Pneumologia

Disseminated *Mycobacterium tuberculosis* following renal transplant: A case report

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Abstract

English:

Miliary tuberculosis (TB) presents a major challenge following a renal transplant in humans. In the current report, we described a patient with disseminated TB following renal transplantation. The article presents the case of a 38-year-old man who presented an 8-month history of fever, chills, sweating, low-back pain and significant weight loss. Chest radiography and computed tomography (CT) scan showed miliary nodules distributed in the two lungs. The transbronchial lung biopsy revealed a granulomatous reaction with caseous necrosis. Magnetic resonance imaging (MRI) of the brain found multiple tuberculomas. Also, MRI of the lumbosacral was indicative of a psoas abscess. Therefore, miliary pulmonary, cerebral and spinal TB was confirmed. The patient was started on an anti-TB regimen and paravertebral aspiration was also done. The patient's condition improved considerably. In conclusion, this case report can remind us of the importance of maintaining a high clinical suspicion and performing a thorough workup to establish a timely diagnosis and treatment of miliary TB.

Keywords

Mycobacterium tuberculosis • renal transplant • miliary tuberculosis

Infectie diseminata cu *Mycobacterium tuberculosis* post transplant renal: prezentare de caz

Rezumat

Romanian:

Tuberculoza miliară (TB) prezintă o provocare importantă după transplantul renal. Descriem în lucrarea prezentă un pacient cu tuberculoză diseminată în urma transplantului renal. Prezentăm cazul unui pacient de 38 de ani cu debut de 8 luni de febră, frisoane, transpirații, dureri de spate, și pierderea semnificativă în greutate. Radiografia toracică și tomografia computerizată (CT) au arătat noduli miliari distribuiți în ambii plămâni. Examenul anatomopatologic a relevat o reacție granulomatoasă cu necroză caseoasă. RMN cerebral a dezvăluit tuberculoame multiple, iar cel lumbosacrat a dezvăluit abces la nivelul psoasului. S-a inițiat tratament antituberculos și aspirație paravertebrală cu evoluție clinică favorabilă. În concluzie suspiciunea de TB trebuie să rămână ridicată la pacienții imunosupresați în țările endemice.

Cuvinte-cheie

Mycobacterium tuberculosis • transplant renal • tuberculoză miliară

Introduction

Opportunistic infections are known to be serious threats in transplanted recipients (1). Such recipients will be susceptible to infection due to immunosuppressive therapy. Also, *Mycobacterium tuberculosis* (TB) is a major and common infection after a solid organ transplant (SOT), particularly in areas where TB is endemic (2). Many studies had confirmed an increased risk of active TB after SOT (3). About 15% of

post-renal transplant cases with TB develop extrapulmonary as miliary TB with a mortality rate of 30% (2,4).

Miliary TB may be very atypical and non-specific regarding clinical features, particularly in kidney transplant recipients, making the diagnosis difficult. Here, we describe a renal transplant recipient who developed miliary TB with multiple organ involvement: lung, brain and spine.

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Case presentation

We present a case of a 38-year-old man with an 8-month history of fever, chills, sweating, low-back pain and significant weight loss.

The patient presented a kidney transplant 6 years ago, being under immunosuppressive treatment with cyclosporine and prednisolone. The patient is also diagnosed with spondylodiscitis based on the results of the lumbosacral magnetic resonance imaging (MRI) that he previously performed for his progressive low-back pain. On admission, there were no significant findings on the physical examination. Laboratory findings were: haemoglobin level of 137 g/L and white blood cell (WBC) counts 7200 cells/mm³ with 72% polymorphonuclear leukocyte. The renal profile was within the normal range, but a slightly increased level of alanine aminotransferase (ALT) was detected. The C-reactive protein (CRP) was 15 mg/dL and the erythrocyte sedimentation rate (ESR) was 103 mm/h. The chest X-ray (CXR) was normal. Sputum culture was not performed because the patient had no cough. Given the systemic persistent symptoms, the immunocompromised status and the presence of spondylodiscitis modification and Pott's disease were suspected. The patient underwent a lumbar biopsy and anti-TB therapy was started. After 6 weeks, the histopathological and bacteriological results from the lung biopsy specimen showed no evidence of TB. Despite a slight improvement in symptoms, the anti-TB treatment was discontinued.

The patient was re-admitted after several weeks with the same set of complaints as previous ones. The physical examination and paraclinical findings were similar. This time a pyogenic spondylodiscitis was suspected and a large spectrum of antibiotics were administered. Also, a repeated biopsy of the affected spinal bones was negative for TB. During hospitalisation, his general status altered. The patient developed respiratory symptoms. CXR and computerised tomography (CT) scans showed distributed miliary nodules in both lung fields (Figures 1 and 2) consistent with miliary TB. Bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial biopsy of the lung were carried out. The pathological examination found a granulomatous reaction with caseous necrosis (Figure 3). Therefore, miliary pulmonary TB has been confirmed. Treatment for TB was initiated with rifampicin (10 mg/kg/day), isoniazid (5 mg/kg/day), ethambutol (25 mg/kg/day), pyrazinamide (15 mg/kg/day) and pyridoxine (10 mg/day). During treatment, the patient developed headache, nausea and vomiting. The MRI of the brain revealed multiple tuberculomas (Figure 4) and systemic corticotherapy was initiated. Given the extension of the back pain to the lower limbs, a new MRI was performed and it revealed a psoas abscess. Therefore, paravertebral aspiration has been done. The polymerase chain reaction

Figure 1. Chest radiography revealing distributed miliary nodules in both lung fields.

Figure 2. CT scan showing distributed miliary nodules in both lung fields. CT, computed tomography.

(PCR) of the psoas abscesses pus was positive for *M. tuberculosis*.

The TB treatment was continued for 6 months and the patient's progress was favourable and his weight returned to normal and his organomegaly calmed.

Discussion

Miliary TB is a potentially life-threatening infection if left undiagnosed and treated timely. It can be hard to diagnose forms of extrapulmonary TB. Up to 30% of TB patients present

Figure 3. The pathological examination showing a granulomatous reaction with caseous necrosis.

Figure 4. MRI of the brain revealing multi-lobar tuberculomas of the brain. MRI, magnetic resonance imaging.

extrapulmonary involvement (5). Some studies confirmed that the miliary TB accounts for <2% of all patients having TB and >20% of all extrapulmonary TB patients (6).

Predisposing factors for miliary TB are as follows: old age, diabetes mellitus, chronic renal failure, organ transplantation, malnutrition, corticosteroids, human immunodeficiency virus (HIV) infection, connective tissue disease, immunosuppressive therapy and pregnancy (7). In our case, the predisposition

factor was immunosuppressive treatment for secondary organ transplantation.

The clinical and laboratory presentations of miliary TB can be non-specific and highly variable. In miliary TB, haematological abnormalities may include anaemia, leukopenia, leukocytosis, monocytosis, agranulocytosis, thrombocytopenia and pancytopenia (6,7). Also, ESR is typically high. In this case, there were no specific clinical manifestations or laboratory findings suggesting miliary TB except for high ESR.

CXR plays an important role in the initial and final detection of miliary TB (8). Differential diagnoses of pulmonary miliary pattern include histoplasmosis, sarcoidosis, hypersensitivity pneumonia, tumour metastases, bronchogenic carcinoma and pyogenic septic embolisation (9). In case of suspicion of miliary TB, quick diagnostic tests are needed to prove the diagnosis and start the treatment as soon as possible. In our case, CXR and CT scans revealed the presence of miliary nodules distributed in both lungs.

Primary diagnosis of TB relies on the detection of acid-fast bacilli. About <20% of miliary TB patients underwent a positive sputum smear (10). In this case, acid-fast bacilli were found neither in the spinal bone biopsy nor in the BAL, but a bronchial biopsy revealed caseating granulomas, which is usually required to make a rapid diagnosis.

Molecular techniques, such as PCR, have provided a new approach to the rapid diagnosis of TB (11). As it was reported in our patient who had psoas drainage abscess, PCR is positive for TB. Skeletal TB is diagnosed in about 3% of all patients, half of whom are due to spinal TB (12).

In our case, the clinical presentation and pulmonary infiltrates combined with radiographic findings of paraspinal abscess were consistent with TB, which was confirmed by molecular and pathologic findings.

The involvement of TB in the central nervous system (CNS) is infrequent. Symptoms may vary, including meningism, nausea, vomiting, headache, papillary oedema, hemiplegia, hemiparesis, monoplegia, aphasia, cerebellar symptoms, epilepsy, seizures and impaired consciousness (13). Our patient presented with pulmonary and cerebral TB several days after his skeletal complaints.

Widespread miliary pulmonary TB has been associated with almost all presented patients with miliary brain tuberculomas, encountered similarly in our patient. Therefore, radiological screening for the CNS is mandatory in all miliary TB cases. Multiple CNS tuberculoma is frequently reported in the HIV infection (14). Our patient was diagnosed with miliary TB but was seronegative for HIV infection. This condition may be due to his immunodeficient state due to immunosuppressive therapy. Also, this case reminds us that it is necessary to check transplant recipients for latent TB with tuberculin skin test (TST) and interferon gamma release assay (IGRA) to

prevent its activation during the immunosuppressive period, especially in endemic areas of the world for TB.

Conclusion

This case report may remind us of the importance of maintaining a high level of clinical suspicion and conducting a thorough review for an early diagnosis of miliary TB. In addition, this case also warns us of the importance of initiating timely TB treatment in the cases high- risk TB cases.

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Ethics approval and consent to participate

Informed consent for publication was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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