Case Report
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Two Elderly Patients with Disseminated Tuberculosis

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Abstract:

Introduction: Disseminated tuberculosis (DTB) is defined as tuberculosis infection involving the blood stream, bone marrow, liver, or two or more noncontiguous sites, or miliary TB. We aimed to review the definition, etiology, diagnosis and treatment of DTB with case reports of two elderly patients with DTB.

Case Reports: This report presented two cases of DTB. The first case was a 71-year-old woman with miliary TB, nondefinitive liver TB (high liver enzymes and miliary nodules on High-Resolution Computerized Thorax Tomography [HRCT]) and TB lymphadenitis. She was admitted to our outpatient clinic with dyspnoea, anorexia, 10 kg weight loss within one month and night sweats. She had no comorbidities, but her mother was treated for pulmonary TB when she was a child. Cervical ultrasonography (USG) revealed right and left supraclavicular LAP. The definite diagnostic test of the first case was left supraclavicular lymph node biopsy. After a treatment regimen of major anti-TB agents and prednisolone, clinical symptoms and hypoxemia were recovered, and infection predictors were reduced.

The second case was a 71-year-old man who was consulted with our outpatient clinic for fatigue, dyspnoea, and 10 kg weight loss within one year.He had pulmonary, pleural, bone marrow TB and TB lymphadenitis with no comorbidity. He had no well-known TB exposure. Evaluation of initial laboratory parameters showed leukopenia and anemia. He was diagnosed by left supraclavicular lymph node also bone marrow biopsies. He was discharged when clinical, radiological and laboratory findings recovered on the 24th day of major anti-TB therapy.

Conclusions: A rapid diagnosis of disseminated TB is desirable, as early initiation of treatment can reduce fatality. The definitive diagnostic tests of DTB are variable owing to atypical presentations and diagnostic difficulties. Our diagnostic tests (radiological, laboratory, histopathological) contributed valuable information about TB to us. We recommend that health providers must be aware of DTB especially in the diagnosis of elderly patients with poor nutritional status in endemic countries, such as Turkey.

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Introduction

Disseminated TB(DTB) is defined as tuberculosis infection involving the blood stream, bone marrow, liver, or two or more noncontiguous sites, or miliary TB (1). Patients with DTB have comorbidities much more than patients with pulmonary TB. HIV (Human Immunodeficiency Virus), liver disease, alcohol and drug abuse are significant risk factors for DTB (2). Incidence of tuberculosis is higher in the elderly, due to the increased prevalence of the infection and the higher rates of reactivation as a result of impairment of T-cell mediated immune response with aging. Other age-associated factors, such as malignancy and chronic diseases, also contribute to the greater risk of reactivation of latent infection (3). We aimed to review the definition, etiology, diagnosis and treatment of DTB with case reports of two elderly patients with DTB who were admitted to our chest diseases clinic for examination and treatment after the first examination in our outpatient clinic.

Case 1

A 71-year-old woman was admitted to our outpatient clinic with complaints of dyspnoea, anorexia, 10 kg weight loss within one month, and night sweats. She had no comorbidities, but her mother was treated for pulmonary TB when she was a child. She never smoked and drank alcohol. During her physical examination, the patient was conscious and cooperative and had normal vital signs. The only pathological system examination finding was bilateral rhonchi. Evaluation of initial laboratory parameters showed mild low hematocrit (34,2%), severe lymphopenia (0,17 10e3/uL), high C-reactive protein level (119 mg/L), mildly increased Lactate Dehydrogenase (355 IU/L), mildly increased Aspartate Transaminase (59 IU/L), hypocalcemia (7,9 mg/dl), and hypoalbuminemia (2,4 g/dl). Arterial blood gas examination revealed moderate hypoxemia (pO2:49,6 mmHg) and mild hypocarbia (pCO2:24,6 mmHg). Chest X-ray revealed bilateral diffuse miliary and micronodular infiltration (Figure 1).

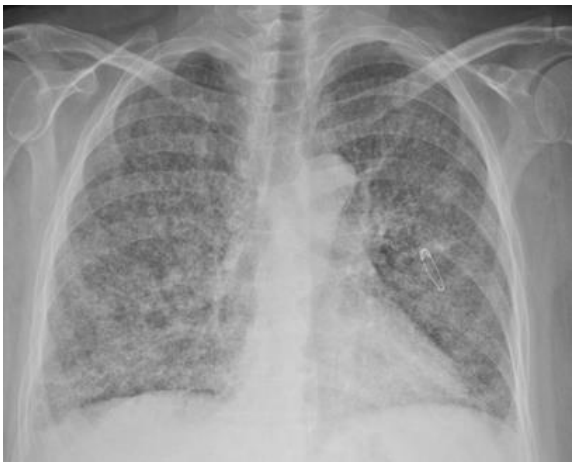

Figure 1. Bilateral diffuse miliary and micronodular infiltration on Chest X-ray.

Initial therapy included empiric antibiotics, bronchodilators, mucolytic, and oxygen supplementation. The intradermal purified protein derivative (PPD) test was negative. No sputum examination was available because the patient could not expectorate sputum, and no microorganism was obtained in hemoculture. The collagen vascular disease parameters were all negative. HRCT revealed right-sided axillary lymphadenopathy (some of which had calcifications), bilateral pulmonic millimetric nodular opacities, 7.5–9 mm nodules in the right upper lobe and lingula, and rare miliary nodules in the liver (Figure 2).

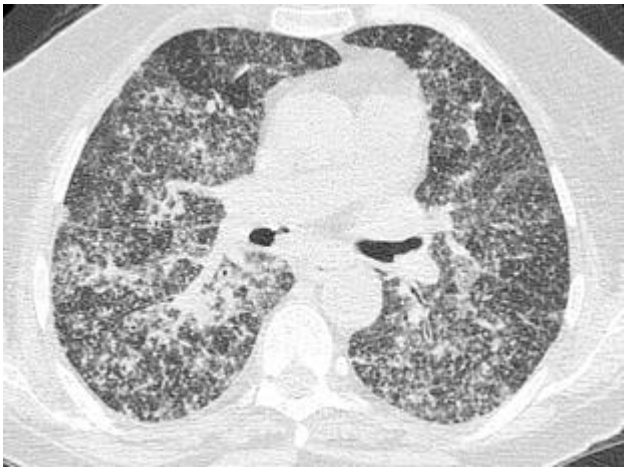

Figure 2. Bilateral pulmonary millimetric nodular opacities, 7.5–9 mm nodules in the right upper lobe and lingula on HRCT.

Bronchoscopy evaluation could not be performed because of hypoxemia. No pathological findings were obtained on abdominal ultrasonography (USG). Cervical USG revealed 13-mm right and 21-mm left supraclavicular LAP. The excisional biopsy of the left supraclavicular lymph node was reported as a small granuloma focus involving huge necrosis and hyalinization.
Treatment regimen was consisted of major anti-TB agents, including Isoniazid 300 mg 1x1/d, Rifampicin 300 mg 1x2/d, Pyrazinamide 500 mg 1x4/d, Ethambutol 500 mg 1x3/d. Prednisolone 1mg/kg/d was added to the treatment. She was observed in our clinic for 1 month and discharged after recovering from clinical symptoms, hypoxemia. She was referred to a local TB dispensary on the 20th day of therapy. The dose of prednisolone was reduced according to the outpatient clinic controls, and it was discontinued after two months.

Case 2

A 71-year-old man was admitted to our outpatient clinic with fatigue, dyspnoea, and 10 kg weight loss within one year. His family history did not reveal any known disease. He had no well-known TB exposure but had a story of smoking 40 packs/per year. Upon auscultation, rhonchi on the apical pulmonary regions and wheezing were noted. He was cooperative and conscious, and all vital signs were normal. Evaluation of initial laboratory parameters showed hypoalbuminemia (2,5 g/dl), mildly increased Aspartate Transaminase (52 IU/L), mildly increased γ-Glutamyl Transferase (86 IU/L), elevated Alkaline Phosphatase (142 IU/L), mild hyponatremia (132 mEq/L). Chest X-ray revealed blunting of the bilateral costodiaphragmatic angle, bilateral nonhomogenous infiltration involving cavitation on the upper zones, and

homogeneous densities on the right and left lungs limited with the posterior 6th and 7th costae, respectively (Figure 3).

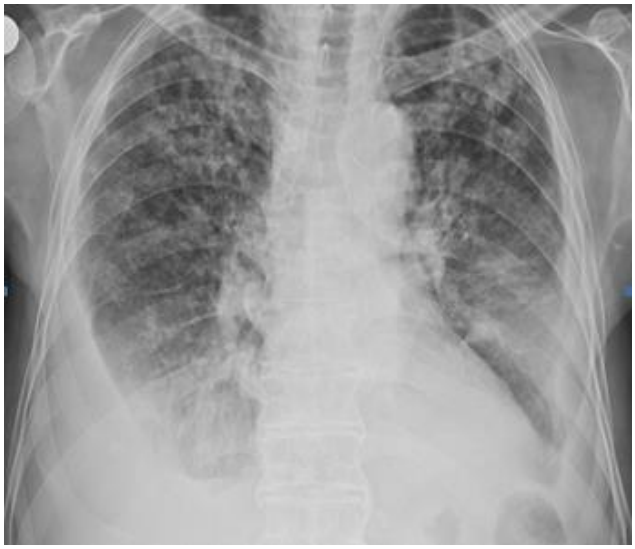

Figure 3. Blunting of the bilateral costodiaphragmatic angle, bilateral nonhomogenous infiltration involving cavitation on the upper zones, and homogeneous densities on the right and left lungs limited with the posterior 6th and 7th costae on Chest X-ray.

Thorax CT revealed pleural effusion with 6 and 5 cm thickness in the right and left lungs, respectively, and bilateral tree-in-bud diffuse infiltration in mostly the upper site decreasing to the basal site (Figure 4).

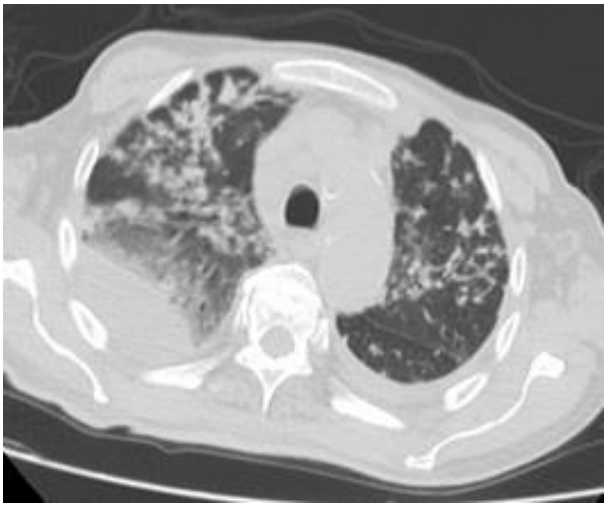

Figure 4. Bilateral pleural effusion and bilateral tree-in-bud diffuse infiltration in mostly the upper site decreasing to the basal site on Thorax CT.

PPD test was negative. The patient's condition was considered clinical-radiological pulmonary TB, and treatment consisting of Isoniazid 300 mg 1 × 1/d, Rifampicin 300 mg 1 × 2/d, Pyrazinamide 500 mg 1 × 4/d, and Ethambutol 500 mg 1 × 3/d was started. The patient had

bicytopenia, anemia (hemoglobin [Hb]: 8.4 g/dL), and leukopenia (white blood cell count: 2.83 $10e^3$/UL), and as a result of hematology consultation erythrocyte and leucocyte suspension transfusion was recommended. Sputum tests could not be examined because the patient could not produce sputum. Pleural fluid was exudative and serosanguinois and consisted of 100% lymphocytes, and Adenosine Deaminase of the fluid was mild high (45.9 U/L). The smear and culture of sputum samples for acid fast-bacilli (AFB) were negative. The fluid cytology was reported as mesothelial cells and lymphocytes.

Bilateral (10-mm right and 21-mm left) supraclavicular LAP was shown on the cervical USG. Excisional biopsy of the left supraclavicular lymph node was reported as necrotizing granulomatous lymphadenitis. Bone marrow biopsy performed by hematology department was reported as hypercellular marrow parenchyma involving tuberculoid granulomatous node. He was followed up for 24 days in our clinic and discharged after radiological, clinical, and laboratory recovery. He was referred to a local TB dispensary on the 14th day of treatment.

Discussion

It is estimated that DTB accounts for 1–2% of all tuberculosis cases (4). Extrapulmonary-TB (EP-TB) is most often manifested by pleural and bone involvement (5,6). The most prevalent form of EP-TB is lymphadenitis which is transmitted by haematogenic and direct spreading. Lymph nodes are solid, painless, mostly more than one and can be fistulized to the skin. The cervical lymph node is the most common location for TB lympadenitis. TB lymphadenitis other than cervical and supraclavicular TB lymphadenitis has a severe clinic and accompanies systemic symptoms (7,8).

Miliary TB is a potentially lethal type of DTB caused by tubercle bacilli spreading hematogenously to the lungs, and other organs. The most significant factor contributing to mortality tends to be a delay in diagnosis and failure to initiate specific antituberculosis therapy (9,10). The patients with DTB usually have immunodeficiency such as HIV, liver disease, alcohol abuse (2). The risk factors of our both two patients were senility and poor nutritional status causing hypoalbuminemia.

DTB has a wide range of clinical symptoms, which vary depending on the organ affected by TB. As a result, available diagnostic tests for particular symptoms must be differentiated. The detection of active TB should require a smear and culture of sputum samples for AFB, as well as nucleic acid amplification tests, according to consensus recommendations. When induced sputum samples are unavailable, flexible bronchoscopic sampling with transbronchial biopsy is preferred, as the yield of bronchoalveoler lavage is uncertain. AFB stain, mycobacterial culture, nucleic acid amplification testing, and histologic analysis can all be performed on suspicious extrapulmonary locations (11). The definite diagnostic test of the first case was lymph node biopsy. The second case was diagnosed by lymph node also bone marrow biopsies.

Abnormal laboratory findings such as hypoalbuminemia, hyponatremia, elevated Alkaline Phosphatase, and -Glutamyl Transferase and anemia can be determined in patients with DTB (1).

TB causes cytopenia in the peripheric blood by destroying the bone marrow anatomy with granulomatous nodules and chronic infection effect. Pancytopenia especially severe pancytopenia is rare and fatal. Except for TB-induced bone marrow granulomatous infiltration, pancytopenia is caused by histiocytic hemophagocytosis (12) and immune reactions (13). We confirmed bicytopenia by biochemical laboratory in the second case. After initiation of antituberculosis drugs Hb level and the count of leucocyte increased.

EP-TB is treated similarly to pulmonary TB, with an initial phase consisting of two months of quadritherapy (Rifampin, Isoniazid, Pyrazinamide, and Ethambutol), accompanied by a four-month continuity phase consisting of dual therapy (Rifampin, Isoniazid). The average recovery time for culture-negative TB can be shortened to four months (continuation phase of two months). When there is skeletal involvement, some experts recommend prolonging treatment to a nine-month schedule, and a twelve-month regimen when there is central nervous system involvement (14).

Conclusion

Treatment for related diseases complicates TB treatment in older people, resulting in a rise in adverse medication effects, treatment failure and higher rates of retreatment and drug resistance (15,16). A rapid diagnosis of DTB is desirable, as early initiation of treatment can reduce fatality. The definitive diagnostic tests of DTB are variable owing to atypical presentations and diagnostic difficulties. Our diagnostic tests (radiological, laboratory, histopathological) contributed valuable information about TB to us. We recommend that health providers must be aware of DTB especially in the diagnosis of elderly patients with poor nutritional status in endemic countries, such as Turkey.

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