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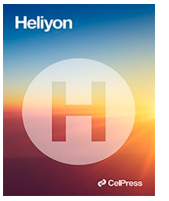

Necrotizing fasciitis due to mycobacterium tuberculosis: A case report

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ABSTRACT

We admitted a patient with extensive and rapidly progressing necrotizing fasciitis, pulmonary tuberculosis, cutaneous tuberculosis, and bacterial infections because of late diagnosis and treatment. Early diagnosis is necessary for both cutaneous tuberculosis and necrotizing fasciitis. However, these are rare clinical manifestations and are difficult to detect. Despite surgical and pharmacologic treatment, the patient had poor outcomes. We discussed the next-generation sequencing test for early tuberculosis diagnosis, especially for atypical ones. The modified and typical laboratory risk indicator for necrotizing fasciitis score was used for diagnosing and identifying patients at high risk for necrotizing fasciitis. Subcutaneous effusions and gas accumulations observed through imaging were useful in assessing necrotizing fasciitis progression. Debridement or tuberculosis treatment should be initiated as early as possible in managing patients with both necrotizing fasciitis and cutaneous tuberculosis. Clinicians should be alert in identifying the condition, whether *Mycobacteria* tuberculosis is the independent cause of necrotizing fasciitis, and treating the condition. The choice of rapid microbial diagnostic tools should be of concern. Debridement or tuberculosis treatment should be initiated as early as possible in managing patients with both necrotizing fasciitis and cutaneous tuberculosis. Multidisciplinary cooperation should be considered.

1. Introduction

Pulmonary tuberculosis (PTB) and cutaneous tuberculosis (CTB) are rare and severe forms of complex tuberculosis [1]. Because of how rapidly these diseases progress, patients are at significant risk if they are not diagnosed early or treated appropriately. Nonetheless, misdiagnosis or mismanagement due to abnormal clinical symptoms and imaging frequently occurs. CTB can develop into widespread necrotizing fasciitis (NF), which is the focus of this case.

2. Case presentation

This study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Informed consent was obtained from the patient for the publication of all images, clinical data, and other data included in this study.

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A 52-year-old man presented to his local dermatology office 5 days before admission, reporting swelling and soreness in his left groin that had persisted for 2 months. Antiviral and antipruritic medications were ineffective. He was admitted to our hospital's emergency room for an abdominal wall and perineal skin defect with necrosis and suppuration. The patient was conscious upon admission, with respiratory rate, heart rate, and blood pressure of 20 breaths/min, 125 beats/min, and 92/77 mmHg, respectively. Skin examination revealed a 40 × 20 cm^2 skin defect in the abdomen, exposing the rectus abdominus muscle, a significant amount of necrotic tissue, and purulent discharge. The scrotum and penis also had black areas with ulcers, defects, erosion, pus, and a foul odor. The testes were not exposed.

The patient had a known history of diabetes with no previous record of treatment or complications; he reported normal daily insulin intake (insulin 5–10 U early and 5–10 U later before meals; Sanofi background Pharmaceutical Co.; insulin glargine [450 U] 10–20 U before bedtime, depending on blood glucose levels; GE, Sanofi-Ayentis Deutschland Gmbh), with no renal, infectious, or other immunosuppressive diseases or unidentified bites. Height and weight data were unavailable because he was bedridden; however, his nutritional assessment was moderate. On admission (day 1), blood tests were performed according to the Manufacturer's instruction (CRP-M100, Mindray), (BC-6800Plus, Mindray), (cobas 8000, Roche Diagnostics CmbH), (G8-90SL, TOSOH CORPORATION), and (cobas 8000, Roche Diagnostics CmbH), and the following results were obtained: high-sensitivity C-reactive protein, 244.34 (0–4) mg/L; white blood cells, 8.79 (3.5–9.5) × 10^9/L; fasting blood glucose, 7.64 (3.9–6.1) mmol/L; glycated hemoglobin, 6.70 (4.0–6.0)%; creatinine, 185.0 (57–97) μmol/L; hemoglobin, 118.0 (130–175) g/L; and sodium, 130.0 (137–147) mmol/L. The modified laboratory risk indicator for necrotizing fasciitis (LRINEC) was 36 at admission, whereas a typical score is 7 [2,3]. Computed tomography (CT) and contrast-enhanced CT scans revealed extensive, rapidly progressing infections in his lungs and skin, as well as subcutaneous effusion and gas accumulation; additionally, the subcutaneous effusion and gas accumulation results also indicated the progression of PTB (Figures A1–C3). On days 1–5, the wound was repeatedly debrided as needed. After 5 days of unsuccessful treatment, full surgical debridement under general anesthesia occurred 6 days after admission (Figure E); intraoperatively, the patient had type I respiratory failure and was transferred to the intensive care unit for ventilatory support after surgery. Abdominal tissue pathology on day 14 showed necrosis with infection of the adipose tissue and infiltration of numerous neutrophils, lymphocytes, and plasma cells; multinucleated giant cells were also observed (Figure D1–3). Ziehl–Neelsen staining revealed acid-fast bacilli, indicating the presence of *Mycobacterium* TB proteins. To further identify the responsible pathogen, we performed bronchoscopy and alveolar lavage. Furthermore, next-generation sequencing (NGS) testing was performed to identify pathogenic bacteria; on day 15, NGS examination of the alveolar lavage fluid revealed 994 sequences. Identifying bacterial cultures from wound secretions revealed multidrug-resistant

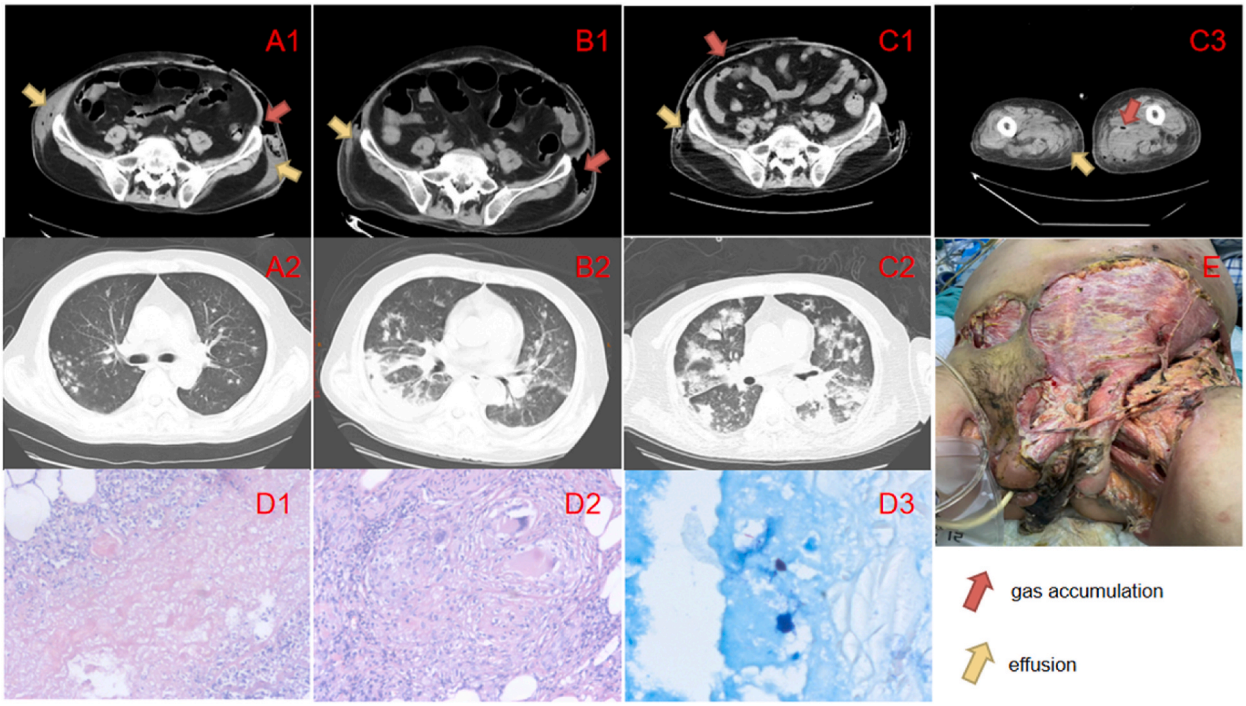

Fig. 1. Imaging (A1-C2), histopathological findings (D1-D3), and gross picture (E) of the patient.
A1, A2:(CT 04/02/2023) Abdominal wall: right side gas, bilateral effusion. Lungs: inflammatory changes B1, B2:(CT 07/02/2023) Abdominal wall: less fluid accumulation and more extensive gas accumulation after debridement and drainage Lung: progression of infection, manifestations of mycobacterium tuberculosis infection. C1, C2, C3:(CT 16/02/2023) Abdominal wall: extensive pneumocystis on the left side. Inner thigh: pneuma in the muscular space. Lungs: infection progresses. D1, D2, D3: (pathological results of abdominal necrotic tissue) necrosis with infection of adipose tissue, infiltration of many neutrophils, lymphocytes, and plasma cells, multinucleated giant cells Ziehl-Neelsen staining found acid-fast bacteria, considering the possibility of MTBC. E1:(09/02/2023) Extensive defects, necrosis, and pus of the skin and soft tissue. Finger test: positive.

Escherichia coli, although no bacteria were recovered from multiple blood cultures.

After admission, the patient was treated with ornidazole (0.5 g, Bid, iv, Sichuan Kelun Pharmaceutical Co. Ltd., Sichuan, China) and meropenem (0.5 g, q8h, iv, PKU HealthCare Corp., Ltd., Peking, China) for infection control and received fluid rehydration, daily wound care, and daily dressing changes. On day 15, we combined CT results, pathological findings, NGS, and clinical manifestations to reach the final diagnoses of NF, PTB, and CTB. The NF was either due to infection from *Mycobacteria* alone or with *E. coli*. On the same day, following the results of NGS and drug sensitivity analysis, we additionally prescribed tigecycline (50 mg, q12h, iv; Hunan Sailong Pharmaceutical Co., Ltd., Hunan, China) to combat the bacteria and isoniazid (5 mg/kg, qd, po, Hangzhou Minsheng Pharmaceutical Co., Ltd., Hangzhou, Zhejiang, China), rifampicin (10 mg/kg, qd, profess to be convinced, Shenyang Hongqi Pharmaceutical Co. Ltd., Shenyang, Liaoning, China), ethambutol (15 mg/kg, qd, po; Shenyang Hongqi Pharmaceutical Co. Ltd., Shenyang, Liaoning, China), and pyrazinamide (25 mg/kg, qd, po; Chengdu Jinhua Pharmaceutical Co., Ltd., Chengdu, Sichuan, China) to treat TB. On day 17, the family requested that the patient be discharged because of his poor prognosis and the family's inability to afford further treatment. The patient died after discharge.

Throughout his hospitalization, the patient and family cooperated with the diagnostic and treatment process by signing multiple consent forms for surgery, diagnosis, and treatment measures.

3. Discussion

TB can be broadly categorized into pulmonary or extrapulmonary TB (EPTB), which can include CTB, depending on the site of infection by *Mycobacteria* tuberculosis (MTBC). The most recent national epidemiological data in China show that CTB accounts for approximately 1 % of TB cases [1]. NF is an aggressive and rapidly progressing infection with initially insidious onset and fulminant course. The lesions extend internally toward the fascia layer, necrotizing the superficial tissue. Some patients may experience severe systemic toxicity, such as septic shock or progressive multi-organ failure.

Early diagnosis of CTB and NF is crucial yet challenging; however, the diagnosis of both conditions has improved with advances in imaging techniques. CT is the preferred imaging modality in diagnosing abdominal TB since it can identify complications, including intestinal obstruction, perforations, and fistulae, and can sample tissue specimens for histopathological and microbiological analysis [4]. Since our patient demonstrated no typical TB symptoms, there may be two potential sources of skin TB in this case as follows: either directly into the skin through the blood or by direct subcutaneous spread after rupture of the inguinal lymph node (since the patient's initial presentation was inguinal pain). If a patient seeks treatment immediately when such groin pain occurs, doctors can identify the cause and obtain pathological slides during the disease's early stage, creating an opportunity to reverse the prognosis.

To diagnose TB, we combined the CT, NGS, and pathological findings; this combination may provide new options for clinical practice, as NGS is not yet widely used in this field. The assessment of soft tissue effusion and gas accumulation using ultrasonography, CT, and magnetic resonance imaging is also helpful for the early diagnosis of NF [2,3,5]. LRINEC scores are considered useful for differentiating NF from other severe soft tissue infections, such as cellulitis. The modified LRINEC score cut-off point is ≥ 17, indicating a high possibility of NF diagnosis in the patient's case [3]. Meanwhile, the typical LRINEC score ≥ 7 is an independent prognostic marker for lethality [6]. These support the need for early diagnosis and identification of high-risk patients for NF. Early debridement leads to fewer serious complications and a better prognosis.

The choice of rapid microbiological diagnostic tools should also be considered for earlier detection, as histology and culture-suggested harmful organisms can guide the use of antimicrobials. Existing rapid microbial diagnostic tools include matrix-assisted laser desorption ionization time-of-flight mass spectrometry, spectroscopic techniques, electrochemical biosensors, integrated molecular diagnostic platforms, and metagenomic sequencing [7]. In this case, the most suitable tools to identify *Mycobacterium* TB infection were GeneXpert and NGS; however, because the patient showed no typical symptoms of TB infection (and since *Mycobacterium* TB is not detected in multiple blood, sputum, and wound secretion cultures), doctors could not identify the specific responsible pathogenic bacteria. Moreover, our hospital does not specialize in TB and could not provide GeneXpert testing. Finally, a metagenomic NGS examination was selected for comprehensive consideration, and *Mycobacterium* TB infection was confirmed.

To date, no high-level case-control studies have investigated MTBC infection as a direct cause of NF. The patients reported here and by Meena [8] were diagnosed with both CTB and NF. Therefore, further research is required to reveal whether CTB is a pathogenic factor independent of NF. Patients with EPTB who require surgical resection of lesions should undergo preoperative anti-TB therapy for a minimum of 6 months [9]. However, this contrasts with the recommended treatment for NF, which requires early and thorough debridement. Researchers are also exploring the effectiveness and safety of a short-term regimen to accelerate the surgical timeline and reduce the incidence of multidrug-resistant TB [10,11]. Moreover, experienced clinicians should comprehensively assess the patient's condition, and debridement or TB treatment should be initiated as early as possible in patients with both NF and CTB. More in-depth research on CTB combined with NF is needed in the future.

This case involved multi-organ TB, NF, and bacterial infections. The patient's illness course suggests two possibilities as follows: first, *Mycobacterium* originating in the lungs spread to the skin of the inguinal region through the bloodstream, where it developed as CTB. Subsequently, the resulting rash, ulcer, and other lesions spread rapidly throughout the abdominal wall and perineum, leading to extensive NF. *E. coli*, a common bacterium within the perineum, was detected twice in the wound secretion because of a medical error. Second, *Mycobacteria* spread from the lungs to the skin, interacted with *E. coli*, and resulted in local perineal inflammation. Subsequently, delayed and incorrect diagnosis and treatment led to the rapid development of widespread NF. We considered the former to be more likely, as the infection of the lungs and skin progressed simultaneously and since the NF continued to progress even when sensitive antibiotics were used.

Although TB is a curable disease, it is still extremely harmful to patients if they do not receive appropriate treatment as soon as

possible. Therefore, in countries and regions with high TB incidence, healthcare workers should increase their awareness and vigilance for latent and atypical presentations of TB and should include TB in more differential diagnoses.

3.1. Limitation

The diagnosis of EPTB in this case report lacks a convincing microbial diagnosis, such as culture or GeneXpert TB and nuclear test. We cannot exclude the possibility that the patient had a disseminated non-tuberculous mycobacterial infection; this possibility should be noted in future clinical studies.

4. Conclusion

CTB combined with NF is a rare clinical manifestation and both are difficult to detect. Clinicians should promptly identify and treat these conditions, foster multidisciplinary cooperation, and increase the use of rapid microbiological detection tools. However, many aspects of this interaction still require further research.

Ethics statement

Informed consent was obtained from the patient for the publication of all images, clinical data and other data included in the main manuscript.

Data availability statement

No data was used for the research described in the article.

CRediT authorship contribution statement

Liying Chen: Writing – original draft, Writing – review & editing. **Yinhui Zhu:** Writing – original draft, Writing – review & editing. **Du Fan:** Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20733.

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