Clinical Problems

Problems in distinguishing tuberculosis of bowel from Crohn's disease in Asians

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Summary

The cases of five immigrants with definite or almost certain intestinal tuberculosis are described. Because of the clinical, pathological, and radiological features all were thought at some time, often for long periods, to have Crohn's disease. Recommendations are made for medical and surgical treatment.

Introduction

Tuberculous disease of the intestine as a complication of pulmonary tuberculosis is well recognized. In an American survey covering the years 1924-49, an incidence of 1 in 16 cases was found on routine alimentary radiography.¹ In Western Europe, however, ulcerative tuberculous intestinal disease is rare. Before Crohn² described regional ileitis, and for some years afterwards, many such cases were treated as alimentary tuberculosis.³ Now, however, such misdiagnoses are rarely made.⁴

We report five cases of intestinal tuberculosis to show that it is common in Britain and that its differential diagnosis from Crohn's disease may still present considerable diagnostic difficulties.

Present series

The five patients were examined by us. All had been under the care of the East Birmingham Hospital, which treats most cases of tuberculosis in Birmingham.

CASE 1

A 23-year-old Pakistani man was admitted to hospital as an emergency on 2 February 1971 with abdominal pain, vomiting, and diarrhoea for three days. He was feverish and tender in the right iliac fossa. A plain erect film of the abdomen showed gas under the right cupola of the diaphragm and paralytic ileus. Perforated duodenal ulceration was diagnosed. He was treated with gastric suction and intravenous fluids and rapidly recovered. Seven weeks later barium-meal examination (no follow-through) showed no abnormality.

In May 1971 he presented with suprapubic pain and dysuria. He was tender in the rectovesical pouch. An intravenous pyelogram was normal. Barium-enema radiography suggested spasm at the rectosigmoid junction with rigidity of the sigmoid colon. Sigmoidoscopy was inconclusive and the urine was normal. A speculative diagnosis of diverticulitis was made.

In November 1971 he was again seen, with abdominal pain, constipation and diarrhoea, dysuria and frequency, and a loss of 6-7 kg in weight. He was afebrile with tenderness in the right lower abdomen and was thought to have a pelvic abscess. Cystoscopy showed nothing abnormal, sigmoidoscopy suggested a fixed bowel with granular mucosa, but a barium enema showed at least three internal fistulae arising from the rectum, rectosigmoid, and distal sigmoid colon. Barium meal and follow-through examination confirmed fistulae between small intestine and sigmoid and rectum and between loops of small bowel. The terminal ileum had a narrowed lumen with proximal stasis and dilatation. The appearances were thought to be almost certainly those of Crohn's disease. A parasitic cause was excluded. His symptoms did not improve with azothiaprime, and prednisolone was added.

In March 1972 he was again admitted with abdominal pain and weight loss. Chest x-ray examination showed a left apical focus suggestive of tuberculosis. *Mycobacterium tuberculosis* was cultured from faeces, urine, and sputum. He responded rapidly to specific chemotherapy, with radiological improvement. The time from initial presentation to diagnosis was 14 months.

CASE 2

A 10-year-old Indian boy was admitted to hospital in August 1962 with apparent acute appendicitis. Laparotomy showed a normal appendix but a large mass was discovered in the caecum. The mesenteric nodes were involved and enlarged. An ileotransverse colostomy was carried out. Histologically the nodes showed conspicuous follicular hyperplasia with per follicular fibrosis thought to be compatible with non-specific mesenteric adenitis. Crohn's disease was evidently considered because of the culture and agglutination techniques used to exclude *Pasteurella pseudotuberculosis*. All gave negative results. Tuberculosis must have been considered because guinea-pig inoculation was done, though there is no record of a report.

He continued to complain of intermittent right-sided pain and was readmitted in November 1963. Barium studies showed a narrowing of the terminal ileum and ascending colon with a functioning colostomy. Though the Mantoux test produced a strongly positive reaction no specific chemotherapy was given because a mass in the right iliac fossa appeared to resolve spontaneously with his other symptoms. Crohn's disease was thought likely.

Chest x-ray examination in February 1964 confirmed a primary, probably calcified, complex. The intermittent abdominal pain continued, and in the November he was readmitted as an emergency with severe pain in the right iliac fossa and flexor spasm of the right hip. Several days later an abscess discharged spontaneously on to the anterior abdominal wall above Poupart's ligament. *M. tuberculosis* was cultured from this. Wound scrapings showed caseating granulomatous inflammation with much secondary infection. Specific chemotherapy was begun. Barium-meal film in January 1965 suggested that the colostomy was not functioning and showed gross disease of the terminal ileum with "skip" areas. The radiologist, reporting blind, thought the features more consistent with Crohn's disease than tuberculosis. The chest lesion looked active.

Despite treatment the fistula continued to discharge periodically for 18 months but with serially negative cultures. The haemoglobin fell to 4 g/dl. His final admission was in October 1966, when his fistula was discharging profusely and he had a swinging temperature. Barium enema confirmed a functioning colostomy and filling of the ileum via this. The ileal loop distal to the anastomosis was grossly dilated and contained faeces. The ascending colon was narrowed and shortened. The external fistula was filled. There was considerable stasis in the dilated blind loop, which emptied slowly via the anastomosis alone and was still filled at 48 hours.

In November 1966 terminal ileostomy and ascending and partial transverse colectomy were carried out. Postoperatively the fistula closed and the patient rapidly regained his health. He remained well.

CASE 3

A Pakistani woman aged 54 was admitted to hospital on 19 February 1970

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with acute intestinal obstruction. Laparotomy showed ileocaecal obstruction secondary to a craggy mass in this region with an ulcer crater some 7.5 by 7.5 cm palpable through its wall and a few tubercle-like lesions on the serosal surface of the ileum. A side-to-side ileotransverse anastomosis operation was performed and an elective right hemicolectomy carried out at a later date. Mesenteric nodes were removed.

Examination of the colonic specimen confirmed that the ulcer and chronic inflammatory exudate extended through all layers and showed many tubercles with giant and epithelioid cells. Exudate was largely lymphocytic. "Tubercles" were also present in the lymph nodes. No caseation was noted, and no tubercle bacilli were found on specific staining. The pathologist thought that the lesion could be Crohn's disease or tuberculosis but that the former was the more likely. The chest x-ray picture was normal. The result of the Mantoux test was not recorded. She was discharged on no specific treatment and lost to follow up.

In November 1973 she was readmitted with a year's history of anorexia, loss of weight, and abdominal pain. Chest x-ray examination showed infiltration of left mid and upper zones consistent with active tuberculosis. A barium follow-through study of the jejunum and ileum showed no abnormality. At the site of the anastomosis there was a consistent narrowed segment of bowel 10 cm long. The mucosa was destroyed and deep "rose-thorn" ulcers were present. Distal to these a segment of large bowel at the splenic flexure was less grossly affected with a further "skip" area and another area of gross disease. The changes were thought to represent the classical features of a granuloma but with reference to the chest x-ray picture probably were tuberculous rather than a result of Crohn's disease.

M. tuberculosis was isolated from three sputum specimens and from one stool culture at seven weeks. She responded rapidly to rifampicin, streptomycin, and isoniazid but three months later had symptoms and evidence on barium-meal examination of subacute obstruction of the descending colon. She did not complain further but proved difficult to persuade to undergo further radiological studies though remaining on drugs.

CASE 4

A 31-year-old Pakistani man presented in August 1973 with severe loss of weight and abdominal pain. He was found to have a low-grade continuous fever and a discrete mass in the right iliac fossa which was not always palpable. Chest x-ray film suggested a focus of doubtful radiological activity in the left upper zone.

On 13 September the appearances on barium meal and follow-through examination were reported as normal. Barium enema several weeks later showed a narrowing of 5 cm of the transverse colon with a cobblestone appearance of the surface pattern and irregular contours. The ascending colon was narrowed, with loss of haustration and "collar-button" ulcers. Radiologically the overall appearance was thought to be strongly suggestive of Crohn's disease. Though the reaction to a Mantoux test was strongly positive, mycobacteria were never cultured. Antituberculosis treatment was begun in October and the patient's condition dramatically improved, with resolution of the temperature and rapid weight gain. Barium-enema examination one month later confirmed the above appearances and also showed a fistula between ileum and ascending colon. A follow-up enema in August 1974 confirmed clearance of the "collar-button" ulcers and resolution of the cobblestone appearance of the transverse colon with smooth contours; the fistula, however, remained.

CASE 5

A 35-year-old Indian woman presented on 6 May 1971 with an apparent appendix abscess. This was treated conservatively with surgery planned for a later date. She failed to attend for the operation.

On 28 March 1972 she again presented but with a loss of 8 kg and occasional fever. A vague mass was palpable in the right iliac fossa. Chest x-ray appearances were normal. Mantoux test result was not recorded. A barium meal and follow-through examination showed delay at the terminal ileum. These loops were dilated, indicating some degree of stenosis or obstruction distally. The hold-up remained at 24 hours. The radiological appearance was thought to be that of ileocaecal tuberculosis. She was given para-aminosalicylic acid and isoniazid for three months at a convalescent hospital, from where she was referred in July 1972 with subacute intestinal obstruction. At operation multiple adhesions were found around the caecum, the distal ileum being distended. Numerous fleshy mesenteric nodes were excised. A right hemicolectomy was carried out and she was discharged on no specific treatment.

The surgical specimen showed ulceration with deep fissures into the muscularis mucosa which in turn exhibited widespread granulomatous giant-cell inflammation. There were multiple giant-cell follicles in the nodes. The specimen was a 15-cm length of bowel. A firm diagnosis of Crohn's disease was made.

Postoperatively the patient gained 12 kg and had a normal pregnancy—perhaps pertinent to a diagnosis of "Crohn's" disease. Chest x-ray examination in April 1973 showed a small opacity in the left mid zone. This was unchanged in November 1973 and observation was continued. She remained well and received only three months of antituberculosis chemotherapy, a decision presumably based on the pathology report. A barium enema in August 1974 showed no abnormality either in the large bowel or at the stoma.

Discussion

In the past 15 years various forms of tuberculosis have been common in immigrants in Birmingham and elsewhere in the U.K.⁵ Though Crohn's disease is rare in India and Pakistan,⁶ it remained the principal diagnosis for long periods in four patients in the present series. Fortunately only one had been given immunosuppressive treatment. In case 4 the patient had radiological features indistinguishable from Crohn's disease but responded well to antituberculosis treatment. This patient was the only one to present to a physician daily seeing tuberculosis patients.

The interval between laparotomy and confirmation of tuberculosis (we include case 5 in this category) varied from 14 to 27 months. With the possible exception of one case, however, tuberculosis was always considered and frequently sought by the surgical teams. In Howell and Knapton's series,³ also from Birmingham, a woman with ileocaecal tuberculosis who had an internal colostomy went 10 years before developing symptoms needing antituberculosis chemotherapy. Two patients in our series (cases 3 and 5) had a hemicolectomy. This and three months of chemotherapy in case 5 may have accounted for the non-recurrence in one case and the interval of three and a half years in the other.

Lee and Roy,⁷ who reviewed 15 cases of granulomatous disease of the ileocaecal area, pointed out that pathologically the only significant alternative to Crohn's disease is tuberculosis. They stressed that the presence of caseation and the demonstration of acid-fast bacilli are the only indicators of distinction from Crohn's disease. In other sections of specimens in which caseation has been found this latter change may be absent. In such areas the appearances are indistinguishable from Crohn's disease. Howell and Knapton³ underlined this pathological difficulty. In favour of tuberculosis, apart from caseation and the demonstration of bacilli, they took to be the presence of large numbers of follicular lesions, some undergoing coalescence. The more typical tuberculous reaction was found in the draining lymph nodes, even when these were not obviously enlarged. Commenting that caseation may be rare in other conditions, they affirmed that its presence even in the absence of bacteriological proof should be considered characteristic of tuberculosis of the intestine.

The presence of tubercles on the serosal surface of the small bowel found at operation in case 4 was compatible with Crohn's disease. Heaton *et al.*⁸ drew attention to this finding at laparotomy in cases of early Crohn's disease—that is, before bowel wall involvement. Tuberculous tubercles are usually more widespread.

With the above factors in mind we believe that a histological diagnosis of tuberculosis could have been made earlier in cases 2, 3, and 5 from the pathological findings. The importance of culturing all specimens direct from the operation and before fixation is worth emphasizing. Caseation should be sought throughout the length of the resected segment.

The radiological problems of differentiating between tuberculous and Crohn's disease of the small and large intestine are well known. Marshak and Lindner¹⁰ commented, "We have been unable to differentiate tuberculosis of small bowel from regional ileitis radiologically. As a rule, in tuberculosis there is deeper ulceration, more irregular scarring and marked stricture formation." Cummack¹¹ also underlined the close radiological similarity between the two conditions. He stated that a barium follow-through study is the best method of examination but that in many instances a barium enema gives further information (see, for example, our case 4). Chronic tuberculosis, he commented, "does lead to shortening, particularly in the caecum and ascending colon, so that the terminal ileum leads directly into the colon without the usual angle at the ileo-caecal valve." Anscombe *et al.*¹² noted that these latter pointers held true when differentiating malignant from tuberculous caecal disease. That this extreme difficulty in differentiation is well recognized was evidenced by the comments of the radiologists reporting on the present five patients.

Hawkins¹³ stated that a normal chest x-ray picture virtually excludes bowel tuberculosis. Singh *et al.*¹⁴ found evidence of lung parenchymal disease in 6% of their cases of tuberculous peritonitis. Panstian and Bockus¹⁵ described one confirmed case in the absence of chest x-ray changes. Kogan and Janowitz¹⁶ commented that extensive tuberculous peritonitis could occur with minimal as well as florid pulmonary disease. In only one of our five cases was there any suggestion of lung parenchymal tuberculosis, and that was doubtfully active. Two patients, however, later developed overt disease and the other two developed changes compatible with inactive disease.

Four of the present patients presented with an abdominal mass, incidences reported by previous workers being 48%, 65%, and 42% respectively.^{17 14 2}

Treatment of intestinal tuberculosis is less problematical if its presence is suspected before or shortly after laparotomy in those patients presenting surgically, though from our experience of other cases there are few hard and fast rules. We agree with Anscombe *et al.*¹² that if the lesion is in the ileocaecal area resection is preferable to a bypass procedure (see, for example, case 2). We do not agree (see case 3) that there may be no necessity for antituberculosis treatment as we believe that a subsequent, more florid tuberculosis may develop. Fistulae may remain open and cicatrization and bowel obstruction may occur later (see cases 2, 3, and 5), necessitating surgery when the hazard of tuberculous peritonitis is much reduced. These latter cases (5 and 2) required surgery at periods of three months and two years respectively after antituberculosis treatment had been begun.

Conclusions

Tuberculous bowel disease should rate particularly highly among the differential diagnoses in immigrant patients presenting with abdominal symptoms and a mass. A clinical, radiological, or pathological diagnosis of Crohn's disease should be viewed with suspicion. We believe there to be a good case for a therapeutic trial of antituberculosis drugs. A positive Mantoux test result in

children under 14 years may be a valuable aid in diagnosis. Normal chest x-ray appearances do not exclude tuberculosis of the bowel.

Resection of affected, indurated bowel is in our opinion preferable to a bypass procedure. If confirmatory a full course of antituberculosis treatment should be given. Later presentation with intestinal obstruction does not necessarily detract from the diagnosis.

We are grateful to the physicians and surgeons of the East Birmingham Hospital for allowing us access to their records. Any conclusions drawn from them are ours alone.

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Potassium para-aminobenzoate was considered to limit progression of the disease,⁵ but a recent controlled trial has not confirmed this.⁶ Penicillamine may be of use in the early active phase of the disease,⁷ but more evidence is needed. Immunosuppressive therapy has been disappointing. It should not be forgotten that spontaneous remission may occur and crippled patients may regain a considerable degree of mobility.

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Does the degree of continuing sexual activity have any connection with the development or otherwise of prostatic disease?

Neither cancer nor benign enlargement of the prostate gland appears to be caused by sexual activity or abstinence, since they afflict the sexually active and the celibate alike.¹⁻³ Acute prostatitis can be secondary to gonococcal or non-specific urethritis, and so related to sexual activity, but in practice is more often seen as a complication of urinary infection and outflow obstruction. Chronic prostatitis is notoriously hard to diagnose objectively and may be associated with undesired, frequent, and painful erections. It is exceedingly difficult to correlate any other alteration in sexual activity with any disorder in the prostate, since benign nodular hyperplasia is universal after middle age, focal carcinoma appears to be the rule in the very old, and the range of normality in human sexual behaviour even in the twilight years is astonishingly diverse.

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A teenage girl has severe perceptive deafness in one ear and total deafness in the other as a result of childhood measles. What treatment, if any, might help her?

An up-to-date powerful amplifier for improved auditory training with special emphasis on lip-watching and speech training can work wonders. The danger of damaging the remaining hearing in the one ear from the increased input of the aid is worth risking. If they have not already done so, the parents should join the National Deaf Children's Society, and meet others with similar problems and they should take the journal of the Royal National Institute for the Deaf, *Hearing*. Recently the improvements in cochlear implants have been enormous—to me, almost miraculous.¹ A few (very few) surgeons, physiotherapists, and other scientists are implanting these electronic devices in carefully selected patients with relative safety. At present only adults are considered suitable. This teenage girl may in the relatively near future be able to seek such an opportunity, but it should not be considered too soon, nor without sensible appreciation of the difficulties.

¹ Michelsen, R P, *Laryngoscope*, 1974, 84, 1883.

What is the treatment for scleroderma?

Treatment has to be symptomatic, as there is no specific remedy, and common-sense measures are important. Physiotherapy should help stiff joints. The hands should be kept warm and if the peripheral circulation is poor a vasodilator is worth trying. Griseofulvin,¹ intravenous low molecular weight dextran,² and hyperbaric oxygen³ for peripheral vascular insufficiency have all had their advocates, but evaluation of their efficacy is difficult. Small doses of systemic steroids may relieve arthritic pain but do not halt progress of the disease.⁴ Other manifestations of the disease such as respiratory infections and cardiac and renal failure should be treated on their own merits. Two remedies, thought to be more specific, have been suggested.