

SHORT REPORT

# The demonstration of monozygosity in twins discordant for sacral agenesis

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Sacral agenesis is usually of sporadic occurrence. It is associated with malformations of the lumbar as well as of the sacral vertebrae and the lower limbs, and also soft tissues including genitourinary tract malformations, anal stenosis or imperforation, congenital heart defect, and cleft lip or palate. The sacral abnormalities that may be seen include hemisacrum, hypoplasia or agenesis of sacral and coccygeal vertebrae, and sacral spina bifida.

The role of genetic factors in the aetiology of sacral agenesis, with its associated urogenital malformations, remains unclear. Despite the fact that most cases are sporadic, with about 15% being associated with maternal diabetes,<sup>1</sup> there have been a number of reports of familial occurrence.

We present here a report of a pair of twins discordant for sacral agenesis. Blood group and HLA determinations and minisatellite DNA probes were used to establish conclusively that these twins were identical.

Twin brothers were born at 34 weeks' gestation on 4.1.63. Twin 2 was of lower birth weight at 2069 g and was born with hypospadias and chordee of the penis. He had sacral agenesis with absence of the sacral vertebrae

below S1 (fig 1), resulting in a neuropathic bladder. He was also found to have a right inguinal hernia and duplication of the right ureter with a ureterocele on the upper pole ureter. He has undergone several surgical repairs of the hypospadias, including more than one urethroplasty, and the right kidney and ureters have been removed. The ureterocele was resected in 1984. He is now 168 cm tall.

His brother, twin 1, had a birth weight of 2552 g. There was a single placenta but the fetal membranes are not recorded. Twin 1 is quite well and has no skeletal or genitourinary abnormality. His present height is 183 cm. Apart from their difference in height the brothers are of similar appearance.

Blood was taken from both twins for blood group determination at the MRC Blood Group Unit and for HLA grouping by the Division of Rheumatology, Clinical Research Centre. Further blood samples were collected for minisatellite DNA determination.

The results of the blood group and HLA determinations, which showed no discordance, are given in the table. Taken together the blood group determinations (using the tables of Smith *et al*<sup>2</sup>) and HLA findings give a



Figure 1 Radiograph of sacrum of proband.

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Blood group and HLA determinations.

	ABO	MN	S	Pl	Rh	Lu <sup>a</sup>	K	k	Le <sup>a</sup>	Le <sup>b</sup>	Fy <sup>a</sup>	Xg <sup>a</sup>	HLA-A	HLA-B	HLA-C	HLA-D
Twin 1	A2	MN	-	+	R1 R2	-	+	+	-	+	-	+	2,28	7, 51, w4, w6	w7, -	DR4, -
Twin 2	A2	MN	-	+	R1 R2	-	+	+	-	+	-	+	2,28	7, 51, w4, w6	w7, -	DR4, -

probability of 99.46% that the twins are monozygotic. The minisatellite DNA studies showed identical patterns of DNA fragments for the two twins (fig 2).

Blood group and HLA markers give either a clear discordance with inevitable dizygosity or

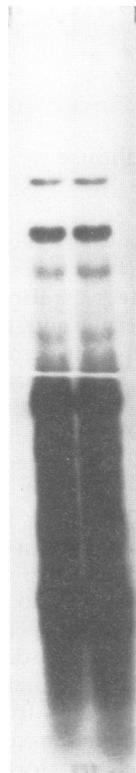


Figure 2 Autoradiograph of genomic DNA of the proband (twin 2) on the right and his twin on the left, probed with the minisatellite probe 33.63 after HaeIII restriction enzyme digestion.

a very high probability of monozygosity, as here, but cannot give absolute certainty of monozygosity. Hill and Jeffries<sup>3</sup> have shown the use of minisatellite DNA probes in zygosity determination of newborn twins. Twins will only give identical autoradiographic patterns with these probes, as here, if they are monozygotic. This approach is likely to prove especially valuable in twins studied after the neonatal period.

These findings suggest the operation of unknown environmental factors in the aetiology of sporadic sacral agenesis, but do not preclude genetic predisposition as well.

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- 1 Welch JP, Aterman K. The syndrome of caudal dysplasia: a review, including etiologic considerations and evidence of heterogeneity. *Pediatr Pathol* 1984;2:313-27.
- 2 Smith SM, Penrose LS, Smith CAB. *Mathematical tables for research workers in human genetics*. London: Churchill, 1961.
- 3 Hill AVS, Jeffries AJ. Use of minisatellite DNA probes for determination of twin zygosity at birth. *Lancet* 1985; ii:1294-5.