



Case Reports

Peritoneal Tuberculosis in a Patient on Tumor Necrosis Factor inhibitors: A Case Report and Review of the Literature

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Abstract

Peritoneal tuberculosis (PTB) is a diagnostic challenge due to its nonspecific presentation, low sensitivity of ascitic fluid microbiologic tests, and possible resemblance to peritoneal carcinomatosis. We describe a case of 51-year-old woman with long-term tumor necrosis factor alpha (TNF- α) inhibitor exposure presented with fever and abdominal distension after returning from the Philippines. Initial tests, including microbiological studies, were inconclusive, despite imaging findings suggestive of carcinomatosis with elevated CA-125. Diagnostic laparoscopy revealed miliary white nodules; however, omental biopsy showed non-necrotizing granulomas without AFB. High clinical suspicion prompted excision of an enlarged axillary lymph node, which demonstrated necrotizing granulomas with rare AFB-positivity and ultimately grew *Mycobacterium tuberculosis*. The patient experienced rapid symptomatic relief and near-complete radiological resolution within four months of tuberculosis (TB) treatment. PTB should remain on the differential for unexplained ascites or peritoneal nodularity – particularly in immunosuppressed travelers from endemic regions – even when early microbiologic tests are negative. Timely invasive sampling and, when warranted, empirical anti-TB therapy is critical. Clinicians must recognize that patients on TNF- α inhibitors remain at heightened risk for extrapulmonary TB despite negative baseline screening.

BACKGROUND

Peritoneal tuberculosis (PTB) is a form of extrapulmonary tuberculosis (TB) affecting the peritoneum. The disease usually unfolds insidiously over weeks to months. Most patients present with abdominal pain and fever; examination often reveals ascites and abdominal tenderness.¹ Paracentesis is typically the first diagnostic step: a serum-ascites albumin gradient (SAAG) < 1.1 g/dL, lymphocyte-predominant leukocytosis, elevated lactate dehydrogenase, and raised adenosine deaminase (ADA) are characteristic findings.² Yet microbiologic confirmation from ascitic fluid is slow and insensitive, frequently delaying treatment. Consequently, diagnostic laparoscopy with peritoneal biopsy remains the gold standard.¹

With rising global migration and a growing population of immunocompromised hosts, clinicians must maintain a high index of suspicion for PTB. Nonspecific symptoms and the low yield of conventional microbiologic tests compound the diagnostic challenge. We de-

scribe a patient receiving tumor necrosis factor-alpha (TNF- α) blockade in whom PTB masqueraded as malignancy and all initial TB studies were negative PTB, underscoring the importance of early invasive sampling and careful clinical judgment.

CASE PRESENTATION

A 51-year-old woman with a history of rheumatoid arthritis, Sjögren's disease, and stage IV endometriosis with bilateral ovarian endometriomas (status post hysterectomy) presented with a two-week history of recurrent fevers and progressive abdominal distension. Her symptoms began shortly after returning from a three-week trip to the Philippines. She had been receiving long-term immunosuppressive therapy, including methotrexate, hydroxychloroquine, and prednisone (5 mg daily). TNF- α inhibitor had been added three years earlier, and her final dose of golimumab was given two weeks before her trip. Then, a single dose of sarilumab was administered the day before departure. Born in the Philippines,

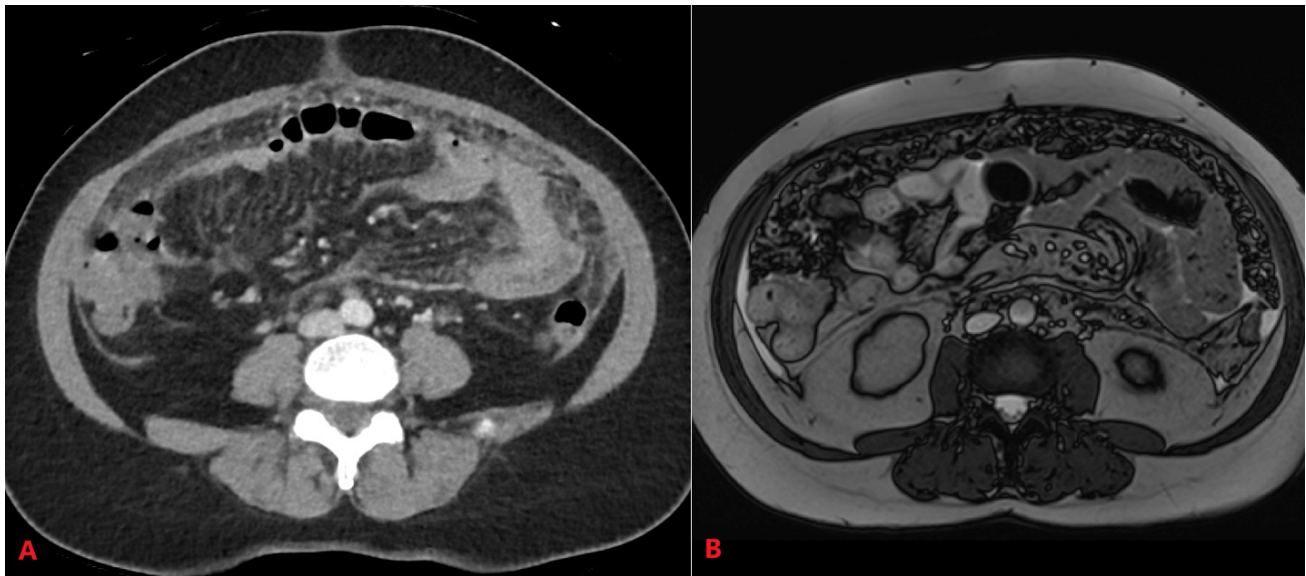


Figure 1. Computed tomography (CT) and magnetic resonance imaging (MRI) scans of abdomen.

A. Axial CT of the abdomen shows peritoneal thickening and fat stranding in the mesentery and omentum, accompanied by small-volume ascites. B. T2-weighted MRI with True Fast Imaging with Steady-State Precession (FISP) demonstrates intraperitoneal nodular dissemination along the omentum and peritoneal surfaces, extending into the pelvis.

she had received Bacillus Calmette-Guerin (BCG) vaccination and immigrated to the United States (US) seven years ago. 15 months prior she had visited the Philippines and, on returning, experienced transient axillary lymphadenopathy (LAD) that resolved spontaneously.

On admission, her white blood cell count was 5.78 K/ μ L with chronic lymphopenia (absolute lymphocyte count 0.57 K/ μ L). Abdominal computed tomography (CT) revealed new ascites, peritoneal thickening, and fat stranding, raising concern for peritoneal infection or malignancy [Figure 1A]. During the first few days of admission, she presented intermittent high-grade fevers reaching up to 103°F. A broad infectious and oncologic work-up ensued. HIV testing was negative, and her cancer antigen (CA)-125 level was markedly elevated at 497 U/mL. Ascitic fluid analysis showed SAAG of 0.7 g/dL, a nucleated cell count 7,080/ μ L (35% neutrophils, 55% lymphocytes), glucose 92 mg/dL, and ADA level 55 U/L [Table 1]. However, *Mycobacterium tuberculosis* (MTB) polymerase chain reaction (PCR) and acid-fast bacilli (AFB) stains on sputum and ascitic fluid samples were negative. QuantiFERON-TB gold testing was indeterminate (nil 0.15 IU/mL; mitogen-nil 0.37 IU/mL; TB1-nil 0.19IU/mL; and TB2-nil 0.23 IU/mL), identical to a result obtained one year earlier (reference range: TB1-nil and/or TB2-nil > 0.35 IU/mL = positive; nil > 8.0 IU/mL or mitogen-nil < 0.5 IU/mL = indeterminate). A baseline test obtained before TNF- α inhibitor initiation had been negative.

Pelvic magnetic resonance imaging (MRI) showed no focal ovarian masses, but abdominal MRI showed moderate left pleural effusion, left axillary LAD, and intraperitoneal nodular dissemination suggestive of peritoneal carcinomatosis [Figure 1B]. Chest CT confirmed

enlargement of the left axillary node to 12.5 mm (previously 7 mm two years earlier). CT-guided omental core biopsies demonstrated non-necrotizing granulomas without malignancy or AFB positivity. She received seven days of empiric ceftriaxone.

Following discharge, thoracentesis confirmed an exudative pleural effusion but showed negative AFB smear and cytology [Table 2]. Positron emission tomography-CT demonstrated intensely fluorodeoxyglucose-avid areas of omental caking, peritoneal thickening, peritoneal implants, and LAD above and below the diaphragm. Laparoscopic peritoneal exam revealed the omentum densely adherent to the anterior abdominal wall and studded with miliary white nodules. Excised omentum biopsy again showed non-necrotizing granulomatous inflammation without malignancy or AFB positivity.

Despite persistently negative microbiologic studies, the clinical picture, degree of immunosuppression, and epidemiologic risk maintained a high suspicion for PTB. Therefore, an axillary lymph node biopsy was pursued to improve diagnostic yield and allow drug-susceptibility testing, given the high prevalence of multidrug-resistant (MDR) TB in the Philippines. After the biopsy, empiric quadruple therapy—rifampin (RIF), isoniazid (INH), pyrazinamide, and ethambutol—was initiated. Soon after, the lymph node biopsy finally revealed necrotizing granulomas containing rare AFB-positive mycobacteria. One month later, cultures from both omental and nodal tissue grew MTB that was resistant to pyrazinamide but susceptible to the remaining first-line agents. Cultures from sputum, pleural fluid, and blood cultures remained negative. Her regimen was streamlined to a nine-month course of RIF and INH. At four months of therapy, follow-up imaging demonstrated complete resolution of

Table 1. Ascitic fluid analysis

Value	Results
Red blood cells, / μ L	5,000
Nucleated cells, / μ L	7,080
Neutrophils (%)	35
Lymphocytes (%)	55
Monocytes (%)	7
Eosinophils (%)	3
Albumin, g/dL	2.8
SAAG, g/dL	0.7
Amylase, U/L	41
Glucose, mg/dL	92
LDH, U/L	407
Total protein, g/dL	6.3
ADA, U/L	55
MTB PCR	negative
AFB smear	negative
Mycobacterial culture	negative
Cytology	No malignant cells identified. Reactive mesothelial cells, abundant inflammatory cells and histiocytes.

Table 2. Pleural fluid analysis

Value	Results
Red blood cells, / μ L	7,000
Nucleated cells, / μ L	3,788
Neutrophils (%)	11
Lymphocytes (%)	85
Eosinophils (%)	2
Basophils (%)	2
Albumin, g/dL	3.2
Glucose, mg/dL	118
LDH, U/L	172
LDH, serum, U/L	164
Total protein, g/dL	6.7
Total protein, serum, g/dL	9.2
pH	7.42
AFB smear	negative
Mycobacterial culture	negative
Cytology	No malignant cells identified. Mesothelial cells and histiocytes. Mixed inflammatory cells.

pleural effusions, marked reduction in axillary LAD, and near-resolution of omental nodularity and ascites.

DISCUSSION

TB continues to pose a formidable global health challenge. In 2023, an estimated 8.2 million new cases were reported – the largest annual total since the mid-1990s. Although TB-related mortality has declined over the past decade, TB remains the world's tenth leading cause of death, and incidence rose again during the COVID-19 pandemic. The Philippines, where the patient was originally from and traveled to, accounts for 6.8% of all TB

cases (fourth worldwide) and 7.2% of MDR or rifampin-resistant TB (fifth worldwide).³ In the US, extrapulmonary disease affected 29% of TB patients, and peritoneal involvement was the fourth most common site.⁴ Recognized risk factors for PTB include cirrhosis, continuous ambulatory peritoneal dialysis, HIV infection, and low socioeconomic status.⁵ Extrapulmonary spread is particularly common in HIV-positive individuals with low CD4 counts.⁶ PTB is usually attributed to reactivation of dormant bacilli lodged in the mesenteric lymph nodes or peritoneum during an earlier pulmonary infection. Less frequent pathways include ingestion of bacilli with translocation through Peyer's patches, contiguous

spread from the genitourinary tract, or hematogenous seeding from active pulmonary or miliary TB.¹

TNF- α antagonists, widely prescribed for autoimmune disorders, blunt host response to TB to regulate cellular immunity and granuloma formation.⁷ Increased risk of TB reactivation with use of TNF- α inhibitors and higher incidence of extrapulmonary TB have been reported.⁸⁻¹⁰ Therefore, current guidelines mandate latent-TB screening—via tuberculin skin test or interferon- γ release assay (IGRA)—before TNF- α blockade; repeat testing is generally reserved for ongoing exposure.¹¹ Our patient's baseline IGRA was negative, but she was a candidate for repeated latent TB screening; IGRA was selected as the patient had a history of BCG vaccination. However, but subsequent assays became indeterminate—an outcome recognized in individuals receiving TNF- α inhibitors, where impaired interferon- γ responses may yield low mitogen and TB-antigen values.¹²

Additional immunosuppression may also have compounded her risk of TB infection. Increased TB risk with prednisone doses ≥ 15 mg daily was reported, however, our patient's lower dose of 5 mg daily likely contributed less than TNF- α inhibitor. She also received sarilumab, IL-6 inhibitor, immediately before traveling. However, its TB risk has not been well understood from clinical studies, but genome-wide association studies suggest no clear link between reduced IL-6 signaling and TB.¹³ Nonetheless, their use might have added to the overall immunosuppressive burden.

Whether the patient reactivated latent infection or acquired TB de novo is uncertain. The transient axillary lymphadenopathy that developed after an earlier trip to the Philippines, followed by an indeterminate IGRA, suggests primary infection during that visit with subsequent reactivation precipitated by cumulative immunosuppression. A false-negative baseline IGRA is also plausible, especially in individuals from endemic regions.

Delayed recognition of PTB carries a significant mortality risk, as a retrospective study linked longer time to therapy with fatal outcomes.¹⁴ Ascitic-fluid microbiology is notoriously insensitive ($\approx 3\%$ smear-positive, 35% culture-positive). Early laparoscopic biopsy, which offers 93% sensitivity and 98% specificity and often reveals diffusely thickened peritoneum with scattered miliary whitish nodules, remains the diagnostic gold standard. Histology and culture with drug-susceptibility testing are essential.¹ When diagnostic studies stay negative, but suspicion remains high, empiric therapy is warranted.¹⁵ In our case, excisional axillary lymph node biopsy was chosen to improve yield and obtain susceptibilities in view of high MDR TB rates in the Philippines, which ultimately confirmed TB. Serum CA-125 is widely used to assess ovarian cancer but is nonspecific and may rise in PTB.¹⁶

Its interpretation in our patient was further complicated by history of endometriosis, which can be another cause of CA-125 elevation.¹⁷ Thus, elevated CA-125 in women with ascites and peritoneal nodularity may mimic peritoneal carcinomatosis and delay the diagnosis of PTB.¹⁶

PTB is treated with the same regimens as pulmonary TB: a two-month of first-line medications (INH, RIF, pyrazinamide, ethambutol), followed by four-month of INH and RIF.¹ When the strain is pyrazinamide-resistant but INH- and RIF-susceptible, a nine-month INH-RIF course is recommended.¹⁸ Our patient responded briskly, with near-complete radiographic resolution by four months of therapy. This case underscores how PTB can masquerade as malignancy in immunosuppressed travelers. With the growing use of TNF- α inhibitors and increasing global mobility, clinicians must remain alert to extrapulmonary TB—even in low-incidence countries or with negative early microbiological tests. A high index of suspicion, prompt invasive diagnostics, and, when appropriate, empiric treatment are essential to minimize morbidity and mortality.

Author contribution

All Authors have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the ICJME criteria of authorship.

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosures/Conflicts of Interest

The authors have no conflicts of interest to disclose.

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