Crohn's disease in monozygotic twins

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Summary: A pair of monozygotic twins with Crohn's disease is described. Both have ileocaecal disease and suffered their first symptoms after living apart for 6 years. The pathogenic role of hereditary and environmental factors is discussed in the light of this and previous reports of twins with Crohn's disease.

Introduction

Seventeen pairs of identical twins concordant for Crohn's disease have been recorded (Table I). We describe a further set of affected twins unusual in that the disease developed simultaneously and at the same site in each patient at a time when they had been living in different environments for 6 years. As in a minority of previous reports (Crismier *et al.*, 1963; Goldstein *et al.*, 1976; Morichau-Beauchant *et al.*, 1977; Klein *et al.*, 1980; Gonzalez *et al.*, 1983), monozygosity in our patients was investigated by histocompatibility typing and blood group analysis.

Case histories

The twins were delivered 6 weeks prematurely in 1956; information about the placenta is unavailable. At the age of 2 years, on account of their mother's mental illness, they were transferred from their parental home into the same residential accommodation. They left this home to live apart in 1978. There was no other family history of inflammatory bowel disease.

Twin A

In early 1984 she had several weeks of abdominal pain, nausea and watery diarrhoea. The symptoms recurred in September and persisted until her referral to hospital in November 1984. Examination, including sigmoidoscopy, was normal. Her haemoglobin concentration was 10.7 g/l, and erythrocyte sedimentation rate (ESR) 47 mm in the first hour. Small bowel enema and barium enema showed narrowing, spasm and abnormal sinus tracks in the terminal ileum and caecum with matted loops of adjacent bowel. Colonoscopy, performed after she had started on steroid therapy, showed mucosal oedema, cobblestoning and

aphthous ulceration around the ileocaecal valve with the opening of a sinus visible just proximal to it; the remainder of the large bowel was normal. Rectal biopsy was normal but biopsies from the caecum showed patchy active inflammation with foci of ulceration; no granulomata were seen. Treatment with prednisolone, iron, folic acid and vitamin B₁₂ injections produced rapid symptomatic and haematological improvement, and at the time of writing she remains in remission.

Twin B

In January 1984 she developed erythema nodosum and reported diarrhoea for several weeks. She was passing loose motions two or three times daily, usually provoked by specific foods such as onions, without blood or mucus. There was no abdominal pain but she had lost weight. Examination was normal. Her ESR was 54 mm in the first hour but there were no other haematological or biochemical abnormalities. Barium studies showed typical Crohn's disease of the terminal ileum with mucosal thickening and ulceration. She made a partial response to a short course of steroids but because of persistent symptoms had a colonoscopy in July 1985: this showed involvement of the caecum and terminal ileum with cobblestoning and serpiginous ulcers. Biopsy showed mucosal ulceration and inflammation and although no granuloma was seen the histology was consistent with the diagnosis of Crohn's disease. She was therefore recommenced on prednisolone 20 mg/day. Her symptoms settled, her ESR fell to 13 mm in the first hour and she regained weight. She is presently well on reducing doses of steroids.

Monozygosity

The twins are of similar appearance. The histocompatibility type of each, determined by the microlym-

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phocytotoxic technique, was A2, A3, B7, B15 (62), BW6, CW3, CW7, DR7, possible DRW8. Their blood groups were also identical: B, R₁r(CD̄₅/c̄dē), MNS̄_s, P₁ positive, Lu^{a-b+}, Kell negative (k̄k), Kp^a negative, Le^{a-b+}, Fy^{a+b+}, JK^{a-b+}.

Discussion

Although in neither patient were granulomata found on microscopic examination of biopsy specimens, there seems little doubt from the clinical, radiological and colonoscopic findings, as well as their response to treatment, that this is the eighteenth pair of monozygotic twins with Crohn's disease, and only the fifth living apart at the onset of symptoms, to be reported (Table I).

Calculations based on the prevalence of Crohn's disease in the general population (about 50/100,000) (Miller *et al.*, 1974) and of monozygotic twins (360/100,000) indicate that there are far more recorded instances of identical twins concordant for Crohn's than can be explained by chance alone (Goldstein *et al.*, 1976; Morichau-Beauchant *et al.*, 1977; Carlisle & Hersh, 1978; Almy & Sherlock, 1966). In addition, published reports suggest that Crohn's disease occurs

more commonly in monozygotic twins than does ulcerative colitis, which has a prevalence of about 80/100,000 (Evans & Acheson, 1965) but for which only 5 concordant pairs of identical twins have been recorded (Mayberry *et al.*, 1982) (χ^2 test, $P < 0.001$).

Crohn's disease occurring in monozygotic twins living together sheds little light on the relative importance of inherited and environmental factors in its pathogenesis. Our twins resembled two other pairs (Niederle, 1961; Morichau-Beauchant *et al.*, 1977) in having the same region of gut affected and a simultaneous onset of symptoms after living for some years in separate environments. Either genetic predisposition or environmental influences operating prior to their separation could theoretically explain these observations; exposure to the same environmental factor after the twins' separation is much less likely. However, no single inherited or environmental factor can be invoked to account for these cases as well as those concordant identical twins living in the same environment but with different distributions of disease (Goldstein *et al.*, 1976; Klein *et al.*, 1980; Gonzalez *et al.*, 1983; Weterman & Peña, 1984) or times of onset differing by up to 6 years (Freysz *et al.*, 1958; Crismer *et al.*, 1963; Goldstein *et al.*, 1976; Gonzalez *et al.*, 1983; Weterman & Peña, 1984): neither can cohabiting

Table I Published cases of identical twins concordant for Crohn's disease

Reference	HLA/blood group analysis	Age at onset (years)	Site in each twin	Environment at onset
Edwards (1954)	—	27/30	Ileum/ileum	Unstated
Freysz <i>et al.</i> (1958)	—	59/63	Ileum, colon/ileum, colon	Same
Niederle (1961)	—	50/50	Ileum/ileum	Different (30 years)
Crismer <i>et al.</i> (1963)	Yes	18/23	Ileum, colon/ileum, colon	Same
Sherlock <i>et al.</i> (1963)	—	44/44	Ileum/ileum	Unstated
Hislop & Grant (1969)	—	27/28	Ileum/ileum	Unstated
Milton-Thompson & Lennard-Jones (1971)	—	Unstated	Colon/colon	Unstated
Berg & Dencker (1972)	—	21/21	Ileum, colon/ileum, colon	Same
Goldstein <i>et al.</i> (1976)	Yes	13/17	Ileum, jejunum/ileum, jejunum, stomach	Same
Morichau-Beauchant <i>et al.</i> (1977)	Yes	32/32	Ileum/ileum	Different (10 years)
Carlisle & Hersh (1978)	—	Unstated	Unstated	Unstated
Hellers (1979)	—	Unstated	Unstated	Unstated
	—	Unstated	Unstated	Different
	—	Unstated	Unstated	Different
Klein <i>et al.</i> (1980)	Yes	14/14	Ileum, colon, oesophagus/ileum, colon, mouth	Same
Gonzalez <i>et al.</i> (1983)	Yes	11/13	Ileum, colon/ileum, colon, oesophagus	Same
Weterman & Peña (1984)	—	20/22	Ileum/ileum, colon	Same
Present report	Yes	27/27	Ileum, caecum/ileum, caecum	Different (6 years)

monozygotic twins discordant for Crohn's (Weterman & Peña, 1984) be easily explained. Other approaches are required to unravel the complex inter-relationships between nature and nurture in the pathogenesis of Crohn's disease.

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