

Case study

Crohn's Disease Mimicking Intestinal Tuberculosis: A Rare Case Series

Abstract-

In the Developing countries like India, differentiating Crohn's disease from tuberculosis is a very difficult task. The overall estimated burden of Inflammatory bowel disease in India in 2010 came out to be 1.4 million.

Aim of our study was to focus on histomorphological findings of rare Crohn's disease and discuss the role of serum Antisaccharomyces cerevisiae (ASCA) antibody level and short standard anti tubercular therapy for 15 days. We reported 4 cases aged 15yrs, 24 yrs, 65 yrs and 42 yrs, as crohn's disease of intestine on histopathology at our institute between june 2021 to march 2022.

On Histopathological examination - sections from all 4 cases showed Transmural involvement comprising of chronic inflammation and architectural distortion along with few microgranuloma . In one case we got only very few freely scattered epithelioid without discrete microgranuloma. Microbiological examination of that case showed absence of tubercular bacilli. Serum ASCA was positive in only 2 cases.

So our definite diagnosis was crohn's disease in 3 cases as we got microgranuloma in those cases. But we were not sure of crohn's disease in 1 case (as we got very few epithelioid cells only), so we go for short standard anti tubercular therapy in that case for 15 days as our area is more prone to tuberculosis . But that patient did not responded. So we go with the management of crohns disease and patient responded well with corticosteroid and immunomodulators.

Both intestinal tuberculosis and Crohn's disease are chronic granulomatous lesion, but the absence of well defined macrogranuloma and caseous necrosis on histopathology are clinching point against intestinal tuberculosis, favouring crohn's disease. Microbiological findings and serum ASCA antibody level were of no use in differentiating crohn's from tuberculosis. We could go for short standard antitubercular therapy in developing countries like india, if there is diagnostic difficulties between crohn's disease and intestinal tuberculosis. The earliest distinction between these two lesion is must as there management are very different from each other.

Key words: Chronic granulomatous lesion, Intestinal tuberculosis, crohn's disease' granuloma, Antisaccharomyces cerevisiae antibody level .

Introduction:

Differentiating Crohn's disease from tuberculosis is very difficult in developing countries due to higher burden of tuberculosis. Only few cases of Crohns have been reported from India. Developing countries like India are at the stage of epidemiological transition with the decreasing incidence of infectious diseases and an increasing trend of chronic non-infectious diseases (1). Chronic

granulomatous disorder of the intestine is one such example of diagnostic dilemma due to the epidemiological transition from intestinal tuberculosis to crohn's disease, a subtype of inflammatory bowel disease. (2). Differentiating intestinal tuberculosis (ITB) from Crohn's disease (CD) is very important as the management of the two are very different. But differentiating TB and Crohn's is very difficult because of overlapping clinical, endoscopic, radiological, serological, and pathological findings. A definite diagnosis of ITB depends on methods that have unsatisfactorily low sensitivities, including 5.3% to 37.5% for acid-fast bacilli tissue staining, and 36.4% to 67.9% for a polymerase chain reaction.(3,4). We are reporting 4 cases of crohn's disease of intestine on histopathology at our institute between june 2021 to march 2022.

CASE SERIES

CASE 1

A 15 year old male child was admitted to the Gastrosurgery department with chief complaints of pain abdomen, lump right lumbar region, fever on and off, and weight loss from last 3 months. He has a past history of pulmonary Kochs at 4 years of age. On per abdominal examination- a hard lump of 5x5 cm size felt in right lumbar region with smooth surface, tender and fixed.

Radiological finding (CT report) -Circumferential hypoechoic thickening of ileocaecal junction and terminal illeal walls with intussusception. Differential diagnosis were malignancy, crohn's disease and intestinal tuberculosis.

CASE 2

A 24 year old male patient was admitted to the Gastrosurgery department with chief complaints of pain abdomen, vomiting and weight loss from last 1 year. There was history of appendicectomy and it is a follow up case of right iliac fossa sinus. On fisulogram, a thin linear track was seen for a length of approximately 2cm which was communicating with a colonic loop in right iliac fossa.

Radiological finding (Endoscopy report)- a polypoidal mass was seen in caecum near ileocaecal valve.

CASE 3

A 65 year old male was admitted in Gastrosurgery department with chief complain of pus discharge from perianal region from last 5mnths. There was history of hematemesis associated with malena

.On per abdomen examination - soft, non tender and a right inguinal scar was present. No fistulous tract was identified. Occult blood in stool was positive.

Radiological finding (USG report). An ulcerative lesion with multiple defects in anterior and anterolateral (12o clock and 11 o clock) position. Multiple external fistulous opening with multiple nodularity was present.

CASE 4-

A 42 year old male was admitted in the Gastrosurgery departement with chief complains of lower abdominal pain, bleeding per anum and weight loss. On perexamination abdomen - a lump was noted in right iliac fossa.

Radiological findings (CT report) - A hypochoic ileal stricture was noted with hepatic nodules.

In all 4 cases surgery was done and specimen was sent to pathology dept for HPE.

There gross findings and histopathological findings are tabulated in table 1 and table 2 respectively.

Table 1. Gross examination findings

Case	Surgical specimen	Cut section	Cobble stone appearance	Mesenteric fat wrap	Skip lesion
1	Hemicolectomy with Part of Ileum	Nodular lesion with stricture	Positive	Positive	Not Seen
2	Hemicolectomy+ Ileum+Transvere Colon	Thickened area	Negative	Negative	Not Seen
3	Rectal fragmented tissue bits	-	-	-	-
4	Ileal segment with hepatic nodule	Stricture with ulceration	Negative	Negative	Not Seen.

In Table 1, Case 1 and 2 were hemicolectomy specimen with part of ileum, having greyish white thickened area .Case 3 was small rectal biopsy in fragmented form, so we don't have its specific findings on gross examination. Case 4 showed ileal segment, having stricture with gross ulceration. Cobble stone appearance, mesenteric fat wrap were noted in only 1st case, but skip lesion was not seen in any case.



Fig 1 (a, b, & c) showing Gross specimens of case 1 , 2 and 4 respectively. Fig 1 (a) shows cobblestone appearance and mesenteric fat wrap. Skip lesion not seen in any of the 4 cases.

Table 2 . Histopathological Findings

Case	Transmural inflammation	Architectural distortion and branching	Microgranuloma +_giant cell	Ulceration	Pyloric gland metaplasia	Dysplasia
1	+	+	Giant cell+ epithelioid cells+	+	+	-
2	+	+	Microgranuloma+	+	-	-
3	+	+	Microgranuloma+	+	-	-
4	+	+	Microgranuloma+	+	-	-

Table 2. shows histopathological findings of all 4 cases. Sections from all 4 cases showed transmural involvement . Both architectural abnormalities and transmural inflammation noted. Architectural abnormalities includes crypt distortion (non parallel crypts and cystically dilated glands), crypt branching (>branched crypts) and crypt shortening (decreased crypt length). Inflammatory features includes transmural inflammation comprising of lymphoplasmacytic infiltration. Microgranuloma (<200um) was noted in all cases except in Case 1 in which we got only very few epithelioid cell . Surface mucosal denudation and superficial ulcer was also noted in all 4 cases. pyloric metaplasia was noted in case 1 only. Dyaplasia was not seen in any case.

MICROSCOPY

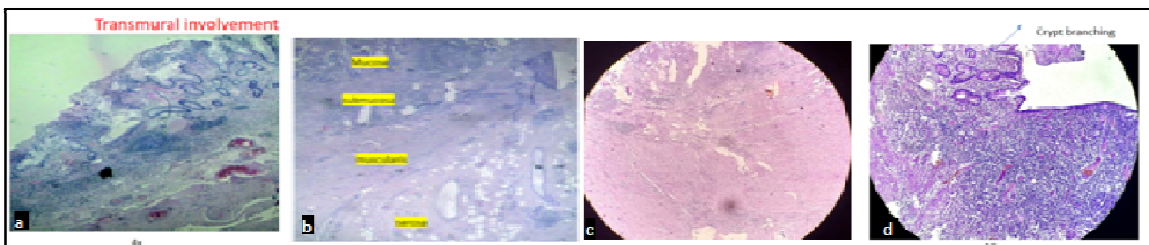


Fig 2(a, b, c, & d) 4x. view showing transmural inflammation in all 4 cases.

Muscular Layer

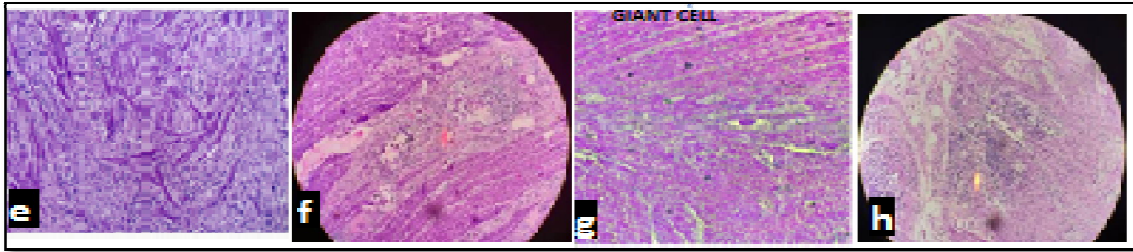


Fig 2(e, f, g, & h) 10x view showing muscular proper layer infiltrated by lymphoplasmacytic infiltration in all 4 cases.

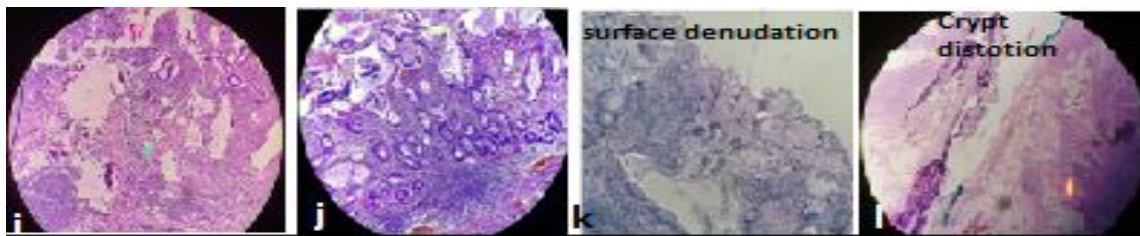


Fig 2(i, j, k, & l) 4x. view showing crypt architectural distortion in all 4 cases.

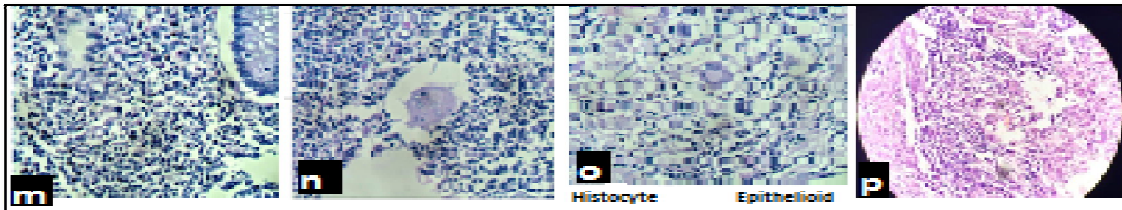


Fig 2 (m, n, o & p) 10x view showing only few epithelioid cells in case 1 (Fig 2m) and microgranuloma in other 3 cases.

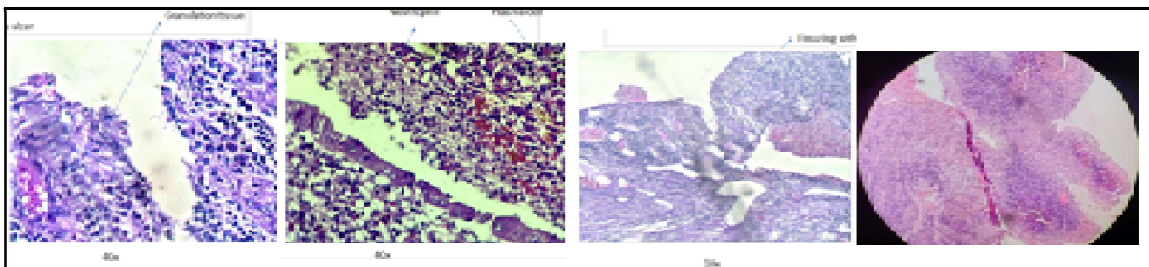


Fig 2 (q, r, s, & t) 10x. view shows surface denudation and superficial mucosal ulceration in all 4 cases.

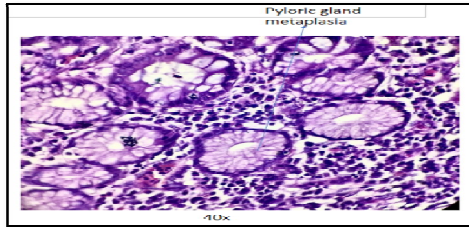


Fig 2 (u) show pyloric gland metaplasia in case 1.

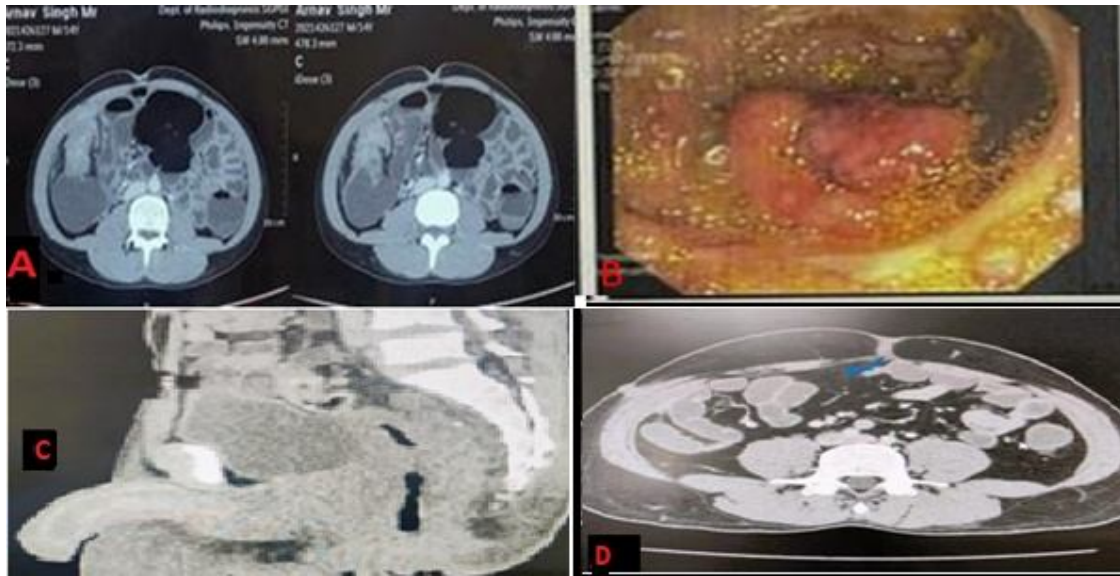


Fig 3(a, c &d) show CT findings of gut wall thickening in Case 1,3 & 4 respectively. Fig 3(b) show endoscopic finding of case 2.

In serological markers we have done Serum ASGA antibody level, which was found raised in case1 and 4. AFB stain and TB -PCR was found negative in all 4 cases.

In all 4 cases, neither well defined macrogranuloma nor caseous necrosis seen on histopathology added by the negative microbiological findings, the chance of intestinal tuberculosis was very less and we were more in favour of crohns disease.

We have started management of cases 2,3 and 4 in line of crohns disease and patient responded very well.

But we were in diagnostic dilemma in Case 1 as patient has history of tuberculosis and discrete microgranuloma not noted. So we gave a short trial of ATT in cases 1 for 15 days, but got no good response. After which we have started management with corticosteroids and immunomodulators.

Patient responded well and was stable.

Discussion:

Diagnosing crohn's disease is very difficult in developing countries due to higher burden of tuberculosis. Very few cases of crohn's have been reported from India.

Among the clinical features, diarrhea, hematochezia, perianal disease, and EIMs favored CD, while fever, night sweats, lung involvement and ascites favored ITB. However, none of these features is exclusive for either disease and alone cannot diagnose CD or ITB. (5). Overlapping clinical features was also noted in our 4 cases.

In recent studies from India, it was found that radiological findings that were more common in patients with CD as compared to ITB were involvement of the left colonic segment (22% vs 6%), long-segment involvement (69% vs 28%), presence of skip lesions (63% vs 42%), and presence of comb sign (44% vs 20%). On the other hand, the involvement of ileocecal area (70% vs 43%), shorter length of involvement, and presence of lymph nodes larger than 1 cm (20% vs 2%) were more common in ITB (6). But these features are also not very specific for either of 2, as seen in our cases.

Both the disorders are characterized by chronic granulomatous inflammation in the GI tract, and pathological features can be classified into architectural and inflammatory features. Architectural abnormalities such as crypt distortion (non-parallel crypts, variable diameter or cystically dilated crypts), crypt branching (> 2 branched crypts), crypt shortening, decreased crypt density) and microgranuloma (<200µm) more common in CD but can also be seen in ITB [9,10]. Inflammatory features including, transmural inflammation, focal cryptitis, aphthoid ulcers, proximal location of ulceration and paneth cell metaplasia and macro granulomas with caseation are more common in ITB. Granuloma is a collection of epithelioid histiocytes (macrophages) with vaguely defined outlines. Tubercular granulomas are usually large (> 200 µm), confluent, dense (> 5-10/hpf), located in submucosa, and are characterized by central caseation, which is diagnostic and exclusive for ITB (7-10). Granulomas in CD are usually small (microgranuloma), discrete, ill-defined and sparse. So, the HPE findings of our 4 cases are more in favour of Crohn's disease than tuberculosis as described in recent studies.

Intestinal TB is a paucibacillary disease and is responsible for poor sensitivity of microbiological tests. Demonstrating the bacillus with acid-fast bacillus (AFB) staining would be easiest, but has very poor sensitivity of 2.7%-37.5%. Polymerase chain reaction (PCR) for AFB in endoscopic biopsies is not exclusive for ITB, hence cannot be diagnostic for ITB. Therefore, among the microbiologic tests, AFB stain, and gene-Xpert MTB are diagnostic for ITB, however, these tests are associated with very poor diagnostic sensitivity, limiting their role in the diagnosis of ITB. (11-13). In our 4 cases AFB stain and PCR are negative, but as sensitivity of these microbiological tests are not so sensitive, so reliability is very less on these tests.

Positive serology for anti-saccharomyces cerevisiae antibody (ASCA) has no role in differentiating CD from ITB, as shown in two studies from India [14]. In all our 4 cases Anti ASCA ab was found to be positive, but it has no specificity for any of two.

Conclusion-

Unfortunately, crohn's remains an under diagnosed disease in developing countries such as India due to overlapping findings with tuberculosis. Age, clinical features, radiological findings are not specific and has no significance. But the absence of well defined macrogranuloma and caseous necrosis on histopathology are clinching point against intestinal tuberculosis, favouring crohns disease. As ITB is a paucibacillary disease, so microbiological tests accounts for poor sensitivity. We could go for short standard antitubercular therapy in developing countries like india, if there is diagnostic struggle between both diseases. The earliest distinction between these two lesion is must as there management are very different from each other.

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