Original Article

Intestinal Tuberculosis: A Case Series from a Single Center over 15 Years

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Key Words
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Purpose. The nonspecific features of intestinal tuberculosis increase the difficulty of accurate diagnosis. This study aimed to familiarize surgeons with common presentations of intestinal tuberculosis and to increase vigilance for this disease.

Methods. A retrospective case series was conducted, collecting data from consecutive patients with intestinal tuberculosis from April 2005 to May 2019 in a single institution. Patients' symptoms, indications for surgery, and complications were recorded as well as the final histology, lesion locations and methods of investigation.

Results. A total of 14 cases was found in the 15-year study period. The cardinal symptoms were abdominal pain, diarrhea, and GI bleeding. The ileocecal region was the most common location. Most cases underwent surgery as a result of obstruction and diagnostic confirmation. Two cases received surgery because of perforation and one had complication-associated mortality. CT was performed in 13 cases and 11 underwent endoscopy. Histology showed typical granulomatous formation in 11 cases. Tuberculosis polymerase chain reaction (TB PCR) was performed in 13 cases. Pulmonary tuberculosis was confirmed in 7 cases and 13 cases received anti-tuberculosis treatments.

Conclusion. A high index of suspicion is essential for early diagnosis of intestinal tuberculosis. Thorough history taking, detailed endoscopic or radiologic exams, and careful histological study, are all paramount for making an accurate diagnosis.

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Extra-pulmonary tuberculosis constitutes about 17.5% of all tuberculosis (TB), from which 3%-4% are abdominal TB.[1] Abdominal TB can occur anywhere within the abdominal cavity, including in the gastrointestinal tract, peritoneum, lymph nodes, omentum or solid viscera. The most common forms of abdominal TB involve the intestine, peritoneum, or liver. Intestinal TB accounts for approximately 28.5% of abdominal TB.[1] Among the multiplicity of different organs that can be affected, presentation is often nonspecific. Furthermore, the nonspecific and obscure symptoms of intestinal TB often make accurate and early diagnosis difficult.

The purpose of the present study was to familiarize surgeons with common presentations of intestinal TB and to increase vigilance for this disease. Here we present 14 patients from our medical center who were diagnosed and treated for intestinal TB within a 15-year span, along with their characteristics such as clinical presentations, imaging findings, diagnostic ele-

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ments and treatments. Associated published studies were also reviewed.

Patients and Methods

Patients who were diagnosed with intestinal TB at Mackay Memorial Hospital, Taiwan, from April 2005 to May 2019 were enrolled. Definitive diagnosis of intestinal TB was made if at least one of the following criteria were present in the specimen:[2] 1) presence of caseated granuloma upon histological examination of diseased tissue; 2) AFB-positive smears on histological sections; 3) AFB-positive cultures; and/or 4) AFB positive TB PCR results. Patients' demographic and clinical data such as age, sex, clinical presentations, and concomitant pulmonary TB were recorded. Imaging studies with computed tomography (CT) scan and/or endoscopy were done for all patients and the general findings were analyzed and categorized.

Other specifics such as lesion locations, surgery indications and type of surgery performed were collected. All data were reviewed until completion of anti-TB therapy or mortality.

Statistical analysis

Microsoft Excel was used for data analyzed.

Results

From April 2005 to May 2019, 14 patients were diagnosed with intestinal TB at Mackay Memorial Hospital, including 9 males and 5 females, accounting for 64.29% and 35.71% of the cases, respectively. Patients' mean age was 56.4 ± 21.1 years. However, patients' ages were fairly widespread, from the youngest at 20 years to the oldest at 92 years. Nine patients presented with clinical symptoms of abdominal pain (64.3%), 6 with weight loss (42.9%), 5 with fever (35.7%), 5 with GI bleeding (35.7%), 5 with diarrhea (35.7%) and 2 with constipation (14.3%). Lesion locations were mostly at the right side of the colon; specifically, 12 were found at the ileocecal region, one at the sigmoid colon (7.1%) and one at the descending colon (7.1%) (Table 1).

Thirteen patients underwent CT imaging study and 11 patients underwent endoscopy. The most common features found in CT scans were wall thickening of the involved intestine (9 patients, 64.29%) and abdominal lymphadenopathy (6 patients, 42.86%). Endoscopy identified mucosal ulcer in 9 patients, strictures in 2 patients, nodularity and/or polypoid lesions in 2 patients and deformed ileocecal valve in 1 patient. Eleven patients had classical histological presentation of granuloma with caseated necrosis (78.6%). Suspected TB was tested with acid-fast stain, culture, and/or PCR test. Three of 14 patients tested with acid-fast stain had positive results (21.43%), two of 6 patients had TB-positive culture results (33%) and eight of 13 patients were PCR positive (61.54%) (Table 2). Not all patients received TB culture because the PCR test provides quicker diagnostic results.

Concomitant pulmonary TB was found in seven patients (50%). All patients received anti-TB treatment. Thirteen of 14 patients (92.9%) completed the anti-TB treatment. The duration of complete anti-TB

Table 1. Demographic and clinical characteristics

	Number	%
Total case	14	
Gender		
Male	9	64.3
Female	5	35.7
Age		
Mean age ± SD	56.4 ± 21.1	
≤ 30	2	14.3
31-44	1	7.1
45-64	6	42.9
≥ 65	5	35.7
Symptoms		
Abdominal pain	9	64.3
Weight loss	6	42.9
Fever	5	35.7
GI bleeding	5	35.7
Diarrhea	5	35.7
Constipation	2	14.3
Lesion locations		
Ileum	6	42.9
Ileocecal region	6	42.9
Sigmoid colon	1	7.1
Descending colon	1	7.1

treatment was 9 months for nine patients (64.3%) and 6 months for four patients (28.6%). Twelve patients (85.7%) were recurrence free at the end-point of follow-up data collection. Mean follow-up time was 50.67 ± 33.09 months, and the longest follow-up period was 94 months. Two patients (14.3%) had complication-associated mortality (Table 3); one was hospitalized and died from pneumonia-induced sepsis 3 months into medical treatment, and the other experienced perforation while under medical treatment.

Ten of 14 patients underwent surgery (71.4%). A majority of these patients received surgery due to emergent conditions such as obstruction (40%) and perforation (20%). Four patients underwent laparoscopic surgery for diagnostic purposes (40%). For types of surgery, four patients underwent right hemicolectomy (40%), three patients underwent small bowel resection (30%), two patients underwent diagnostic laparotomy or laparoscopy (20%), and one patient underwent sigmoidectomy (10%). One patient had postoperative mortality. The other nine patients had no morbidity or mortality (Table 4).

Table 2. Diagnostic investigations

	Number	%
CT findings	13	
Wall thickening of involved intestine	9	64.3
Abdominal lymphadenopathy	6	42.9
Endoscopy findings	11	
Ulcer	9	81.8
Strictures	2	18.2
Nodules/polypoid lesions	2	18.2
Deformed ICV	1	9.1
TB survey		
TB AFB stain	3/14	21.4
TB culture	2/6	33.0
TB PCR	8/13	61.5
Histology		
Granuloma w/caseated necrosis	11	78.6

Table 3. Pulmonary TB, anti-TB treatment and follow up

	Number	%
Pulmonary TB	7	50.0
Anti-TB treatment		
Received anti-TB therapy	14	100.0
Complete anti-TB therapy	13	92.9
Duration:		
9 months	9	64.3
6 months	4	28.6
Follow up		
Mortality	2	14.3
Recurrence free	12	85.7

Table 4. Surgery

	Number	%
Received surgery	10	71.4
Surgery indications		
Obstruction	4	40
Diagnostic	4	40
Perforation	2	20
Surgery types		
Right hemicolectomy	4	40
Small bowel resection	3	30
Diagnostic laparotomy/laparoscopy	2	20
Sigmoidectomy	1	10

Discussion

The tubercle bacilli, the bacteria causing intestinal TB, mainly enter the intestinal tract through ingestion of infected milk or sputum. Other pathways include hematogenous spread from the tubercular focus from elsewhere in the body to abdominal solid organs, direct spread to the peritoneum from infected adjacent foci, or spread through lymphatic channels from infected nodes.[3] After tubercle bacilli enter the intestinal tract, they invade the submucosa and form granuloma, which are surrounded by Langhans' giant cells. The center of the granulomas is digested by macrophage and neutrophils and becomes caseation necrosis. Caseation necrosis can cause overlying mucosal ulceration and spread into deeper layers, even into adjacent lymph nodes and the peritoneum.[4]

Symptoms

A majority of patients have non-specific symptoms with abdominal pain, weight loss, and diarrhea, with fever being the most common symptom.[5-7] The present series showed similar results but with the addition of GI bleeding (35.7%) as another common presentation.

Location

Lesions are reported to be predominantly located at the ileum and ileocecal region, ranging from 64%-80%.[5,8] This location may be common due to Peyer patches in the ileum mucus membrane and the stable physiology of the ileum, which increases the bacterial contact time. Colonic lesions (10.8%) are far fewer and usually involve the ascending colon.[7,9] The present study showed similar results to those of the above previous reports.

Diagnosis

Other than direct histologic confirmation, the diagnosis of abdominal TB may be established definitively by demonstration of *M. tuberculosis* in a biopsy specimen of an involved site via mycobacterial culture and/or PCR.[5] Despite their high specificity, the poor sensitivity of both PCR (47%) and culture (19%-70%) can increase the difficulty of diagnostic confirmation.[10,11] However, a higher rate of PCR (61.5%) and culture (33.0%) sensitivity was seen in the present study compared with the rates in previous studies. The better sensitivity is most likely due to obtaining sufficient specimens and bacterial count from the surgery site.

Caseation granulomas and positive acid-fast stain are observed in fewer than 33% of cases.[5] On the other hand, in the present study, 78.6% of the patients exhibited granuloma with caseated necrosis.

Poor sensitivity of culture and PCR may lead to false negative results. When intestinal TB is highly suspected by clinical presentations, definitive diagnosis is difficult to make solely by a single histologic examination. Combining acid-fast stain, TB culture and PCR provides the best way to make an early and timely diagnosis.

Shi et al. stated that evidence of concomitant pulmonary TB is an important indicator for suspecting and/or diagnosing intestinal TB.[12] Luh et al. in Taiwan showed that 82% of patients with abdominal TB have concomitant pulmonary TB.[13] In the present study, 50% of patients had concomitant pulmonary TB.

CT and endoscopy

Several authors have concluded that radiological features do not reliably predict intestinal TB diagnosis.[14,15] For example, CT features such as necrotic lymph nodes and ileocecal area involvement have been shown to have calculated pooled sensitivity of 23% and specificity of 100%, and pooled sensitivity of 64% and specificity of 77%, respectively. These radiological features are not specific to the disease, and the low sensitivity rate limits their widespread applicability.[16] In the present study, wall thickening of the involved intestine (64.3%) and abdominal lymphadenopathy (42.9%) were the most common features identified in CT. On the other hand, endoscopy features of intestinal TB can be non-specific and mimic inflammatory bowel disease or malignancy.[17-19] Mucosal ulcer (81.8%) is the primary endoscopic finding in the present study, followed by strictures (18.2%), nodules/polypoid lesions (18.2%) and deformed ileocecal valve (9.1%).

Types of surgery

Surgery is warranted in cases with complications, including obstruction, perforation, severe hemorrhage, IAA/fistula formation, and uncertain diagnosis.[20,21] In the present study, surgery was performed for obstruction (40%), diagnostic examination (40%), and perforation (20%). The morbidity rate of surgery was 0%, and the mortality rate of surgery was 10%. In case of emergent conditions or uncertain diagnosis, surgery is a feasible option.

Management of intestinal TB

Mukewar et al. recommended 6-9 months of anti-TB therapy depending upon patient response.[22] Saurabh et al. determined that the majority of ulcers (87.2%), nodules (84.6%), polypoid lesions (85.7%), luminal narrowing (76.2%), and ileocecal valve deformities (76.5%) could be resolved with anti-TB treatment.[13] In the present study, 92.9% of patients, whether they underwent surgery or not, completed anti-TB treatment with resolution of symptoms. Anti-TB therapy was the first option for those with confirmed diagno-

sis of intestinal TB. If the patient presents with an emergent or uncertain condition, surgery should be added on. Patients in the present study who underwent surgery were recurrence-free during follow-up.

Limitations

This was a retrospective, single-center study with a relatively small sample, which limits statistical power and limits generalization of results to other populations or locations. Follow-up data were limited to 3 months without allowing long-term evaluation of treatment results. Further prospective, multicenter study may yield evidence to confirm the present findings.

Conclusions

A high index of suspicion is essential for early diagnosis of intestinal TB. Thorough history taking, detailed endoscopic or radiologic exams, and careful histological study are all paramount for making accurate diagnosis. Anti-TB medication is the backbone of treatment for intestinal TB. However, surgical intervention is a safe and feasible treatment method for patients with emergent conditions and uncertain diagnosis.

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Conflicts of Interest

No potential conflicts of interest was reported by the authors.

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原　著

腸結核：單一醫學中心十五年間的病例系列研究

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目的　腸結核的非專一性表現會使準確診斷變得困難。本篇的目標是幫助外科醫師熟悉腸結核的常見表徵並增加疾病的警覺性。

方法　本篇為回溯性病例系列，資料蒐集自單一醫學中心，時間從 2005 年四月到 2019 年五月。記錄症狀、手術適應症、併發症、最終病理結果、病灶位置和診斷方法。

結果　十五年研究期間共有十四個病例。主要症狀有腹痛、腹瀉和腸胃道出血。大部分病例接受手術，適應症是阻塞和診斷。兩個病例經歷手術是因為穿孔，且其 中一位死亡。迴盲瓣附近的位置占大多數，各占大約 43 個百分比。十三個病例執行電腦斷層，十一個病例做大腸鏡。十一個病理報告顯示典型的肉芽腫構造。十三個病例有接受結核菌核酸增幅檢驗。七個病例被證實有肺結核。十三個病 例有接受抗結核菌治療。

結論　高度懷疑對於早期診斷腸結核是必須的。包括過去病史在內，全面性的臨床檢查是至關重要的。本篇呈現我們中心的腸結核病例經驗。雖然資料簡短而有 限，我們期望能在本篇的基礎上，對未來進行更詳細的分析以供研究及參考。

關鍵詞　腸結核、診斷、保守治療、手術。