Original Article

Differentiation Between Ileocecal Tuberculosis and Crohn's Disease using a Combination of Clinical, Endoscopic and Histological Characteristics

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ABSTRACT

Background: Differentiation between ileocolonic tuberculosis (TB) and Crohn's disease (CD) is difficult but very important. Data on this issue is scarce and inconsistent.

Methods: Clinical, endoscopic and biopsy results of 27 TB patients and 33 CD patients were analyzed and compared.

Results: The only useful clinical feature to distinguish TB from CD was host immune status (odds ratio 51 for CD, p <0.001). The presence of immunocompetency was associated with sensitivity, specificity, PPV and NPV of 100%, 39%, 68% and 0%, respectively for the diagnosis of CD. The only endoscopic feature that helped distinguishing CD from TB was the number of ulcers of 4 or more (odds ratio 4.67 for CD, 95% CI 1.12-19.54, p = 0.004), with sensitivity, specificity, PPV and NPV of 84%, 47%, 70% and 33%, respectively for CD. A single biopsy session, together with searching for evidence of extraintestinal TB led to the diagnosis of TB in all patients, whereas in CD, even multiple colonoscopies and biopsy sessions could definitely diagnose CD in only 11.8%.

Conclusion: Patient immune status, number of ulcers and result of single biopsy session could distinguish ileocolonic CD from TB in most patients.

Key words : clinical, Crohn's disease, differentiate, distinguish, endoscopy, histology, tuberculosis

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INTRODUCTION

Intestinal tuberculosis (TB) and Crohn's disease (CD) are chronic granulomatous diseases of the intestine. Both diseases usually involve the terminal ileum and the colon, causing difficulty in clinical practice to differentiate the two conditions. Although histologic findings from endoscopic biopsy can definitely diagnose intestinal TB by identifying acid-fast bacilli or positive TB culture, it is not so sensitive. On the other hand, histology is usually not specific enough to diagnose CD, thus diagnosis is usually based on clinical grounds and after excluding other diseases, including TB. Since the treatment and prognosis of both diseases are quite different, misdiagnosis leading to treat-

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ing TB as CD or vice versa will delay proper treatment and can be harmful. In clinical practice therefore, differentiation between the two conditions is critical.

Thus far, there have been only few studies trying to determine clinical, endoscopic or histologic features to differentiate between the two diseases[1-6]. The results were either inconsistent or impractical to use.

The purpose of this study is to identify clinical, endoscopic and histologic characteristics that may help differentiating between ileocolonic TB and CD.

Material and Method

Data records of all patients diagnosed as ileocolonic TB and CD at Siriraj Hospital, Bangkok, from January 2005 to January 2011 were retrieved and were retrospectively reviewed and analyzed.

Diagnosis of TB and CD

Ileocolonic TB was diagnosed by any of the followings: histologic finding of caseating granuloma microscopic finding of acid-fast bacilli positive culture for *Mycobacterium tuberculosis*, positive polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*, or concurrent active TB in other organ(s) with response to antituberculous therapy.

Ileocolonic CD was diagnosed by the presence of two of the followings: stricture or fistula on radiographic study, macroscopic appearance of induration in the bowel wall, mesenteric lymphadenopathy "creeping fat" at laparotomy, inflammation of the bowel wall on microscopic appearance, and response to immunosuppressive drugs (i.e. corticosteroids, azathioprine, or sulfasalazine/5-aminosalicylates)

Data collection

Clinical and histopathological data were collected from chart reviews. Endoscopic data were collected from both endoscopic reports and all photos were rereviewed by two of the authors (S.A. and S.P.). Discordances were solved by the third author (S.L.), or by consensus.

Statistical analysis

Statistical evaluation was performed using SPSS software (Version 17). Continuous variables, e.g. age and size of lesions, were presented in mean, median, standard variation and range. Categorical data and proportions were compared by using Pearson's chi-squared test, or Fisher's exact test as appropriate. A p-value of less than 0.05 was considered to be significant. Sensitivity and specificity of the identified features were calculated.

This study was approved by Siriraj Institutional Review Board.

Results

One-hundred-thirty-four patients with ileocolonic lesions were initially identified. After long-term follow-up, 27 patients had definite ileocolonic TB and 33 patients had CD. Clinical data were complete in all patients. For colonoscopic findings, 9 TB and 7 CD patients were excluded because of incomplete colonoscopic results, either due to failure to reach the caecum or to enter the terminal ileum. Thus, colonoscopic data of 18 ileocolonic TB and 27 ileocolonic CD were finally obtained.

Clinical features

Comparison of demographics data, symptoms and signs between patients with ileocolonic TB and CD is shown in Table 1. The only clinical data that was significantly different between the two diseases was the underlying diseases. CD was universally found in normal hosts, while all immunocompromised patients had TB ($p = 0.001$). History of oral aphthous ulcers was more common in CD than in TB (27.2% vs. 3.8%, respectively, $p = 0.053$). Other demographic and clinical features were not significantly different between TB and CD.

Endoscopic features

Details of the colonoscopic features of TB and CD are compared in Table 2. Sites of involvement were not different. Ulcer sizes were similar, however CD were more commonly multiple with ≥ 4 ulcers than TB (84% vs. 53%, $p = 0.029$). Ulcer shapes were also similar, since both TB and CD ulcers are mostly transverse (77.8% and 84.6%, $p = 0.432$). Patulous ileocaecal valve favored TB than CD, whereas pseudopolyps, cobblestone appearance, scar and stricture were more commonly found in CD than in TB, but without statistical significance.

Performance of tissue diagnosis

Diagnosis of ileocolonic TB was achieved in all patients with only one session of colonoscopy. Histo-

Table 1. Comparison of demographic data, symptoms and signs between patients with ileocolonic TB and CD.

	TB (n = 27)	CD (n = 33)	*p*-value
Male gender, n (%)	16 (59.3)	19 (57.6)	0.895
Age (years), mean ± SD	45.1 ± 16.7	44.2 ± 21.6	0.544
Underlying diseases, n (%)			
Normal	15 (62.5)	33 (100)	0.001
HIV	6 (25)	0	
Others	3 (12.5)	0	
Fever, n (%)	10 (38.5)	11 (33.3)	0.683
Abdominal pain, n (%)	19 (73.1)	24 (72.7)	0.976
Abdominal mass, n (%)	3 (11.5)	2 (6.1)	0.453
Diarrhea, n (%)	12 (54.5)	21 (80.8)	0.051
Lower GI bleeding, n (%)	4 (15.4)	12 (36.4)	0.072
Weight loss, n (%)	19 (79.2)	26 (81.3)	0.846
Aphthous ulcer, n (%)	1 (3.8)	7 (27.2)	0.053
Perianal lesions, n (%)	4 (15.4)	6 (18.2)	0.776
Arthritis, n (%)	0	1 (3.0)	0.371
Uveitis, n (%)	0	1 (3.0)	0.371

Table 2. Comparison of colonoscopic features between ileocolonic TB and CD.

	TB (n = 18)	CD (n = 26)	*p*-value
Location, n (%)			
Terminal ileum alone	2 (11.1)	8 (30.8)	0.161
Colon alone	7 (38.9)	9 (34.6)	0.772
Terminal ileum + caecum	1 (5.6)	2 (7.7)	0.782
Terminal ileum + colon	9 (50)	9 (34.6)	0.307
Ulcer shape, n (%)			
Transverse	14 (77.8)	22 (84.6)	0.432
Longitudinal	0	1 (3.8)	
Combined	1 (5.6)	2 (7.7)	
Unclassified*	3 (16.7)	1 (3.8)	
Ulcer characters, n (%)			
Aphthoid	6 (33.3)	8 (30.8)	0.858
Flat ulcer	14 (77.8)	22 (84.6)	0.697
Ulcerative mass	3 (16.7)	3 (11.5)	0.676
Number and size of ulcers			
Number ≥ 4, n (%)	9 (52.9)	21 (84.0)	0.029
Size (cm), mean ± SD	2.0 ± 1.6	2.6 ± 1.4	0.209
Others, n (%)			
Patulous ileocaecal valve	4 (28.6)	3 (11.5)	0.422
Pseudopolyps	3 (16.7)	9 (34.6)	0.303
Cobberstone appearance	3 (16.7)	6 (23.1)	0.716
Nodularity	5 (21.8)	3 (11.5)	0.240
Scar	0	6 (23.1)	0.067
Stricture	1 (5.6)	3 (11.5)	0.634

*Aphthoid or small round ulcers

Table 3. Comparison of the number of colonoscopy needed and the performance of tissue biopsy to diagnose ileocolonic TB or CD.

	TB (n = 18)	CD (n = 26)	*p*-value
Number of colonoscopy			
1	18 (100)	14 (53.8)	<0.001
2	0	6 (23.1)	
3	0	3 (11.5)	
4	0	3 (11.5)	
Pathological diagnosis			
Definite	15 (83.3)	3 (11.5)	<0.001
Not definite	3 (16.7)*	23 (88.4)	

*Diagnoses were made by the presence of extraintestinal TB

Table 4. Diagnostic performance of the two distinguishable features between TB and CD.

	OR (for CD)	95% CI	*p*-value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Immunocompetence	51	NA*	< 0.001	100	39	68	0
Number of ulcer ≥ 4	4.67	1.12-19.54	0.041	84	47	70	33

*NA: not assessable

Table 5. Prediction of the likelihood of ileocolonic CD or TB based on the presence or absence of the two distinguishable features.

Host	Ulcer number	n	CD	TB
Immucompetent	≥ 4	24	21 (87.5)	3 (12.5)
Immucompetent	< 4	8	4 (50)	4 (50)
Immunocompromised	≥ 4	5	0 (0)	5 (100)
Immunocompromised	< 4	4	0 (0)	4 (100)

pathology could promptly diagnose TB in 83.3% of the cases. In the remaining cases (16.7%) with non-diagnostic biopsy, the diagnosis of TB was made from the presence of concomitant extraintestinal TB (1 patient), positive culture (1 patient), and response to antituberculous medications (1 patient). The sensitivities of AFB stain, culture and PCR for diagnosing TB were 76.5%, 44.4%, and 14.3% respectively. In contrast, 46.2% of CD patients needed more than one session of colonoscopy, and even then, definitive diagnosis was achieved in only 11.5% (Table 3).

Diagnostic performance of the distinguishable features

Diagnostic performances of the 2 distinguishable features between TB and CD, namely the host immune status and the number of ulcers ≥ 4, are shown in Table 4. Prediction of the likelihood of CD or TB based on the presence or absence of these two features is shown in Table 5.

Discussion

In the present study, we could identify 2 parameters, 1 clinical and 1 endoscopic, that could help distinguishing between ileocolonic TB and CD, namely the host immune status and the number of ulcers. Crohn's disease always occurred in immunocompetent patients the number of ulcers was usually ≥ 4, whereas TB could affect both the immunocompromised and the immunocompetent patients and the number of ulcers were often < 4. Other clinical and endoscopic features

were not helpful, in keeping with the diagnostic difficulty in those two diseases. Additionally, the present study indicated that the combination of single tissue biopsy session and evidence of extracolonic TB was very sensitive for diagnosing of TB, making repeating colonoscopic biopsy unnecessary. Crohn's disease, on the other hand, could not usually be diagnosed by histology, even with multiple repetitions. Repeating colonoscopy and biopsy are rarely helpful in CD.

The results of the present study differ from previous reports. Regarding clinical features, our study fails to confirm that hematochezia[2], weight loss[2], fever[2], diarrhea[2], perianal lesions[1,5], pulmonary TB[5] or ascites[5] are useful for distinguishing TB from CD. Previous surgery has been shown useful in favor of CD in one study[5], but not in our study with very few operative cases. Positive fecal occult blood was shown to favor CD, while positive PPD skin test was for TB (the latter two tests are not commonly used in Thailand, however, and so not in our study). The reasons why our results differ from others are not obvious, but may be from the small number of our cases. We found host immune status very helpful for distinguishing CD from TB, immunocompromised always TB. This finding has not been reported previously.

Our study did not indicate that endoscopic characteristics, particularly ulcer alignment (transverse or longitudinal) were helpful. Some studies previously suggested that transverse ulcers favored TB while longitudinal ulcers favored CD. In our study, we noted that both TB and CD ulcers usually were transverse, and longitudinal ulcers were uncommon and would when present indicate CD. We also found that to describe ulcer shape as transverse or longitudinal was not easy, as most cases had both, and no standard definition exists on how to classify ulcer shape. Thus, we assumed that transverse ulcers mean number of transverse was more than 2/3 of all ulcers (and similarly for longitudinal ulcers) and combined ulcers were called when the numbers of each ulcer type were between 1/3 to 2/3. A patulous IC valve was also not helpful in our study. Instead, we found that number of ulcers, which was more easily determined, helped distinguish CD from TB (more ulcers, more likely to be CD). This finding has not been mentioned in any previous study.

An important finding in our study was that single biopsy session was sufficient to diagnose TB, whereas repeating biopsy was not enough for CD. Repeating colonoscopy and biopsy, therefore, may not be necessary for either TB or CD. This finding together with the above mentioned clinical and endoscopic features may enable an earlier diagnosis and treatment as well as avoiding repeat investigations.

There were some limitations in the present study. Firstly, the retrospective nature of the study inevitably resulted in some incomplete data record. However, due to very low prevalence of the diseases in Thailand particularly CD[7], a prospective study design would be very difficult. Secondly, the number of patients in each group was rather small. Thus, many potentially distinguishable features were short of statistical significance. The completeness of colonoscopic description of lesions was another problem. Therefore only patients endoscoped after 2005 were chosen as captured colonoscopic photos had since been systematically recorded and available for review.

In conclusion, patient immune status, number of ulcers by colonoscopy and result of the first biopsy can help distinguish between ileocolonic TB and CD.

Conflict of interest

None

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