

Ileo-caecal tuberculosis

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EDITORIAL SYNOPSIS Seven patients with proven ileo-caecal tuberculosis and six others in whom the presumptive evidence of intestinal tuberculosis was very strong were admitted to the United Birmingham Hospitals in the period 1951-62. The features of the condition are described, and the difficulties of diagnosis, both clinical and pathological, are discussed. Any lesion of the bowel showing follicular lesions with giant cells should be carefully searched for tubercle bacilli.

Tuberculous ulceration of the intestine has been recognized from antiquity as a serious complication of advanced pulmonary tuberculosis. In India, Ukil (1942) found that of 1,000 cases of intestinal tuberculosis 95% were secondary to the pulmonary disease. In western countries in recent years this form of intestinal tuberculosis has become uncommon, probably due to the more effective control of tuberculosis, and Mitchell and Bristol (1954) found intestinal complications in comparatively few patients with pulmonary tuberculosis.

Ileo-caecal tuberculosis without apparent lung disease was frequently diagnosed in the earlier part of this century but the diagnosis has been made less often since Crohn, Ginsburg, and Oppenheimer (1932) described the entity of regional ileitis. Both conditions involve the region of the terminal ileum and are grossly, and sometimes microscopically, similar. Hence papers on ileo-caecal tuberculosis published before Crohn's original contribution are open to considerable doubt unless accompanied by bacteriological proof. Since 1932 case reports of ileo-caecal tuberculosis have been few and all suggest that the condition is distinctly uncommon, at least in the western hemisphere (Hoon, Dockerty, and Pemberton, 1950; Fridjohn and Ellis, 1957; Paustian and Bockus, 1959) and some observers have doubted the existence of this entity (Warren and Sommers, 1948). In India the condition appears to be much more common (Anand, 1956), a point of some importance in the context of the present paper.

Interest in ileo-caecal tuberculosis was stimulated by the study of a bacteriologically proven case (A.M.). Subsequently an investigation was undertaken to

assess the frequency and to study the clinical and pathological features of tuberculous lesions of the bowel situated at, or in fairly close proximity to, the ileo-caecal valve, among patients admitted to the United Birmingham Hospitals during the 12-year period 1951-62, and on whom laparotomy or resection of bowel had been performed.

MATERIAL

In 12 cases a diagnosis of tuberculosis had been made after histological examination of resected portions of bowel. In a further patient a hypertrophic bowel lesion with constriction was found at laparotomy but was not resected; other collateral evidence for the tuberculous nature of this lesion was very strong.

In seven of the 12 resected specimens bacteriological proof of the disease was obtained either by demonstrating alcohol-acid-fast bacilli in the tissue sections (five cases) or by culture (two cases). The remaining five cases had histological features, discussed later, which made a diagnosis of tuberculosis highly probable, but in the absence of bacteriological proof by no means certain.

CLINICAL FEATURES

The 13 patients consisted of 10 men and three women whose ages varied at diagnosis from 24 to 62 years. Six men and one woman were immigrants from India or Pakistan, but the length of time spent in England was not recorded in all cases. Language difficulties made taking adequate histories difficult in certain instances. The most frequent symptom (Table I) was a constant, dull, aching abdominal pain, which was present in 11 patients. In five it was situated either in the central abdomen or in the right iliac fossa. In five, the onset of abdominal

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TABLE I

SYMPTOMS AND SIGNS

<i>Symptoms and Signs</i>	<i>No. of Cases</i>
<i>Gastrointestinal</i>	
Abdominal pain	11
Vomiting	7
Abdominal distension	6
Abdominal mass	5
Anorexia	3
Diarrhoea	3
Constipation	2
Alternating diarrhoea and constipation	2
Wind	2
Post-prandial pain	2
Melaena	1
Fistulae	1
<i>General</i>	
Weight loss	8
Anaemia	6
Weakness	2
Night sweats	1

pain was sudden, with vomiting and other manifestations of acute intestinal obstruction. Three patients had diarrhoea, two constipation, and a further two diarrhoea alternating with constipation. In eight there was a variable degree of weight loss and in two this was the major complaint.

A mass in the right iliac fossa was found in five patients. Six were suffering from iron-deficiency anaemia but only one patient had obvious melaena. Low fever was present in five patients when admitted to hospital.

The following histories illustrate some of the main clinical features in bacteriologically proven cases.

CASE REPORTS

CASE S.T. An English woman of 62 presented with loss of weight, anorexia, and lassitude of eight months' duration. There were no abdominal symptoms. Physical examination revealed a fullness in the right iliac fossa. After occult blood had been found in the stools, a barium enema showed deformity of the caecum and ascending colon thought to be due to a carcinoma. A chest radiograph was normal. Laparotomy was performed and an oedematous mass involving the caecum and colon was resected and an ileo-colic anastomosis performed. She remained well for 10 years without antituberculous drugs until 1961 when she became unwell with recurrence of a mass in the right iliac fossa. This became progressively smaller when streptomycin, para-amino-salicylic acid, and iso-nicotinic acid hydrazide were prescribed, and she apparently recovered completely.

CASE A.M. An English woman of 47 complained of loss of 2 st. in weight, epigastric discomfort, and lassitude for one year. Appetite remained good. A brief period of diarrhoea preceded admission to hospital, when examination revealed wasting, anaemia, and a temperature of 99°F. There was a diffuse tender mass in the right iliac fossa. Barium enema showed a lesion, possibly granulomatous, involving the terminal ileum and caecum. Chest radiographs showed calcification at both hila and a less dense shadow in the left mid zone; but these changes were not considered to be tuberculous. At laparotomy the terminal ileum and caecum were thickened with small nodules on the serosal surface; three other areas of ileum showed the same changes and were resected together with the caecum (Fig. 1). The mesentery was thickened and the lymph nodes enlarged. After operation, and repeated examinations, the sputum was found to contain tubercle bacilli. She was treated with streptomycin, para-

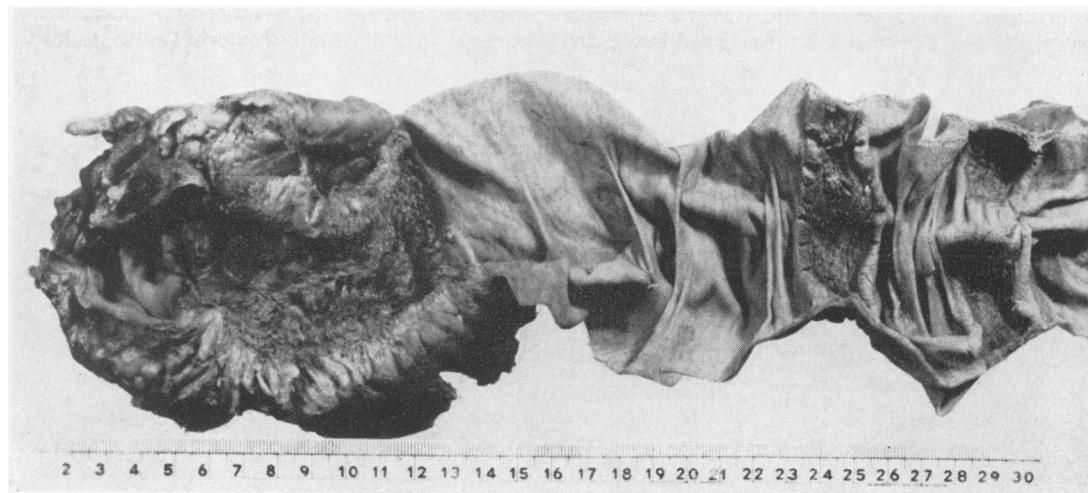


FIG. 1. Caecum and terminal ileum showing ulceration and thickening of the caecum with appearances like those of carcinoma. Note the two segmented lesions in the ileum showing thickening and ulceration.

amino-salicylic acid, and iso-nicotinic acid hydrazide with slow resolution of the softer pulmonary shadow, disappearance of the abdominal symptoms, and a steady gain in weight.

CASE H.H. An English man of 42 complained of intermittent diarrhoea and constipation, sweating, and loss of weight of six months' duration. Examination revealed a large firm mass in the right iliac fossa which after x-ray examination was considered to be a carcinoma of the caecum. A right hemicolectomy was performed. A chest radiograph showed a diffuse miliary mottling but tubercle bacilli were not found in the sputum either on direct examination or on culture. Streptomycin, para-amino-salicylic acid, and iso-nicotinic acid hydrazide were given post-operatively and the lung changes and all abdominal symptoms resolved within six months.

CASE M.M. A Pakistani man aged 28 presented with attacks of abdominal colic and vomiting. He had been admitted to hospital on two previous occasions when a diagnosis of subacute intestinal obstruction had been made, but with resolution of symptoms no active treatment had been undertaken. A barium meal between attacks had shown a stricture in the terminal ileum. On his third admission with acute small bowel obstruction, laparotomy revealed in the terminal ileum three distinct areas of thickening and stenosis, the lesions being separated by normal bowel; the lesions were resected. Chest radiographs showed soft opacities in both upper lobes, but no tubercle bacilli were identified or cultured from sputum or stools. The lung lesions resolved after five months' treatment with streptomycin, para-amino-salicylic acid, and iso-nicotinic acid hydrazide, and bowel symptoms have not returned.

PATHOLOGY

MACROSCOPIC APPEARANCES In this retrospective survey, the gross descriptions of resected specimens

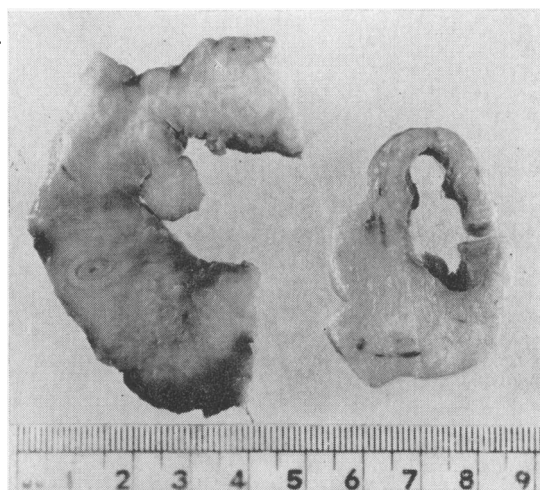


FIG. 2. Cross section of caecum (left) and ileum (right) showing great thickening of bowel wall with obscuration of all layers. Note extension of the process into the attached mesentery.

have been culled from the operative findings and the description of the specimen as received in the pathology laboratory (Table II). The appearances were similar whether or not tubercle bacilli were subsequently identified.

The caecum alone was involved in two cases, in one of which tubercle bacilli were found. Both showed great thickening of the bowel with rather superficial mucosal ulceration. The bowel wall was replaced, and its muscle layers obscured by grey or white friable tissue (Fig. 2) which in one case extended into the attached mesenteric fat. In one specimen small white subserosal nodules were present. In both, the mesenteric lymph nodes were

TABLE II

Case	Sex	Age	Nationality	Site of Lesion	RESECTIONS OF TUBERCULOUS BOWEL							Chest Radiograph	Acid-fast Bacilli in Sputum
					Pathology of Resected Bowel								
					Thickening	Ulcer	Stenosis	Serosal Nodules	Segmented Lesions	Lymphadenopathy	Acid-fast Bacilli		
S.T.	F	62	British	Caecum	+	+	-	-	-	+	+	Normal	-
A.A.	M	46	Pakistani	Caecum	+	+	-	+	-	+	-	Tuberculosis	-
H.H.	M	42	British	Caecum and ileum	+	+	+	+	-	+	+	Tuberculosis	-
G.D.	F	25	Indian	Caecum and ileum	+	+	-	-	-	+	+	Normal	-
H.C.	M	35	British	Caecum and ileum	+	+	-	-	+	+	-	Normal	-
A.M.	F	47	British	Caecum and ileum	+	+	-	+	+	+	+	Tuberculosis	+
M.M.	M	28	Pakistani	Ileum	+	+	+	-	+	+	+	Tuberculosis	-
P.D.	M	44	British	Ileum	+	+	+	-	+	+	+	Tuberculosis	-
M.S.	M	24	Pakistani	Ileum	+	+	+	-	-	+	+	Normal	-
F.D.	M	29	Pakistani	Ileum	+	-	+	-	+	-	-	Normal	-
P.S.	M	25	Indian	Ileum	+	+	-	+	-	-	-	Normal	-
M.E.	M	34	Pakistani	Ileum	+	+	+	-	-	+	-	Tuberculosis	-

enlarged, and replaced by tissue similar to that which involved the bowel wall. The appearances were thus very similar to those of carcinoma.

Both caecum and terminal ileum were involved in four cases, in three of which tubercle bacilli were identified. All showed thickening of the bowel, mucosal ulceration, and one showed ileal stenosis. Small subserosal nodules were present in two, but all four had enlarged mesenteric lymph nodes. The appearances of the caecum resembled carcinoma (Fig. 1).

In six cases the terminal ileum only was involved, and in three tubercle bacilli were found. The bowel was thickened in all specimens (Fig. 2), and all but one showed mucosal ulceration, but in only two examples was the ulceration described as circumferential. Significant stenosis was present in five, lymph glands were enlarged in four, and small subserosal nodules present in one.

The case in which the terminal ileum was involved but which was not resected occurred in a British male aged 59 and is not included in Table II. The bowel was involved in a granulomatous inflammatory reaction causing almost complete stenosis. As he was known to have active pulmonary tuberculosis and also extensive ulceration of the anal canal, which on biopsy had been shown to contain large numbers of tubercle bacilli, the presumptive evidence of a tuberculous bowel lesion is very strong.

MICROSCOPIC APPEARANCES

BACTERIOLOGICALLY PROVEN CASES There were seven cases in which acid alcohol-fast bacilli were demonstrated either in the tissue sections or else cultured from lymph nodes. The basic histological changes were those of tuberculosis, with many follicular lesions characterized by epithelioid cells, giant cells of Langhans type, and a peripheral zone of chronic inflammatory cells. The lesions were mainly in the submucosal and serosal layers and involvement of the muscle layers appeared to be a relatively late manifestation when the follicular lesions were undergoing coalescence. In some instances sheets of epithelioid cells interspersed with multinucleated giant cells and chronic inflammatory cells, constituting tuberculous granulation tissue, were a marked feature.

Caseation, though not a prominent feature, was present in all specimens, although sometimes prolonged search was required to find it. Fibrosis varied in amount, but occasionally there was a fairly brisk reaction around the follicles, and not infrequently there were areas of focal fibrosis consistent with partial healing. Usually there was a fibroblastic reaction separating muscle bundles and

the serosal layer was thickened and fibrotic. Some specimens showed pronounced oedema involving all layers of the wall, but especially the submucosa, and this combined with the fibrosis, the progressive nature of the tuberculous reaction, and the diffuse chronic inflammatory cell infiltration which was present in all parts explained the great thickening and hypertrophic appearance of the bowel wall.

The oedematous mucosa showed superficial ulceration which did not penetrate the muscle layers. In only one example were pseudo-polypi found. Very frequently there were sinus tracks filled with polymorphs which burrowed from the mucosa into the muscle layers. Endarteritis of submucosal vessels was a prominent feature in many specimens and might have been responsible for the mucosal ulceration.

In general the lymph nodes showed a histological reaction more typical of tuberculosis than the bowel lesion. Discrete follicular lesions, associated with epithelioid cells, giant cells, and caseation were more marked than in the bowel. Most of the nodes from all the specimens examined showed this reaction.

BACTERIOLOGICALLY NON-PROVEN CASES The histological features of these cases showed no major differences from those cases in which tubercle bacilli were demonstrated. In every instance the bowel wall contained granulomatous lesions with foci of caseation similar to those already described. The reaction in draining lymph nodes was also similar.

In all 12 specimens prolonged search was made for other possible causative agents—amoebiasis, actinomycosis, etc.—but none was ever found.

DISCUSSION

The finding of seven bacteriologically proven cases of tuberculosis of the ileo-caecal region together with six other cases in which there was strong presumptive evidence of tuberculosis during a 12-year period indicates that this condition is rare. Nevertheless it must be considered in the differential diagnosis of intestinal obstruction and carcinoma of the colon, especially in patients with abnormal chest radiographs and in the immigrant Indian population.

The symptoms and signs of ileo-caecal tuberculosis as encountered in this series (Table I) are sufficiently similar to those of regional ileitis as to make the differential diagnosis extremely difficult and in no case was a pre-operative diagnosis of tuberculosis made.

When the caecum is involved a mass can frequently be felt; Anand (1956) reported this sign in 48% of patients and Paustian and Bockus (1959) in 65% of patients. A mass was present in six of the 13 cases in

the present series pre-operatively, and was usually presumed to be neoplastic.

Even at laparotomy the true aetiology was obscure as was emphasized by the provisional diagnosis (when given) on the request form for pathological examination. When the ileum alone was involved the operation diagnoses included regional ileitis, chronic granulomatous inflammation of obscure origin, and in one case ileal sarcoma. In all but one of the cases where the caecum was involved, the lesion was thought at operation to be neoplastic.

Segmented lesions of the bowel, common in regional ileitis, were present in five specimens in the present series (Fig. 1) and a further one was found involving the colon, but this was not resected with the main lesion. In most cases the bowel was thickened with a reddened serosa and could be described as showing hose-pipe thickening. The thickening extended into and involved the adjacent mesentery. Minute subserosal nodules, enlarged soft lymph nodes, adhesions between involved segments and adjacent structures, sometimes with a little excess fluid in the peritoneal cavity, were frequently present. All these gross features are common to both tuberculosis and regional ileitis.

Thus it is virtually impossible to confirm the diagnosis of intestinal tuberculosis without laparotomy and bowel resection followed by full histological and bacteriological examination of the specimen. The microscopic differentiation between tuberculosis and regional ileitis also presents considerable difficulties because several features are common to both conditions. Important points in favour of tuberculosis included the presence of large numbers of follicular lesions, some undergoing coalescence. In regional ileitis the follicular lesions tend to be scattered, small and few in number, but this may depend upon the stage of the disease at which resection is performed. The presence of caseation is of importance in the diagnosis of tuberculosis, but it must be stressed that in the present series, even in those cases with bacteriological proof, caseation was not a prominent feature and frequently several sections had to be examined before small foci were found. Of equal importance was the presence in the draining lymph nodes, even when these were not obviously enlarged, of follicular granulomatous lesions which generally showed a more typical tuberculous reaction than did the bowel. Whilst it is recognized that there are very rarely causes for caseation other than tuberculosis, nevertheless it is considered that intestinal lesions with caseation, together with similar lesions in draining lymph nodes, is sufficiently characteristic to give considerable support to a diagnosis of tuberculosis even in the absence of bacteriological proof.

It must also be stressed that although in one or two examples large numbers of tubercle bacilli were present, in others very prolonged search was necessary to find them. The amount of caseation bore no relationship to the ease with which the bacilli were demonstrated.

It is of great importance to determine whether the intestinal lesion is secondary to another tuberculous focus in the body. All the patients in the present series had chest radiographs and in seven there was evidence of tuberculosis, the activity of which was in doubt, radiologically, and in only two cases were tubercle bacilli subsequently recovered from the sputum. One of the two with positive sputum was the patient who did not have a bowel resection. In six patients chest radiographs were entirely normal and there was no evidence of tuberculosis elsewhere. This raises the difficult question of how the bowel becomes involved in the absence of overt tuberculosis in some other site. It seems that spread from involved lymph nodes in a retrograde fashion is a possibility. The more advanced tuberculous lesions in the lymph nodes compared with the bowel lend some support to this suggestion.

The peculiar histological appearance in the bowel with the interplay of progressive tuberculous granulation tissue, oedema, and reactive fibrosis producing hypertrophy of the bowel without the extensive breakdown of tissue as observed in tuberculosis in all other situations in the body appears to be a characteristic of this form of the disease. It is not possible to give any explanation for this, but it has been suggested by Stewart (1928), writing before regional ileitis had been described, that it is due to a high degree of immunity to the tubercle bacillus, or infection produced by small numbers of bacilli, or that a relatively avirulent strain of the organism is involved.

Resection combined with antituberculous drugs would appear to be the treatment of choice for this condition because otherwise progressive fibrosis with accentuation of the stenosis might occur as the lesions heal under the influence of antituberculous chemotherapy. In the present series complete recovery has occurred in all cases with great improvement in general well-being, and with resolution of any pulmonary involvement present at the time of diagnosis. There have been no recurrences except for one patient (S.T.) to whom no chemotherapy was given at the time of initial diagnosis. The recurrence resolved on appropriate chemotherapy.

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