

(A)typical (Extra) Pulmonary Tuberculosis in Kidney Patients

Böbrek Hastalarında, Atipik Ekstrapulmoner Tüberküloz

ABSTRACT

Tuberculosis is still a major health problem especially among immunocompromised hosts. Another problem is making diagnosis due to the unexpected presentation and localization of disease. Extrapulmonary disease may clinically and radiographically mimic other infectious or neoplastic diseases. In this report we presented three tuberculosis cases; a kidney allograft recipient and two patients with end stage renal disease including soft tissue abscess, lytic bony lesions and pathological fractures without any pulmonary symptoms. Tuberculosis should be kept in mind during atypical generalized inflammatory conditions especially in immunocompromised hosts. Atypical localization and symptomatology may arise due to the more potent immunosuppressive agents. Delay in diagnosis may cause significant mortality and morbidity in patients with high risk. Starting anti-tuberculosis treatment empirically in most cases due to the difficulties in establishing diagnosis is another problem. Classical anti-tuberculosis treatment is sufficient to control disease in most cases. Early management may be a life saving approach.

KEY WORDS: Tuberculosis, Immunocompromised host, Extra-pulmonary involvement, Lytic bony lesions

ÖZ

Tüberküloz, özellikle immün sistemi baskılanmış kişilerde, ciddi bir sağlık problemi olmaya devam etmektedir. Beklenmedik bulgu ve semptomlarla ortaya çıkabilmesi sebebiyle tanı koymada zorluklara sebep olmaktadır. Pulmoner sistem dışı hastalık formu, benzer klinik ve radyolojik bulguları sebebi ile diğer birçok enfeksiyöz ve/veya neoplastik hastalığı taklit edebilmektedir. Biz bu makalede, iki son dönem böbrek yetmezliği hastası ve bir transplant hastası olmak üzere 3 hastamızda; yumuşak doku absesi, kemik lezyonları ve patolojik kırıklarla seyreden, hiç pulmoner semptom oluşturmayan tüberküloz vakalarımızı irdeledik. Özellikle immün sistemi baskılanmış hastalarda, atipik yaygın inflamasyon varlığında tüberküloz akılda tutulması gereken bir hastalıktır. Semptomatoloji ve lokalizasyondaki farklılık, etkinliği güçlü immün sistem baskılayıcı ajanlardan kaynaklanıyor olabilir. Tanıda gecikme özellikle bu hastalarda anlamlı mortalite ve morbiditeye sebep olabilir. Kesin tanı koymadaki zorluklar sebebiyle çoğu vakada genellikle ampirik anti tüberküloz tedavi başlatmak gerekliliği bir diğer problemidir. Klasik anti-tüberküloz tedavi, hastalığın control altına alınmasında yeterlidir. Erken müdahale hayat kurtarıcı olabilir.

ANAHTAR SÖZCÜKLER: Immün sistem baskılanmış hasta, Tüberküloz, Pulmoner sistem dışı tutuluş, Litik kemik lezyonu

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INTRODUCTION

Mycobacterium tuberculosis (MT) infection has been still continuing to be a major health problem especially among dialysis patients since 1974 that was the first report of increased risk of tuberculosis (Tb) in patients with chronic renal failure (1) the most well-known acquired immune compromised state. The prominent feature that is a matter of great importance is an insidious presentation of anorexia, malaise, fever and weight loss mimicking uremic symptoms (2) and often extrapulmonary localization (3) of disease. The strange symptoms such as due to the ectopic vit-D production result in an unexplained hypercalcemia (4) or any lymph node (5) or skeletal lesions (6) with or without classical symptoms can be a final clue to make diagnosis. Early diagnosis mostly is centered on only clinical suspicion without specific signs, symptoms and diagnostic powerties may decrease the risk of mortality in such uremic patients (7).

Case 1:

A 30 year old man with an uneventful post transplant course was admitted to our hospital with his painful, swollen right ankle and suffering from fatigue, fever and weight loss. In physical examination; his temperature was 38.5°C and swollen, painful, redness of distal part of right leg was detected. The complete blood count was normal except, erythrocyte sedimentation rate was 140mm/hr, CRP 15.6 mg/dL (Normal range: < 0.5 mg/dL) and white blood cell count 25.500/mm³ suggesting infectious process. Serial blood and urine culture specimens and chest X-ray on admission was normal. X-ray film of distal tibia and right ankle bilaterally showed lytic bone lesion with minimal periosteal reaction suggesting osteomyelitis. Magnetic resonance scan confirmed the lytic bony lesions extended to whole tibia bilaterally (Figure 1) and right ankle tenosynovitis.

Bone scintigraphy was showed intense uptake of Tc99m MDP (methylene diphosphonate) in the distal and proximal parts of the right tibia and the left distal tibia. Fine needle aspiration of the swollen right ankle lesion yielded purulent material with acid resistant bacilli positive. In turns provocative sputum was also revealed acid resistant bacilli although there was normal chest X-ray.

Case 2:

The 68-year-old hemodialysis patient was admitted our hospital with suffering from weight loss, anorexia, subfebrile fever, abdominal discomfort, and intermittent low back pain and headache. On her physical examination abdominal distention and left inguinal lymph node enlargement were detected. The abnormalities in routine blood tests were: serum calcium 12.6 mg/dL erythrocyte sedimentation rate 97mm/hr and CRP 22,4 mg/dL (Normal range: < 0.5 mg/dL). Serum intact parathyroid hormone level was 56 pg/mL. Hypercalcemic blood picture and



Figure 1: Magnetic resonance imaging of tibia. Bilaterally lytic bony lesions.

abdominal findings with palpable left inguinal lymph node were highly suspicious for malignancy. Routine lung X-ray showed a picture like resembling lymphangitic lung metastasis and increased reticulo-nodular density in lung parenchyma.

Cranial bone X-ray due to intermittent headache indicated multiple lytic bone lesions (Figure 2) and thoracic and abdominal CT scan pointed out mediastinal and retroperitoneally located lymph nodes mimicking lymphoma (Figure 3A,B)

Pathological findings of inguinally localized lymph node biopsy revealed chronic granulomatous lesion with caseous foci in harmonious with MT infection although there was no seen acid-fast bacilli in tissue specimen. A diagnosis of miliary tuberculosis was made and tuberculostatic treatment was started empirically.

Case 3:

The 73-year-old hemodialysis patient was admitted our hospital with suffering from weight loss, anorexia and fever. On physical examination there were no pathological findings except subfebrile fever. Her blood picture showed an increased in CRP level, erythrocyte sedimentation rate and leucocyte count. Protein electrophoresis showed polyclonal gammopathy. There



Figure 2: Multiple lytic bony lesions in the skull on X-Ray.



Figure 3A: Multiple mediastinally localized lymphadenopathies.



Figure 3B: Multiple retroperitoneally localized lymphadenopathies on abdominal CT scan.

were three lytic lesions on occipital bone on cranium X-ray films. Bone marrow examination was normal. Whole body CT scan showed multiple pathological lymph node enlargements with calcification and necrosis in mediastinum (Figure 4).

Tumor markers including CA 125 and viral serological tests were normal. Bronchoscopic aspiration and trans-bronchial fine needle biopsy were performed with yielding no result. According to our previous experience, we started anti-tuberculosis treatment empirically.

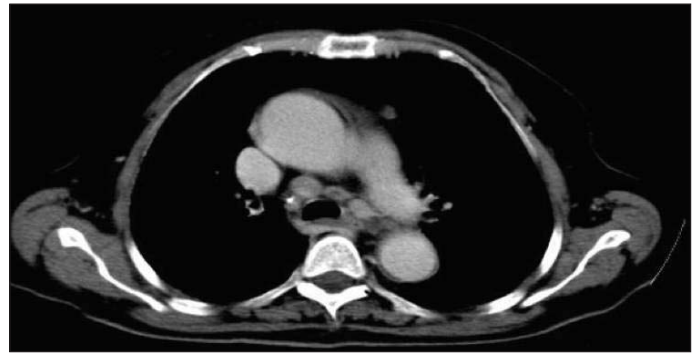


Figure 4: Multiple pathological lymph node enlargements with calcification and necrosis in mediastinum on thorax CT scan.

DISCUSSION

Because of the defective cellular immune response either due to the potent immunosuppressive agents or uremia, Tb has become an interesting infection with increasing prevalence especially in solid organ transplant recipients mostly occurred in first year of transplantation as in our first case (8). Tb mostly arises in reactivation nature which is generally originated from old caseous foci located mostly in lungs, lymph nodes and bone (9). In fact extrapulmonary tuberculosis is more common among these patients than in normal host (10). In the literature chest X-ray is abnormal in approximately 80% and miliary pattern can be seen up to 44% of the transplant patients (9). In our cases there were no any abnormalities on chest X-ray films except second one. However, in the first case provocative sputum revealed MT. In the third case there was no any abnormality on chest X-ray and CT images. In second case miliary pattern can be seen easily on chest X-ray.

Major problem of Tb in kidney patients is the insidious onset of symptoms with fever, anorexia, and loss of weight being the main complaints, mimicking uremic symptoms. In a review of the literature, Pien et al. (11) found fever occurring in a mean of 72% of the cases (range 29–100%), malaise in a mean of 69% (range 29–100%), and weight loss in a mean of 54% (range 10–100%). However, cough and hemoptysis, classic symptoms of Tb in the general population, are less frequently reported in dialysis patients (mean 22% of cases; range 5–71%) as in our cases there were no hemoptysis, cough or positive sputum.

Bone scintigraphy is useful for detecting multiple foci of skeletal tuberculosis. Also it helps to evaluate the response of treatment and useful in the follow up of skeletal tuberculosis (12). Bone scintigraphy was performed to evaluate the extent of bone infection in first case. The bone scintigraphy showed intense uptake of Tc99m MDP (methylene diphosphonate).

Interestingly soft tissue abscess combining ipsilaterally and controlaterally lytic bony lesions and multiple lytic cranial bony lesions with pathological fractures mimicking multiple myeloma as in our patients with end stage renal disease have not been reported previously from the first report of bone tuberculosis by Sakhuja et al (6).

We would like to point out that the patient in first case has been coming from south east region of Turkey where Tb prevalence is twice more common as compared to whole country with low-socioeconomic state. Patients coming from such regions must be carefully examined before transplantation about cessate pulmonary lesion and PPD skin test or after transplantation about continuing the potency and duration of immunosuppressive agents. Shorter duration of isoniazid prophylaxis for patients coming from risky region as in this case may be brought into application especially during the post transplant course. More recently a published letter from Pakistan and India focused isoniazid prophylaxis may be logic approach in such risky patients coming from endemic areas (13,14).

Due to the difficulties in symptomatology, laboratory markers and screening parameters; any unsolved complaints as discussed above with any unexpected laboratory and radiological findings, showed in figures, as in the literature (4-6) should be taken Tb into physician's mind in immunocompromised hosts. Insidious strange symptoms in these population should be carefully evaluated.

We used conventional anti-tuberculosis regimen in our patients according to guidelines (15).

In conclusion we can speculate that whenever the patients who suffered from kidney disease either due to the primary disease itself or medication procedures with non specific symptoms and amazing radiological findings, Tb should be kept in mind in all scenes. Suspicion of clinician may be a final clue for diagnosing Tb which is mostly arised in extrapulmonary localization and carries high mortality rates.

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