are that our first patient had Dandy-Walker malformation and her clinical course was extremely grave. It is interesting that our second patient's condition could be strongly suspected prenatally by ultrasound scans from the middle of the second trimester of pregnancy. If similar observations could be carried out in other cases, prenatal diagnosis could be offered to couples at risk.

1 Wiedemann HR. An unidentified neonatal progeroid syndrome: follow-up report. *Eur J Pediatr* 1979;**130**:65–70.
2 Rautenstrauch T, Snigula F. Progeria: a cell culture study and clinical report of familial incidence. *Eur J Pediatr* 1977;**124**:101–11.
3 Devos EA, Leroy JG, Fryns JP, Van den Berghe H. The Wiedemann-Rautenstrauch or neonatal progeroid syndrome. Report of a patient with consanguineous parents. *Eur J Pediatr* 1981;**136**:245–8.
4 Zeder E. Uber Progerie, eine seltene Form des hypophysaeren Zwergwuchses mit diffuser Sklerodermie. *Monatsschr Kinderheilkd* 1940;**81**:167.
5 Snigula F, Rautenstrauch T. A new neonatal progeroid syndrome. *Eur J Pediatr* 1981;**136**:325.
6 Martin JJ, Ceuterick CM, Leroy JG, Devos EA, Roelens JG. The Wiedemann-Rautenstrauch or neonatal progeroid syndrome. Neuropathological study of a case. *Neuropediatrics* 1984;**15**:43–8.
7 Rudin C, Thommen L, Fliegel C, Steinmann B, Buhler U. The neonatal pseudohydrocephalic progeroid syndrome (Wiedemann-Rautenstrauch). Report of a new patient and review of the literature. *Eur J Pediatr* 1988;**147**:433–8.
8 Toriello HV. Wiedemann-Rautenstrauch syndrome. *J Med Genet* 1990;**27**:256–7.