Case reports

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Hirschsprung disease associated with polydactyly, unilateral renal agenesis, hypertelorism, and congenital deafness: a new autosomal recessive syndrome

HELOISA SANTOS, JOÃO MATEUS, AND MARIA J LEAL

From the Department of Pediatrics, Santa Maria Hospital, Lisbon, Portugal.

SUMMARY An association of Hirschsprung disease with polydactyly, unilateral renal agenesis, hypertelorism, and congenital deafness is described in sibs (brother and sister) of consanguineous parents. It is suggested that this might represent a new autosomal recessive syndrome.

The incidence of Hirschsprung disease is about 1:5000 births, with a sex ratio of four males to one female.¹ This condition is generally regarded as a multifactorial disorder and three major family studies¹ have been useful in estimating the recurrence risk in sibs. Congenital intestinal aganglionosis may also occur in a number of other chromosomal,^{1 2} Mendelian,^{1–6} and neural crest disorders.^{1 3 7 8} We present here a genetic, previously undescribed association of Hirschsprung disease with polydactyly, unilateral renal agenesis, hypertelorism, and congenital deafness.

Case report

The patient was a three year old boy (fig 1) from the Portuguese islands of Azores. There was no history of exposure to drugs during pregnancy.

The delivery, after spontaneous onset of labour, was normal and occurred at home with no medical support. The infant was in good condition and his birth weight was 3750 g. Polydactyly of the toes was noted.

At three months of age he was first referred for constipation and abdominal distension. Diagnosis of classical Hirschsprung disease was made on the basis of rectal biopsies, which showed absence of ganglion cells up to 6 cm above the anus. At three years of age a Soaves procedure was carried out and during

operation absence of the left kidney was suspected. Ultrasound confirmed left renal agenesis.

On clinical examination (fig 1) the child had hypertelorism (inner and outer canthal distances of 3 cm and 8.5 cm respectively) and polydactyly of the toes (fig 2). ERA revealed a moderate degree of congenital sensorineural deafness (cochlear type, with an auditory level of 40 to 50 dB SPL). He had brown eyes, brown hair, and no depigmented patches on the skin. Cardiac malformations were excluded.

FIG 1 The patient at three years of age.

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FIG 2 Radiograph of the feet showing bilateral polydactyly of the toes.

Developmental evaluation using the Griffiths scale showed subnormal results (general quotient 37.4%, mental age 14.1 months, chronological age 40.6 months).

Cytogenetic studies of peripheral blood cultures revealed a normal 46,XY karyotype.

Family history

The proband was the sixth child of a consanguineous marriage; the parents were first cousins. The oldest sister died during the second week of life after a surgical procedure for intestinal obstruction and had polydactyly of the hands and feet. There was no other family history of polydactyly, Hirschsprung disease, or deafness.

Discussion

Classical Hirschsprung disease is believed to be inherited as a multifactorial trait.^{1 2 5} Defective embryonic migration of the neural crest cells or

abnormalities of their intestinal target seem to be the result of the action of both genetic and probably unknown environmental factors.¹ Several genetic disorders where Hirschsprung (classical and long segment) disease occurs with other anomalies have been previously described and some Mendelian disorders, almost all autosomal recessive, are associated with intestinal aganglionosis.

It is interesting to note that isolated abnormalities described in association with congenital intestinal aganglionosis are neural tube defects,⁸ neural crest cell diseases,¹ and intestinal malformations.^{1 2} In this particular family, aganglionosis was not investigated in the oldest sister, but it is possible that one may be dealing with a new disorder with autosomal recessive inheritance, distinct from the one reported by Laurence *et al*,² in which two male infants were described with Hirschsprung disease and polydactyly. These also had congenital heart malformations in contrast to the hypertelorism, renal agenesis, and congenital deafness which were present in our patient.

The association of defects in the present family may not be fortuitous but the result of a common pathophysiological cause, which may help us to understand more fully the embryogenesis of Hirschsprung disease.

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Correspondence and requests for reprints to Dr Heloisa Santos, Unidade de Genética, Serviço de Pediatria, Hospital de Santa Maria, 1699 Lisboa Codex, Portugal.