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Original Article

Differential Diagnosis of Intestinal Tuberculosis from Crohn's Disease: A Diagnostic Dilemma

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Abstract

Background: In geographical regions where both intestinal tuberculosis (ITb) and Crohn's disease (CD) coexist, the differential diagnosis of these two conditions poses a challenge to clinicians, because of similar clinical, radiological, and endoscopic findings, and hence, there are high rates of misdiagnosis in both conditions.

Methods: A total of 345 cases of gastrointestinal (GI) endoscopic biopsies and resected specimens were received during the period January 2009–June 2011. Of the cases, 40 were clinically suspected to be suffering from Tb. These cases were analyzed with clinical, endoscopic, radiological, and pathological findings used acid-fast bacilli stain and culture along with newer ancillary techniques such as polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* DNA and anti-Saccharomyces cerevisiae antibody (ASCA): ASCA - IgG and IgA for CD.

Results: Of 40 clinically suspected patients, 20 (50%) were suffering from Tb, 4 (10%) from CD, 8 (20%) from ischemic enteritis, 6 (15%) from chronic non-specific enteritis, 1 (2%) from adenocarcinoma cecum, and 1 (2%) from inflammatory fibroid polyp.

Conclusions: ASCA test was not found useful in differentiating CD from GITb. Tissue PCR was most reliable technique to confirm GITb. Serological assay is used to some extent, and it is sensitive when IgG and IgA are combined. The best way to diagnose CD, is by exclusion of GITb and to correlate histology with clinical finding.

Key words: Anti-Saccharomyces cerevisiae antibody, Crohn's disease, Intestinal tuberculosis, Polymerase chain reaction

INTRODUCTION

Tuberculosis (Tb) can involve any part of gastrointestinal (GI) tract and is the sixth most frequent site of extrapulmonary involvement. *Mycobacterium tuberculosis* (M. tb) reaches the GI tract through hematogenous spread, ingestion of infected sputum, or direct spread from infected contiguous lymph nodes and fallopian tubes.[1] The incidence of abdominal Tb is increasing globally with the spread of AIDS.[2] Crohn's disease (CD) is found to show cumulative increase from fewer than 5000 in 1987 to 21061 in 2001.[3] Unfortunately, traditional methods (acid-fast bacilli [AFB] stain and culture) for confirming Tb suffer its own limitations: (a) Finding AFB in only, one-third of patients. (b) AFB can be recovered, in culture of the involved tissues (in only 50% and it takes about 6–8 weeks).

The ultimate course of these two disorders is different. ITb is curable; in contrast, CD is a progressive-relapsing illness. For this reason, newer ancillary techniques have been attempted to distinguish these two conditions.

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METHODS

A total of 345 cases of GI endoscopic biopsies and resected specimens were received, during the period January 2009–June 2011. Of the cases, 40 were clinically suspected to be suffering from Tb. A complete clinical, endoscopic, and radiological finding was obtained for these cases, and specimens were also collected.

Macroscopic examination of GI surgical specimens was done after 24 h of fixation. Representative bits were taken from ulcerated lesion and stricture site, and mesenteric

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lymph nodes were also taken. Histological sections were studied with hematoxylin and eosin wherever needed. Ziehl–Neelsen (ZN) method of staining and culture for the presence of AFB, tissue polymerase chain reaction (PCR) for Tb, and serological assay anti-Saccharomyces cerevisiae antibody (ASCA) - IgG and IgA for CD was performed.

RESULTS

Table 1 shows morphological findings of CD and ITb. In the rest 10 of GITb showed serosal tubercles in 8 cases and caseating mesenteric nodes in 2 cases. Table 2 shows histopathological findings of CD and ITb.

a. Mycobacterial culture was found to be positive in 10 cases, AFB stain positive in 5 cases, and PCR positive for M. tb DNA in 3 cases.
b. Serological assay: ASCA - IgG and IgA positive in one case.

Of 40 cases, 20 cases was diagnosed to be Tb, 17 cases showed caseating granuloma and 3 non-caseating granulomas in which PCR for M. tb DNA were positive for 3 cases. AFB identified in 5 cases by ZN method, and culture was positive in 10 cases of 20 cases.

In suspected CD cases, 4 were diagnosed as CD as 2 cases presented with non-caseating granuloma, 1 case was positive for ASCA - IgG and IgA. Morphological features of CD were deep fissures and skip lesion, and enterocutaneous fistula was seen in 4 cases. PCR for M. tb was negative in all 4 cases.

Table 1: Morphological findings of CD and intestinal Tb

Colonoscopy	CD (4)	GITb (20)
Ulceration	3 (75)	6 (30)
Skip lesions	3 (75)	0 (0)
Pseudopolyps	1 (25)	0 (0)
Strictures	3 (75)	4 (20)

CD: Crohn's disease, ITb: Intestinal tuberculosis, GITb: Gastrointestinal tuberculosis

Table 2: Histopathological findings of CD and ITb

Histological features	CD	GITb
Granuloma	2 (50%)	19 (95%)
*Caseating	0	17
*Non-caseating	2	2
*Confluent	0	6
*Discrete	2	13
Ulceration	3 (75%)	5 (25%)
Lymphoid aggregates or follicles	3 (75%)	15 (75%)

CD: Crohn's disease, ITb: Intestinal tuberculosis, GITb: Gastrointestinal tuberculosis

DISCUSSION

There is a close resemblance in clinical, radiological, surgical, and histological features of CD and GITb, thus differential diagnosis is a major challenge. In India because of diagnostic similarity, definite diagnosis of CD is must to avoid unnecessary antitubercular therapy (ATT). Most of the CD cases respond to mesalamine preparations, immunotherapy or steroid treatment. Only a small proportion will respond to ATT, and in such cases, problem is more confusing.

For definite diagnosis of CD, there are certain criteria,[4] which are based on morphological and pathological criteria; (a) morphological criteria are discontinuous/segmental and asymmetrical mucosal involvement, deep mucosal or longitudinal fissures, rigid and stricture intestinal wall, and presence of enterocutaneous or enteroenteric fistula or chronic perianal disease. (b) Pathological criteria: Normal mucus content in the goblet cells of the inflamed region, lymphocyte aggregation in the mucosa or submucosa, non-caseating granuloma, longitudinal ulcers/fissures, and transmural inflammation or inflammation beyond mucosa. For definite diagnosis of CD, presence of at least 3 different criteria or presence of non-caseating granuloma on histology with at least one test to exclude Tb (by histological, microbiological, and PCR studies) is required.

For this reason, many investigators have attempted to find specific differential diagnostic methods to distinguish these conditions. A variety of clinical, endoscopic, and radiological criteria has been recommended for the differentiation[5-9] but does not give good result. However, histology can give clue such as ITb showing well-defined large, confluent granuloma often with caseation and with more than four sites of granulomatous inflammation per site, presence of epithelioid cells. The granulomas in CD are fewer, smaller, and never confluent.

Tissue culture takes a long time and its sensitivity is low. As per studies on tissue culture, in case series, the sensitivity of tissue culture in the diagnosis of ITb is between 21% and 54.5% and the specificity is 100%.[10-14] In another case series, comparing 26 patients with CD and 26 patients with ITb were found to be 40%, 86%, and 41%, respectively. In another case series, comparing 26 patients with CD and 26 patients with ITb, the tissue culture sensitivity was between 25% and 35% and the specificity was 100%.[13]

On colonoscopy, colonic Tb may present as an inflammatory stricture, hypertrophic lesions resembling polyps or tumors, and segmental ulcers. In one study, endoscopically the distribution of macroscopic lesions was similar in the two conditions, with 60–70% of the patients showing ileocecal

involvement and about 50% showing involvement of the transverse or distal colon. Involvement of the ileocecal valve, deformity of the cecum, and stricture/stenosis were, however, more common in the Tb patients, while fistulae were more in patients with CD. Recently, ASCA and tissue PCR for M. tb were employed for the diagnosis. TB PCR was found highly specific for the diagnosis of GITb but lacked sensitivity, the analysis of result can be done quickly and result can be obtained in 48 h. This test is very specific for Tb but occasionally may be positive in patient with CD. Several studies suggest a role for PCR for mycobacterial DNA in the differential diagnosis of ITb. Sensitivity of positive ASCA for the diagnosis of CD reaches up to 76% and 98% in various trials.[15] IgA ASCA and IgG ASCA are considered to be 95% specific for the diagnosis of CD when individually tested but 100% when tested in combination.[15,16]

REFERENCES

1. Sharma MP, Bhatia V. Abdominal tuberculosis. Indian J Med Res 2004;120:305-15.
2. Marshall JB. TB of GIT and peritoneum. Am J Gastroenterol 1993;88:989-99.
3. Das K, Ghoshal UC, Dhali GK, Benjamin J, Ahuja V, Makharia GK. Crohn's disease in India: A multicenter study from a country where tuberculosis is endemic. Dig Dis Sci 2009;54:1099-107.
4. Burke GJ, Zafar SA. Problems in distinguishing tuberculosis of the bowel from Crohn's disease in Asians. Br Med J 1975;4:395-7.
5. Das P, Shukla HA. Clinical diagnosis of abdominal tuberculosis. Br J Surg 1976;63:941-6.
6. Segal I. Intestinal tuberculosis, Crohn's disease and ulcerative colitis in an urban black population. S Afr Med J 1984;65:37-44.
7. Aoki G, Nagasako K, Nakae Y. The fibre colonoscopic diagnosis of intestinal tuberculosis. Endoscopy 1975;7:113-21.
8. Tandon HD, Prakash A. Pathology of intestinal tuberculosis and its distinction from Crohn's disease. Gut 1972;13:260-9.
9. Brahme F, Hildell J. Angiograph in Crohn's disease revisited. AJR Am J Roentgenol 1976;126:941-51.
10. Sato S, Yao K, Yao T, Schlemper RJ, Matsui T, Sakurai T, *et al*. Colonoscopy in the diagnosis of intestinal tuberculosis in asymptomatic patients. Gastrointest Endosc 2004;59:362-8.
11. Bhargava DK, Kushwaha AK, Dasarathy S, Shriniwas, Chopra P. Endoscopic diagnosis of segmental colonic tuberculosis. Gastrointest Endosc 1992;38:571-4.
12. Almadi MA, Ghosh S, Aljebreen AM. Differentiating intestinal tuberculosis from crohn's disease: A diagnostic challenge. Am J Gastroenterol 2009;104:1003-12.
13. Amarapurkar DN, Patel ND, Rane PS. Diagnosis of Crohn's disease in India where tuberculosis is widely prevalent. World J Gastroenterol 2008;14;741-6.
14. Leung VK, Law ST, Lam CW, Luk IS, Chau TN, Loke TK, *et al*. Intestinal tuberculosis in a regional hospital in Hong Kong: A 10 year experience. Hong Kong Med J 2006;12:264-71.
15. Amarapurkar DN, Patel ND. Serology markers of inflammatory bowel disease. Gastroenterol Today 2005;9:9-13.
16. Ruemmele FM, Targan SR, Levy G, Dubinsky M, Braun J, Seidman EG. Diagnostic accuracy of serological assays in pediatric inflammatory bowel disease. Gastroenterology 1998;115:822-9.

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