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Two Sites - One Major Problem

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Abstract The authors present the case of a 36-year-old woman with disseminated tuberculosis shown by pulmonary nodules and urogenital involvement. Positive cultures for *Mycobacterium tuberculosis* in urine and bronchial secretions made the diagnosis. After three months of multidrug treatment, there was a clinical and radiologic improvement. This case highlights an uncommon case of an immunocompetent patient with disseminated tuberculosis. A delay in the diagnosis of pulmonary tuberculosis can result in serious public health problems with disease spread.

Keywords: *mycobacterium tuberculosis, disseminated tuberculosis, infectious diseases*

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1. Introduction

Tuberculosis (TB) is a serious public health problem, being one of the leading causes of death by infectious diseases worldwide. TB can affect every organ [1]. Off all forms of extrapulmonary TB (EPTB) urogenital TB (UGTB) varies according to geographical region, from 2 to 20% [1,2].

2. Case Presentation

A 36-year-old non-smoking black woman, who was born in Angola, living in Portugal for the past five year with no relevant personal medical history, including medications, alcohol, or substance abuse is presented. She was a uniparous woman with complaints of inability to conceive despite having regular unprotected intercourse for over one year.

The patient was admitted to the hospital with a one-week history of lower left back pain, dysuria, and pollakiuria. She had no fever or hematuria and denied other complaints. A diagnosis of urinary tract infection was established, and she was empirically treated with amoxicillin/clavulanic acid but had a poor response.

One month later, she returned to the hospital with the same complaints and also with a persistent nonproductive cough. At that time, she denied shortness of breath, pleuritic chest pain. and constitutional symptoms such as fever, night sweats, decreased appetite, or weight loss.

Physical examination showed a woman who appeared healthy with normal vital signs: blood pressure of 125/70 mmHg, heart rate of 80 beats/minute, afebrile, and eupneic with oxygen saturation of 98% on room air. Pulmonary auscultation was normal. She had no abnormal findings.

She underwent laboratory testing that showed negative results for hepatitis B and C viruses, human immunodeficiency virus (HIV), and venereal disease laboratory test, hemoglobin 12 g/dL, 4700 leucocytes/mm^3, urea 18 mg/dL, creatinine 0.90 mg/dL, and C-reactive protein 0.8 mg/dL. The patient's urine analysis revealed a leukocyturia and the chest X-ray showed bilateral nodules.

Gynecological and renal ultrasound showed renal size asymmetry with enlargement of the left kidney and parenchymal heterogeneity associated with homolateral hydroureteronephrosis. A ureteral stricture in the pelvic region of the left ureter and a dense, multi-septated fluid in the pouch of Douglas were also detected.

In light of these findings, the hypothesis of an ovarian primitive lesion with invasion and compression of the ureter and metastatic involvement of the lung, was considered.

A tumor marker study revealed a cancer antigen 125 of 41 U/mL and a human epididymis protein 4 of 45 pmol/L. The risk of ovarian malignancy algorithm was 6.2%.

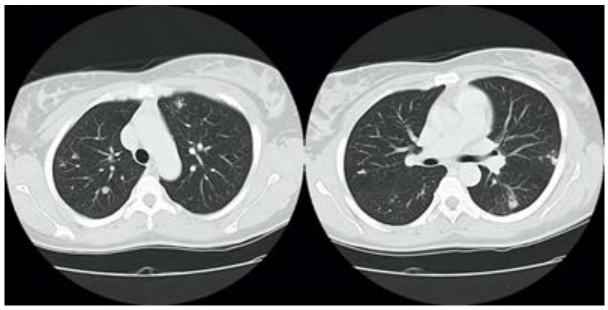

Figure 1. Chest CT scan in lung window. Axial cut revealing bilateral nodules, some with central necrosis and a bilateral centrilobular micronodular pattern

A chest-abdominal-pelvic computer tomography (CT) scan revealed bilateral lung nodules with well-defined contours, some of them with central necrosis. A bilateral centrilobular micronodular pattern, compatible with secondary dissemination was also detected (Figure 1). The CT also revealed left renal hypodense zones and three cysts in the parenchyma. The largest one measured 41 x 28 mm and had a non-pure, septated content and a pyelocaliceal dilation of the left ureter on the pelvic extremity with a 35 x 30 mm non-pure cystic formation.

Next to the renal hilum, left para-aortic enlarged lymph nodes were also described (Figure 2).

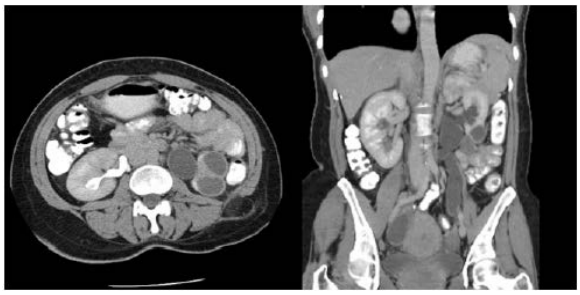

Figure 2. Abdominal-pelvic CT scan in mediastinal window. Axial cut (A) and coronal cut (B) showing left kidney cysts, the largest one with non-pure, septate content and pyelocaliceal dilatation of the left ureter with a non-pure cyst formation

These findings revealed that the ureteral changes did not seem to be associated with the gynecological system even though the initial ultrasound findings had indicated that association. In light of these new findings, tuberculosis was considered as a possible diagnosis.

Next, the patient underwent a bronchoscopy that did not reveal any abnormal endoscopic findings. Bronchial lavage cytology analysis showed a chronic inflammatory process with no malignant cells, and microbiological culture and Ziehl-Neelsen staining were negative. The polymerase chain reaction for *Mycobacterium tuberculosis* was also negative. On the other side, cultural examination of the bronchial secretions and urine culture was positive for *M. tuberculosis*.

Thus, a diagnosis of disseminated TB with lung and urogenital involvement was established, and the patient was started on an empirical multiple-drug TB regimen with isoniazid, rifampicin, pyrazinamide, and ethambutol. Anti-TB drug susceptibility testing revealed no drug resistance to first-line drugs.

She underwent a urological procedure with left ureteral stent placement.

At a 3-month follow-up, the patient presented with clinical, radiological, and analytical improvement with negative urine culture for *M. tuberculosis*.

3. Discussion

TB is a serious public health problem and, even though its incidence is declining, it is still the leading cause of infectious disease-related deaths worldwide.

TB is a multisystemic disease that can affect any organ.

Pulmonary TB is the paradigm of the infection as it is the contagious form of the disease. Disseminated TB is recognized as an important cause of morbidity and mortality. This form of TB is unusual in immunocompetent patients and corresponds to less than 2% of all TB cases. Disseminated TB is defined by lung injury associated with an extrapulmonary focus or two or more concomitant extrapulmonary lesions [1,2,3].

The predisposing conditions for disseminated tuberculosis are HIV, immunosuppressants, alcoholism, older age, diabetes mellitus, and hematological diseases [3].

EPTB is also clinically relevant as it contributes to the burden of disease. EPTB is most common in HIV-positive patients, and this form of the disease represents 10% of all TB forms. This form is very difficult to diagnose because any organ or tissue may be affected. The most commonly affected sites for EPTB are lymph nodes [2,4]. Of all forms of EPTB, UGTB ranges from 2% to 20% according to the geographical region and represents 0.2% to 21% of infertility cases [1,2]. It is difficult to estimate the exact prevalence of UGTB because patients can be asymptomatic. *M. tuberculosis* affects the urinary more than the genital system. UGTB is the third most common form of EPTB in low incidence countries. In Europe, UGTB is diagnosed more often in migrants [1,2,3].

Usually, UGTB arises from pulmonary spread of the bacilli directly via hematogenous or lymphatic seeding. The order of frequency of urogenital track involvement is kidney, bladder, fallopian tube, and scrotum [1,2,5].

The diagnosis is challenging because of the lack of specific symptoms. Therefore, the patients may have long-standing, unexplained urological symptoms before the diagnosis is established. The diagnosis of UGTB can be obtained with a positive culture for *M. tuberculosis* or DNA identification [2,5].

Factors as age, gender, immunosuppressive drugs, and immunodeficiencies, such as HIV, influence UGTB frequency among the population [2,3,5].

The authors present a case of an immunocompetent patient with disseminated TB. The combination of the patient's clinical history, CT imaging, and cultural examination for *M. tuberculosis* in urine and bronchial secretions helped to establish the diagnosis. The patient had lung, renal, and ureteral involvement of the disease.

The kidney is the most affected site by UGTB, and up to 10% of patients have concurrent, active pulmonary disease. Involvement of the ureter is commonly associated with renal TB as the lower third of the ureter is the most affected site followed by the ureteropelvic junction as described in our patient [2].

Although uncommon, TB must be considered as a primary or secondary cause of infertility, especially in patients from less developed countries. In this patient case, TB could not be ruled out as the cause of infertility. The presence of inflammatory debris in the pouch of Douglas may have been associated with pelvic involvement of the disease with bacilli seeded in the fluid. Additional investigations should be done after anti-tuberculous therapy is administered.

TB is a curable infectious disease, and drug therapy is the main treatment. The clinical outcome is positive when there is good compliance with the therapeutic regimen. Treatment for disseminated TB may require 12 months of drug therapy. For susceptible *M. tuberculosis*, the treatment period is six months with two months of a

multidrug regimen of isoniazid, rifampicin, pyrazinamide, and ethambutol. The following four months should involve a combination of isoniazid and rifampicin [1,2]. The continuation phase should be extended to three additional months if patients present with cavitary pulmonary lesions with a positive sputum culture after the initial 2-month treatment. Also, patients with major kidney involvement or compromised renal function may need prolonged treatment for 9 to 12 months. Surgery may be needed as an adjunct to drug treatment in certain cases [2].

4. Conclusion

TB is a big masquerade. Initially, radiologic assessment pointed out malignancy as the likely diagnosis. Our case report highlights an uncommon case of an immunocompetent patient with pulmonary and UGTB.

In conclusion, it is extremely important to have a high suspicion of TB, because a delay in the diagnosis of pulmonary TB can result in serious public health problems with disease spread and progressive end-organ disease.

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