

Tuberculous appendix: a review of clinical presentations and outcomes

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ABSTRACT

Introduction: Tuberculous appendix is surprisingly rare, even in countries where this infection is common. We report our experience with tuberculous appendix over a 15-year period.

Methods: A search for cases of tuberculous appendix was conducted from January 1995 to December 2009 on the databases of the National Tuberculosis Centre and the Departments of Pathology and Surgery of Raja Isteri Pengiran Anak Saleha Hospital.

Results: There were five cases of tuberculous appendix, giving a cumulative incidence of 0.08 percent of all appendectomies (n is 6,593), 0.2 percent of tuberculosis (TB) cases (n is 2,876) and 8.6 percent of abdominal TB (n is 58). Three patients were male and two were female, with a median age of 27 (range 25–48) years. Four patients presented with symptoms of acute appendicitis and one with an appendiceal mass following treatment for acute gastroenteritis. Only one patient had constitutional symptoms. Four patients had appendectomies (one laparoscopic and three open) within the same admission and one had interval appendectomy. Operative findings included perforated appendix (n is 1), appendiceal mass (n is 1) and acute appendicitis (n is 3). In all cases, the diagnoses were made only after review of the histology. None of the patients had pulmonary TB. Delay in initiating anti-TB treatment in one patient resulted in the development of an ileo-cutaneous fistula following appendectomy. This was resolved by excision, followed by anti-TB treatment.

Conclusion: Tuberculous appendix can present as acute appendicitis, and the diagnosis is often made after surgery. Any delay in treatment can lead to significant complications.

Keywords: appendectomy, appendicitis,

gastrointestinal tuberculosis, granuloma, tuberculosis

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INTRODUCTION

Acute appendicitis is a common surgical illness, and in some cases, it may have protean manifestations that can result in a delay in diagnosis.⁽¹⁾ Diagnosis of acute appendicitis is mainly clinical, with supporting laboratory and radiological investigations. In the United States, acute appendicitis occurs in 7% of the population, with an incidence of 1.1 cases per 1,000 people per year.⁽²⁾ The incidence of appendicitis is lower in cultures with a higher intake of dietary fibre.⁽³⁾ However, in countries where infections like tuberculosis (TB) remain endemic, tuberculous appendix is an important cause. Although gastrointestinal TB is common in endemic regions, TB appendicitis is surprisingly rare.⁽⁴⁾ We report our experience with tuberculous appendix from a tertiary referral centre in a developing Southeast Asian nation, where TB infections are still endemic.

METHODS

Patients with tuberculous appendix or TB appendicitis were identified through searches conducted from January 1995 to December 2009 on three databases: the National Coordinating Centre for TB database, which captures all TB cases in the country; the Department of Surgery operation theatre database; and the Department of Pathology database. The cases notes of patients with tuberculous appendix were retrieved and the data retrospectively collected using a predefined proforma. The data collected included the demographics (age, gender and ethnicity or nationality), clinical presentations, laboratory (human immunodeficiency virus [HIV] serology) and radiological (chest radiograph) investigations, operative details, treatment and outcome of follow-ups.

All histology reports and slides were retrieved and reassessed by a single pathologist. A diagnosis of TB appendix/appendicitis was considered if either acid-fast bacilli (AFB) on Ziehl-Neelsen stain or caseating/non-caseating granulomas with large epithelioid Langhans giant cells was present, and on exclusion of other

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Table I. Overall cumulative incidence of tuberculous appendix over the study period (1995–2009).

Case type	No. (%)
All appendectomy (n = 6,593)	5 (0.08)
All tuberculous cases (n = 2,876)	5 (0.2)
Abdominal tuberculosis* (n = 58)	5 (8.6)

* Consists of involvement of the gastrointestinal tract, liver, biliary, gallbladder, abdominal lymphadenopathy and spleen.

granulomatous disorders, such as Crohn's disease, on evaluation or follow-up.

All patients diagnosed with TB were treated with the standard anti-TB treatment, and two regimes were used during the study periods. Up till 1997, the first choice regime was SRIP (streptomycin 15 mg/kg/day, rifampicin 10 mg/kg/day, isoniazid 5 mg/kg/day and pyrazinamide 30 mg/kg/day). After 1997, the standard first choice regime was RIPE (rifampicin, isoniazid, pyrazinamide and ethambutol 20 mg/kg/day each). Both the quadruple regimes were given for two months, followed by dual rifampicin and isoniazid for an additional four months. All patients were also administered pyridoxine (vitamin B₆) to counteract the side effects of isoniazid.

RESULTS

Over the 15-year period, five cases of tuberculous appendix were identified (Table I). There were three male and two female patients, with a median age at presentation of 27 (range 25–48) years. Three patients were locals and two were expatriates from the Indian subcontinent. None of the patients had chest radiological changes that were consistent with pulmonary TB. Only one patient had right costophrenic changes. The details of the patients are shown in Table II.

Four patients presented with symptoms that were consistent with acute appendicitis (generalised abdominal pain that later localised to the right iliac fossa) and fever. All of them had right iliac fossa pain (100%), while four (80%) had fever, three (60%) had anorexia and one complained of weight loss. The duration of symptoms prior to presentation was 2–21 days. The patients underwent appendectomies within the same day of admission; one laparoscopic and three open procedures. However, one patient (Case 1) was initially treated for acute gastroenteritis and was re-admitted with right iliac fossa pain and mass. Conservative treatment was opted, but the mass failed to resolve on follow-up, and the patient eventually underwent an interval appendectomy four months after the initial presentation.

Surgical findings included a retrocaecal appendiceal mass (Case 1), perforated appendix (Case 3) and inflamed

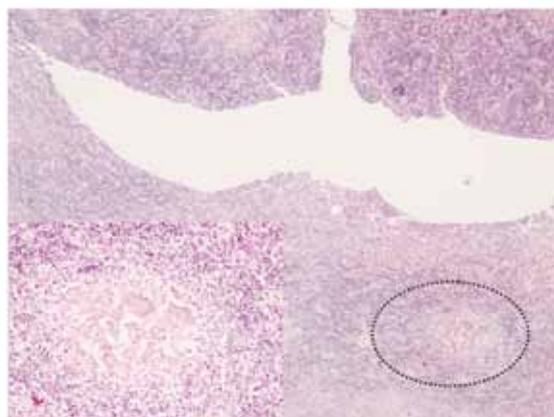


Fig. 1 Histology of the appendix shows granulomas (circled) near the inflamed lumen (Haematoxylin & eosin, × 10). Insert shows the granuloma (Haematoxylin & eosin, × 40).



Fig. 2 Axial CT image shows the ileocutaneous fistula (arrow).

appendix (Case 2, 4 and 5). Histology results were immediately available for four patients, with all the changes consistent with TB (Figs. 1 & 2), and they were started on standard anti-TB treatment. The histologies showed caseating granuloma, but no AFB was identified in the histology of any of the patients. Unfortunately, the histology result of one patient (Case 4) was not retrieved, and she was not immediately started on anti-TB treatment. This resulted in the formation of an ileocutaneous fistula (Fig. 2), which required a laparotomy and fistula excision. The resected specimen showed changes that were consistent with TB (chronic inflammatory changes, with caseating granuloma but no AFB). This was complicated by wound infection and fistula recurrence. The patient was started on anti-TB treatment, and the fistula eventually resolved completely.

All patients were negative for HIV serology. The local patients remained well and had no evidence of recurrence on follow-up. The two expatriates were well on short-term follow-up (less than two months) before returning to their homeland.

Table II. Profiles of the five patients with tuberculous appendix.

Case	Age/gender/ nationality	Symptoms*	Duration from 1st presentation (days)	Treatment	Operative findings	Outcome
1	47/M/expatriate	Pain/fever RIF mass	10	Interval OA	Acute/chronic appendicitis/ ileocaecal TB	Self-limiting hearing loss
2	27/M/expatriate	Pain/anorexia/ fever/nausea	4–5	LA	Acute appendicitis	Uncomplicated
3	25/M/local	Pain/fever/ anorexia	2	OA	Perforated appendix	Uncomplicated
4	30/F/local	Pain/anorexia/ fever/nausea	7	OA	Retrocaecal mass	Complicated by ileocutaneous fistula
5	26/F/local	Pain/anorexia/ weight loss	21	OA	Acute/chronic appendicitis/ peritoneal TB	Uncomplicated

* Pain symptoms were all initially generalised abdominal pain, which later localised to the right iliac fossa.

M: male; F: female; OA: open appendectomy; LA: laparoscopic appendectomy; RIF: right iliac fossa; TB: tuberculosis

DISCUSSION

Our study showed that tuberculous appendix is uncommon, accounting for 0.08% of all appendectomies and 0.2% of all TB cases during the 15-year study period. Among abdominal TB, tuberculous appendicitis accounted for 8.6% of cases. Interestingly, tuberculous appendix is uncommon even in countries where TB infection is still a major public health issue. In a review of 2,921 appendectomies carried out in a tertiary centre in India, only 5% of cases were granulomatous appendicitis. This consisted of tuberculous appendix in 2.3% and parasitic infestations in 2.3%.⁽⁵⁾ Older studies have reported a prevalence of 0.1%–3.0% among all appendectomies, and higher among patients known to have TB (1.5%–30%) or intestinal TB (46%–70%).^(6,7) In fact, most of the reported cases have come from underdeveloped and developing nations.^(8–12) However, these numbers are likely to be underestimation of the actual prevalence. Even with evaluation of such cases with colonoscopy and computed tomography, it is often not possible to diagnose appendix involvement unless laparoscopy is performed or the appendix is removed for various reasons.

The underlying pathogenesis of tuberculous appendicitis is not known. However, concomitant involvement of other parts of the gastrointestinal tract is common, especially the ileocaecal region.⁽⁹⁾ Singh et al proposed a new aetiopathological classification that categorised tuberculous appendix into primary or secondary involvement. Primary involvement occurs through contact with infected intestinal contents or through haematogenous spread from sources that are not clinically detectable. Secondary involvement occurs through local extension from ileocaecal involvement,

retrograde lymphatic spread from distant lesions in the ileum or ascending colon, or peri-appendicitis from peritoneal involvement.⁽⁹⁾ Some cases may have both types of involvement as multi-organ involvements are not uncommon.

The clinical presentation of tuberculous appendix is nonspecific. Singh et al categorised the presentations into three types, depending on the underlying degree of appendix involvements.⁽⁹⁾ The most common type is chronic disease presenting with mild to moderate intermittent right fossa pain, which may be associated with nausea and vomiting. This is clinically indistinguishable from ileocaecal TB. The other two types consist of one that resembles acute obstructive appendicitis and the less common latent type that is often discovered after incidental appendectomy during other kinds of surgery.⁽⁶⁾ In this study, most of our patients presented with the acute obstructive type. The presentations of our patients were similar to those of acute appendicitis of other causes, with the exception of Case 5, which on hindsight, had consistent features of gastrointestinal TB infection. Therefore, the diagnosis of tuberculous appendix was unexpected and was made only after examination of the resected appendix.^(8,9) All our patients had caseating granulomas, but no AFB was identified. Unfortunately, no TB cultures were done as none was suspected to be tuberculous in origin. There are generally no specific features on history, clinical examination or investigations that can differentiate appendicitis of different aetiologies from TB. None of our patients had typical features on radiography that were consistent with pulmonary TB. One patient had costophrenic changes that could have been due to TB. Up to 50% of patients with

abdominal TB have pulmonary involvements.⁽¹³⁾ With the exception of parasite-related appendicitis, other causes of granulomatous appendicitis, including Crohn's disease, sarcoidosis and foreign body-induced inflammation, are rare.⁽⁵⁾

In patients presenting with TB, especially in less commonly affected sites, it is important to rule out an immune-compromised state. All our patients were negative for HIV serology. In our local setting, all patients diagnosed with TB infections are tested for HIV. Additionally, all expatriates undergo compulsory HIV testing prior to employment. To our knowledge, there had only been two patients with pulmonary TB who also had HIV infection.

The initial management of acute presentations of tuberculous appendix is surgical. In fact, it is extremely rare for a diagnosis to be made before surgery. Anti-TB treatment should be started as soon as possible. There is no specific guideline for the treatment of tuberculous appendix, and the treatment recommendation for gastrointestinal TB, which is similar to that for pulmonary TB, is followed. As highlighted by our case, a delay in treatment can result in serious complications. With the ever-increasing patient loads, it is possible for cases to be missed or treatment to be delayed. Review appointments may be long, and some patients may not even get reviewed, especially if the interventions had been uncomplicated. Therefore, it is important for patients, or at least the results of the histology, to be reviewed early so that treatment will not be delayed in patients found to have TB in the resected specimens. Alternatively, a system should be in place so that clinicians are made aware and patients can be recalled for treatment.

In conclusion, we have shown that tuberculous appendix is a rare but important cause of appendicitis. The

acute presentations resemble those of acute appendicitis of other aetiologies. Any delay in treatment can be associated with significant complications. Despite the rarity of this condition, even in endemic areas, it is important for clinicians to be aware of this infection, especially as there are ongoing changes in the population demographics due to population movement and the resurgence of TB.

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