



## Perianal Fistula Due to Tuberculosis Infection: A Case Report

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### ABSTRACT

**Background:** Approximately 5% of all cases of tuberculosis are extrapulmonary. A rare extrapulmonary variant of the disease is known as perianal tuberculosis, which accounts for 0.001% of all extrapulmonary tuberculosis cases.

**Case Report:** A 28-year-old male presented with intermittent chronic anal pain and purulent discharge from the anal for 6 months, without respiratory complaints. Chest X-ray examination shows minimal infiltrate on the right lung apex and broncho vascular pattern partially covered with infiltrate. Fistulotomy has been done three times in this patient within 6 months. Colonoscopy examination shows a recti polyp, and the histopathology result from the biopsy specimen taken from the last fistulotomy is a tuberculosis-specific chronic inflammatory process. The Human Immunodeficiency Virus test is negative. This patient has been treated with anti-tuberculosis treatment for 7 months and 2 months after consuming it the wound on the perianal is healing and the patient's weight is gaining 10 kg within 7 months and anti-tuberculosis treatment is continued for up to 12 months.

**Conclusion:** The diagnosis of perianal tuberculosis is challenging, especially in the absence of pulmonary focus. Tuberculosis should be considered in the differential diagnosis of perianal ulcers and fistulas, mainly in non-healing and recurrent anal lesions, especially in regions where tuberculosis is endemic. Management with anti-tuberculosis treatment can provide complete recovery.

**Keywords:** Extrapulmonary tuberculosis; perianal tuberculosis; tuberculosis infection; fistulotomy; Anti-tuberculosis treatment

### ABSTRAK

**Latar belakang:** Sekitar 5% dari semua kasus tuberkulosis adalah ekstrapulmoner. Varian penyakit ekstrapulmoner yang langka dikenal sebagai tuberkulosis perianal, yang menyumbang 0,001% dari semua kasus tuberkulosis ekstrapulmoner.

**Laporan Kasus:** Seorang pria berusia 28 tahun mengalami nyeri anus kronis intermiten dan keluar cairan bernanah dari anus selama 6 bulan, tanpa keluhan pernapasan. Pemeriksaan rontgen dada menunjukkan infiltrat minimal pada puncak paru-paru kanan dan pola pembuluh darah bronko, sebagian ditutupi dengan infiltrat. Fistulotomi telah dilakukan tiga kali pada pasien ini dalam waktu 6 bulan. Pemeriksaan kolonoskopi menunjukkan polip rekti, dan hasil histopatologi dari spesimen biopsi yang diambil dari fistulotomi terakhir adalah proses inflamasi kronis spesifik tuberkulosis. Tes Human Immunodeficiency Virus (HIV) negatif. Pasien ini telah diobati dengan pengobatan anti-tuberkulosis selama 7 bulan dan 2 bulan setelah mengkonsumsinya, luka pada perianal sembuh dan berat badan pasien bertambah 10 kg dalam waktu 7 bulan dan pengobatan anti-tuberkulosis dilanjutkan hingga 12 bulan.

**Kesimpulan:** Diagnosis tuberkulosis perianal bermasalah, terutama dengan tidak adanya fokus paru. Tuberkulosis harus dipertimbangkan dalam diagnosis banding ulkus dan fistula perianal, terutama pada lesi anus yang tidak sembuh dan berulang, terutama di daerah di mana tuberkulosis endemik. Manajemen dengan pengobatan anti tuberkulosis dapat memberikan pemulihan total.



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**Kata kunci:** Tuberkulosis ekstrapulmoner; tuberkulosis perianal; infeksi tuberkulosis; fistulotomi; Pengobatan anti-tuberkulosis

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## 1. Introduction

Tuberculosis (TB) is a widespread disease that affects many parts of the world [1]. Indonesia has the second-highest TB incidence worldwide and accounts for 8.5% of the global burden of TB despite the enormous efforts in the last two decades [2]. Extrapulmonary instances of tuberculosis account for about 5% of all cases. Perianal TB is an uncommon extrapulmonary variation of the illness. Perianal TB is a spontaneous presentation of cutaneous *M. tuberculosis* infection. It makes up 0.001% of all extrapulmonary TB cases and is more common in men than in women. [3-5]. It is usually secondary to intestinal or genitourinary tuberculosis, developing through direct extension or hematogenous or lymphatic spread from regional lymph nodes [4]. Perianal tuberculosis can manifest with local pain, mucopurulent secretion, and multiple complex perianal fistulas [5].

Diagnosis of perianal tuberculosis is difficult and needs a high suspicion index, especially in patients with perianal involvement as the first presentation of tuberculosis. The diagnosis is confirmed after surgery and histological examination of excised tissue in most cases [6]. Microbiological confirmation through the isolation of *Mycobacterium tuberculosis* from fistula drainage or tissue biopsy is essential for definitive diagnosis [7]. However, the prevalence might be underestimated, as it can be misidentified as Crohn's disease or other inflammatory bowel diseases [3]. Consequently, especially in areas where tuberculosis is common, perianal tuberculosis should be taken into account while making a differential diagnosis for discharge, lump at the anal, and persistent anal pain. One special and difficult side effect of mycobacterial infections is extrapulmonary tuberculosis, which is more common in those with weakened immune systems, such as those who also have HIV infection. The interplay between HIV and tuberculosis creates a milieu conducive to atypical presentations and heightened morbidity [8]. Access to HIV testing in extrapulmonary tuberculosis patients is pivotal, as it not only guides therapeutic decisions but also influences the overall prognosis [9].

In this case report, we will discuss the history, physical examination, investigations, and treatment of the patient who presented with perianal fistula caused by *Mycobacterium tuberculosis*, which presented with anal pain and discharge without respiratory complaints. From this case report, clinicians can increase awareness of the presence of perianal tuberculosis, which can be identified from patient symptoms, and find out what diagnostics test can be carried out and how to manage the patient.

## 2. Case Report

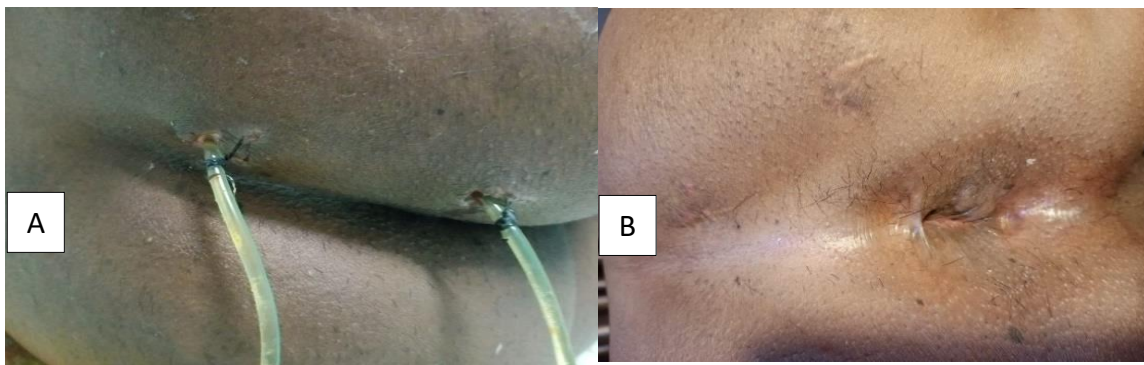
A 28-year-old male presented history of intermittent chronic anal pain and purulent discharge from the anal for the last 6 months. This complaint started by a patient who realized there was a lump around his anal for the past 6 months. The patient reported having a history of bloody stool once, 10 months before the patient was diagnosed with perianal TB. The blood was fresh red and remained on the surface of the stool. The patient had no complaints of respiratory symptoms. Complaints of chronic cough and shortness of breath were not found. Constitutional symptoms such as night sweats were not found in the patient, but the patient had experienced weight loss in the last 3 months about 5 kgs. This was accompanied by a fever of variable degrees. A history of chronic medical conditions such as diabetes mellitus and hypertension were not found in this patient. History of Anti Tuberculosis Treatment (ATT) was not found.

During the clinical examination, the patient, with a weight of 60 kg was relatively weak. Physical examination revealed normal limit with body temperature 36.5°C, blood pressure 122/54 mmHg, heart rate 87 bpm, and respiration rate 18 breaths per minute. No lymphadenopathy was found on palpation. The lung examination showed a vesicular breath sound with no Ronchi and no wheezing. The perianal region examination showed multiple infected abscesses and fistulas followed by pus. During the physical examination, the patient experienced intensely painful anal to the touch. Laboratory investigations showed a hemoglobin level of 15.4 g/dL, a normal white blood cell count of 7.770/μL in addition to normal erythrocyte sedimentation rate of 7 mm/h. The other laboratory data were within normal limits.

An amount of pus was drained from the incisional perianal abscess. The abscess had formed a fistula to the perianal region, indicating a perianal abscess. According to his medical history, he was treated for a perianal

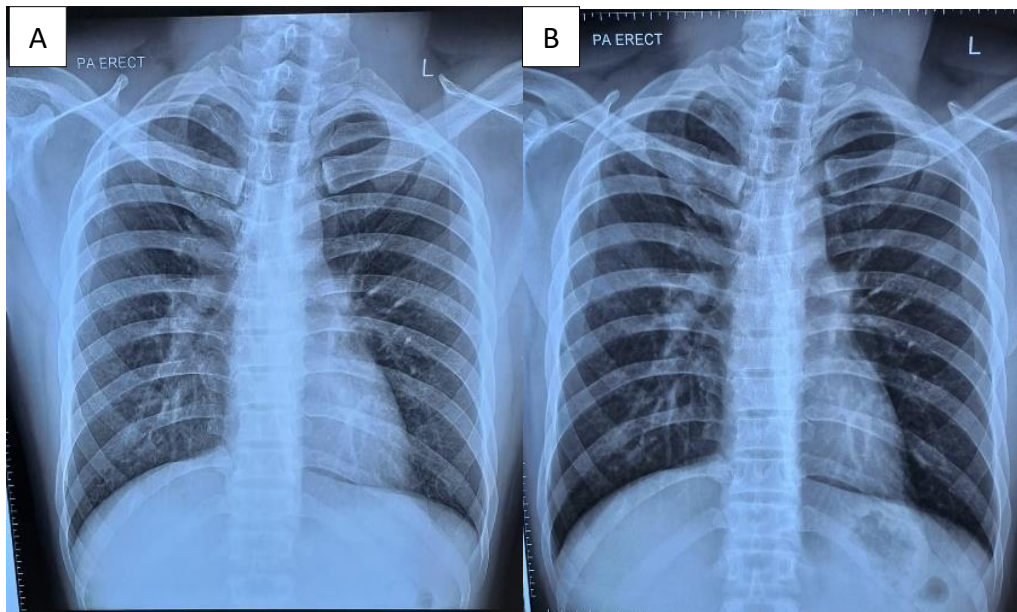
fistula and underwent a fistulotomy procedure, yet, despite the initial healing, the patient still had pain around his anus. In the perianal area, there were fistulous perianal tracts with an outflow of seropurulent secretion after fistulotomy (Figure 1A). However, the discharges remained draining and a fistulotomy had been done three times in this patient within 6 months. To evaluate the patient, a chest x-ray was carried out, those were done two times in the patient before starting the ATT. Chest X-ray examination shows minimal infiltrate on the right lung apex and broncho vascular pattern partially covered with infiltrate followed by lymphadenopathy at the right perihilar. (Figure 2A, 2B). During the colonoscopy, the device progressed with visualization of the recti polyp. Biopsies of lesions at perianal tissue from the last fistulotomy were performed. The histopathology analysis result from the biopsy specimen showed the appearance of epithelioid cell groups and multinucleated giant cells with necrotic masses. No signs of malignancy were found. Those results suggested tuberculosis-specific chronic inflammatory process. Apart from imaging, the patient underwent an HIV test and the result was nonreactive.

We made a diagnosis of perianal abscesses + fistula caused by tuberculosis infection with suspected pulmonary involvement based on chest X-ray results. The patient has been treated with ATT for 12 months, consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months, and rifampicin and isoniazid for 10 months.



**Figure 1** (A) Fistulous perianal tracts with an outflow of seropurulent secretion. (B) The perianal fistula began to heal after two months of consuming ATT.

The patient's symptoms vanished, and the perianal fistula began to heal within two months of treatment (Figure 1B). Afterward, the patient is healthy and has no symptoms. However, the patient has reported a documented weight gain of 10 kg within 7 months. He is now able to ambulate freely. Overall, the patient is showing signs of considerable clinical improvement.



**Figure 2** (A) Chest X-ray examination shows minimal infiltrate on the right lung apex and broncho vascular pattern partially covered with infiltrate 1 month before treated with ATT. (B) Chest X-ray examination shows minimal infiltrate on the right lung apex and broncho vascular pattern partially covered with infiltrate after 1 month when ATT was started (remained as Figure 2a).

### 3. Discussions

Extrapulmonary tuberculosis of the gastrointestinal tract constitutes 1% of all cases of tuberculosis. It may involve any part of the gastrointestinal system, such as the peritoneum, stomach, duodenum, ileocecal region, colon, rectum, and anus. Yet, tuberculous peritonitis is the most common [10]. A perianal fistula may result from perianal TB, an uncommon kind of extrapulmonary tuberculosis. Perianal tuberculosis is thought to make up only 0.001% of cases of extrapulmonary tuberculosis; however, because it can be mistaken for other illnesses, including Crohn's disease and other perianal disorders, its frequency may be understated [3]. Perianal tuberculosis can manifest in a variety of ways, often resembling other common or uncommon illnesses, making diagnosis difficult. [11].

Anal tuberculosis should be considered in the differential diagnosis of chronic or recurrent anal fistulas [12]. Perianal TB can manifest as ulcerative lesions or perianal fistulas [5]. Perianal fistulas resulting from *Mycobacterium tuberculosis* infection present a unique and intriguing facet of extrapulmonary tuberculosis, necessitating a nuanced understanding for effective clinical management [3]. Literature reports a greater prevalence of anal TB in males (ratio 4:1) and primarily in the fourth decade of life. This lesion can happen concurrently with pulmonary infection or manifest earlier than the pulmonary lesion [11]. In addition to the hematogenous dissemination of a pulmonary focus, causes of perianal TB include the ingestion of sputum containing active pulmonary disease bacilli, lymphatic dissemination of intestinal or genitourinary disease from regional lymph nodes or even direct extension from neighboring regions [11,13]. Currently, Indonesia is the second largest contributor to TB cases in the world [14]. Therefore, it is important to consider anal tuberculosis in the differential diagnosis of chronic or recurrent anal fistulas.

Perianal TB can manifest with local pain, mucopurulent secretion, and multiple complex perianal fistulas [5] which we also observed in the case described here. These fistulas can persist and have a prolonged and relapsing course despite proper surgical management. Inguinal adenopathy, perianal ulceration with purulent exudates, abscesses, anal stenosis, anal ulceration, and fissures have also been reported [13,15]. Before developing into fistulas, the patient in our study had perianal abscesses with purulent exudates. In tropical nations like Indonesia, there are several reasons why people get perianal cutaneous ulcerations, including bacterial, viral, and parasitic ones. The differential diagnosis for the TB ulcerative lesions in the perianal region includes amoebiasis, sarcoidosis, syphilis, lymphogranuloma venereum, malignancies, and foreign body reactions. Anorectal abscesses are linked to mixed flora. [10]. Those diseases may be difficult to distinguish from each other by macroscopic evaluation. That is why a microscopic examination is needed. When tuberculosis is considered, a biopsy needs to be taken from the lesion; acid-fast staining and polymerase chain reaction should be used for a rapid and accurate diagnosis. Histopathology and microbiology are of great value in diagnosis [16]. The diagnosis of perianal TB can also be made through the

Xpert MTB/RIF test with a sample using secretions through the perianal fistula or from the tissue biopsy taken during surgery. Apart from the high sensitivity and specificity of the Xpert MTB/Rif, the other advantage of this test is the ability to detect resistance to Rifampicin drug.

Histopathological findings usually include ulceration surrounded by a nonspecific inflammatory infiltrate and extensive caseous necrosis. Granulomas composed of epithelioid, and Langhans-type giant cells can also be seen in the dermis [17], as seen in this report. The biopsy from the last fistulotomy of the patient revealed a chronic granulomatous inflammatory process with epithelioid cell groups, multinucleated giant cells, and necrotic masses. The detection of mycobacterial DNA by PCR in clinical samples contributes to the rapid diagnosis of TB infection [5]. This minimally invasive test can detect bacterial DNA within 48 hours with high sensitivity and specificity. In this report, PCR was not performed. PCR has the highest sensitivity (79.4%), followed by histopathological examination (73.5%), cultures (29%-47%), and smear of material from the perianal region (5.8%) [5].

Regarding treatment, the initial approach is the use of a chemotherapy regimen consisting of rifampin, isoniazid, pyrazinamide, and ethambutol for six months [16]. Oral administration of fixed-dose combination regimens containing isoniazid, rifampicin, ethambutol, and pyrazinamide was initiated in a case report, and the clinical course was favorable after an anti-TB regimen lasting 6-9 months. Although in certain cases the fistula may heal after antituberculosis treatment, surgical removal of tuberculous fistulas is necessarily recommended in addition to anti-tuberculosis drugs [10]. The prognosis of anal TB with the proper drug regimen is excellent with complete remission of the disease [11]. However, the long duration of anti-TB therapy leads to treatment non-compliance by the patient, which leads not only to the recurrence of the fistula but also to the emergence of multidrug-resistant TB strains [17]. This lesion may appear before the pulmonary lesion or concurrently with the pulmonary infection. The transmission of infection from the lungs to the perineum occurs through endogenous sources, typically as a result of breathing in respiratory secretions containing high concentrations of bacilli. Other mechanisms of transmission include hematogenous, lymphatic from regional lymph nodes, and direct extension from adjacent regions, even if the former is the main source of infectivity [18,19]. Extrapulmonary tuberculosis can affect any viscera in the human body, regardless of whether the lungs are affected. The incidence of tuberculosis has increased dramatically in parallel with the rise in AIDS patients worldwide. By releasing growth factors from the bacilli, HIV and tuberculosis (TB) encourage each other's growth and make HIV more infectious in the host. Similarly, HIV-induced immunosuppression can enhance the latent mycobacterium reawakening capacity of lymphoreticular cells. Although anal lesions are rather prevalent in AIDS patients, ranging from 16 to 34%, anal TB is relatively uncommon [20].

Garg et al conducted a study of 637 samples from 410 patients with ani fistula that tested positive for TB in 43 patients. The examinations performed to confirm the diagnosis of TB in ani fistula are histopathology of tissue, tissue Polymerase Chain Reaction (PCR), and pus PCR. In this study, it was found that tissue (polymerase chain reaction) was significantly better than tissue (histopathology) ( $p < 0.00001$ ) and pus (polymerase chain reaction) was significantly better than tissue (polymerase chain reaction) ( $p < 0.0009$ ). Similar to tissue histopathology, pus-PCR demonstrated a noticeably greater detection rate of tuberculosis [18].

To Takahashi et al report, the biopsy of the patient's intergluteal region showed a persistent granulomatous inflammatory process. Additionally, the biopsy of the perianal fistula tract revealed an epithelioid granulomatous process with the presence of multinucleated giant cells (Langhans cells), although there was no caseous necrosis. Both biopsy specimens tested negative for alcohol-resistant fungus and bacilli. The PCR test conducted on the intergluteal tissue yielded a positive result for *M. tuberculosis*, whereas the test yielded a negative result in the material obtained from the fistula tract [5].

Hasani et al also report histological examination of all biopsies from perianal lesions showed epithelioid granulomas and Langhans' type multinucleated giant cells, with the presence of caseous necrosis. Culture swabs from the perianal lesion confirmed mycobacterium tuberculosis [21].

Garg et al demonstrated the treatment with a 6-month prescription of standard 4-drug-ATT was given. The treatment plan consisted of Rifampin, Isoniazid, Pyrazinamide, and Ethambutol for 2 months followed by Rifampicin and isoniazid for 4 months. During the initial 2 months of ATT, patients with a complicated fistula received a daily deep intramuscular injection of 750 mg streptomycin, either in the gluteus maximus muscle or mid-lateral thigh, in addition to anti-tuberculosis treatment. For the first three months following surgery, regular patient follow-up was conducted at the surgeon's office every two weeks. This procedure was performed every week for the subsequent 3 months or until the fistula achieved full healing. A cure was defined as the complete cessation of purulent discharge from all the tracts for a minimum of 6 weeks. The failure of the operating procedure was determined by the continued presence of purulent discharge from the

main fistula or any of the fistula tracts (in the case of a fistula with numerous tracts). Patients who tested positive for tuberculosis (TB) and experienced failure to heal the fistula underwent reoperation. Anti-tuberculosis medications were administered until the specified deadline. Long-term follow-up was initiated six months post-surgery [18]. According to The Guidelines of the Indonesian Society of Respiriology, extrapulmonary TB treatment may take 9-12 months with 2 months of the initial phase followed by 7-10 months of the continuation phase [22].

The patient in this case reported being treated with ATT for 12 months that was consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol in the first 2 months and followed by 10 months of treatment with Rifampicin and Isoniazid. After 2 months of treatment, improvement was seen in the fistula area and the patient's weight increased.

#### 4. Conclusions

Perianal TB is a rare extrapulmonary variant of the disease. The diagnosis of perianal tuberculosis is challenging, especially in the absence of pulmonary focus. Tuberculosis should be considered in the differential diagnosis of perianal ulcers and fistulas, mainly in non-healing and recurrent anal lesions, especially in regions where tuberculosis is endemic. Treatment with anti-tuberculosis agents can provide complete recovery but surgery is often necessary in severe cases.

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