

Concordant expression of Hirschsprung's disease in monozygous twins

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ABSTRACT

A monozygous pair of twins with long segment Hirschsprung's disease born to non consanguineous parents is presented. Mother's history was uneventful. In the absence of prenatal and postnatal illness, the concordant lesions in this pair could be attributed to genetic factors.

Keywords: Hirschsprung's disease, twin children.

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Absence of ganglion in Hirschsprung's disease (HD) is attributed to the failure of distal migration of the neuroblasts in the gut in the early developmental stage.¹ Both environmental and genetic factors have been suggested as a cause of HD. Its occurrence in twins has attracted considerable attention, while considering the etiogenesis. Concordance of HD is rare, and has been described earlier.² Here we present an additional incidence of HD in twins born to non-consanguineous Arab parents. Both the twins had a similar history of presentation as well as similar extent of involvement of the bowel. The occurrence of long segment disease in this twin pair may well be genetically determined.

Case Report. Twin males were born after one and half hours of labor to a 30 year old mother at 36 weeks gestation. She was neither hypertensive nor diabetic and had no serious illness, nor taken drugs during the pregnancy.

Twin 1 was a 2.7 kg newborn and did not pass meconium for the next 5 days. Glycerine suppositories were prescribed by a general practitioner following which he was able to pass stools frequently but gradually developed abdominal

distension. This treatment was continued for 4 months and at this time the parents brought him to our hospital for further advice. Clinically HD was suspected and barium enema studies were performed which revealed a long narrowed segment with coning (Figure 1). Diagnosis of HD was further confirmed by full thickness posterior wall rectal biopsy. Since frozen section biopsy facilities were not available in our hospital, laparotomy was carried out to decide the exact level of presence of ganglion and also to perform the diversion proximal transverse colostomy to relieve the distension and as a preliminary procedure prior to a future definitive operation. The colonic sites of biopsies were marked with colored threads to identify them at the next surgical stage. In this patient, the aganglionic segment extended up to the splenic flexure. The patient recovered from this procedure and is awaiting a definitive operation at a later date.

Twin 2 also had a history of failure to pass meconium for the next 5 days after birth but later started passing stools 2-3 times a day after the use of suppositories. However, gradually abdominal distension developed and at 5 months of age he was brought to our unit. The reason for this visit was that he had not passed stools continuously for 5 days

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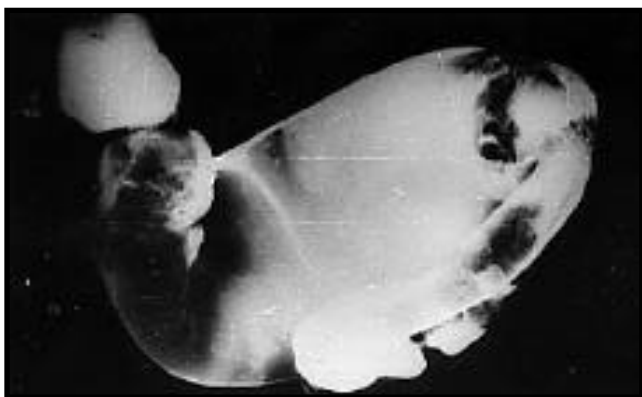


Figure 1 - Barium enema study showing typical coning and narrowing segment of colon.

and had developed severe abdominal distension. He was admitted immediately and similar initial investigations and surgical procedures were performed in this twin as the first. At laparotomy, the extent of the aganglionic segment and coning was exactly similar to the first twin.

The obstetrical history of the mother indicated that the placenta was single and common for both the twins. The blood group of both was A, Rh positive. We were not able to do human leukocyte antigen typing as facilities were not available. There was no history of consanguinity in the parents and they were not from the same tribe. A first pregnancy had ended in abortion but another 2 male and 2 female children were healthy. The uncles and aunts of these infants were normal. They had no symptoms suggestive of HD.

Discussion. Here in these twins, monozygosity was supported by sharing a single common placenta. Low birth weights, progression of the disease and the extent of the aganglionic segments in the left colon were almost the same. Whatever may have been the cause of the arrest of the neuroblasts or destruction of the existing ganglion cells, it had affected both the twins in a similar way. In both of them, various etiological possibilities could be considered to explain the symmetrical involvement of left colon. Since pregnancy was drug free and the mother had no illnesses during the gestation period, it is unlikely that these were the causative factors. Experimental attempts have demonstrated that destruction of the ganglion cells is possible under certain circumstances. Destruction of colonic mesenteric plexus was achieved in dogs by occlusion of the colon and inferior mesenteric artery along with perfusion of the artery by Tyrode's solution for 4 hours.³ A number of years later Moore et al⁴ described an occurrence of HD discordant in monozygous twins. One of their patients

experienced extreme stress due to respiratory distress, prolonged umbilical catheterization, necrotizing enterocolitis and seizures. It was thought that the postnatal stress would have contributed to the destruction of the ganglion cells in their seriously ill patient. Similarly, presence of an unknown cause during the perinatal period was suggested to explain the gradual destruction of ganglion cells in one of the HD discordant twins.⁵ In our patients no similar situation was present which could have contributed to the disease.

Hirschsprung's disease has been described in the families^{6,7} thus strongly supporting the etiological role of genetic factors in some patients. Both dominant and recessive mode of transmission have been proposed. Reyna⁸ has reported an extended family of index patients with 54 members, of which, proved HD was encountered in 6. The disease occurred in offsprings of both affected and unaffected parents indicating a possibility of autosomal dominant inheritance. Others⁹ found that in a long segment HD, the mode of inheritance was compatible with a transmission by a dominant gene with incomplete penetrance, while in a short segment HD not extending above the rectosigmoid, the inheritance pattern was suggestive of autosomal recessive with a low penetrance. Considering the family history and absence of detectable positive perinatal factors, it is reasonable to suggest, that long segment disease observed in our patients may have been the expression of an incomplete penetrance of an autosomal dominant gene.

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