DISSEMINATED TUBERCULOSIS (POTT'S DISEASE AND BILATERAL TUBERCULOUS PLEURAL EFFUSION) ASSOCIATED WITH PULMONARY THROMBOEMBOLISM

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Abstract

Background. Spinal tuberculosis, also known as Pott's disease, is diagnosed generally based on clinical and radiographic signs. There are rare reports of the association of Pott's disease with Pulmonary thromboembolism (PTE) worldwide.

Methodology. For the patient presented in this study, we faced the difficulty of diagnosing Pott's disease. To confirm the diagnosis, several examinations were used, such as Computed Tomography (CT scan) with contrast of the thoracic and abdominal region to detect pulmonary thromboembolism, bony destruction of the vertebral bodies, and bilateral pleural effusion; pleural fluid examination to establish the diagnosis of pleural effusion; and scientific literature was also consulted to determine the patient's diagnosis.

Case report. We report a case of Pott's disease with bilateral tuberculous pleural effusion in a 55-year-old male (Z.M) who presented with chest pain, cough, persistent fever, weight loss, and night sweats over 2 months. He also had progressive lower back pain, the classical kyphosis deformity of the dorsal spine, legs weakness with changes in posture and gait for more than 2 years. He was mistakenly diagnosed with cancer of the spine with destruction of L1, and L2. The interferon-γ release assay QuantiFERON®-TB Gold and the tuberculin skin test was negative. The fluid was an exudate with lymphocytes 80%, an adenosine deaminase 83.50 U/L, Xpert MTB/RIF positive. A CT scan with contrast of the thoracic and abdominal region and was obtained which showed PTE of right pulmonary artery, bilateral pleural effusion, bony destruction of the T12-L1-L2 vertebral bodies. After ruling out all the other thrombosis causes, we concluded that disseminated TB led to PTE in this case.

Conclusion. Pott's disease should be suspected in the diagnosis of spinal pain in patients with the presence of signals like a prolonged history of progressive back pain, and constitutional symptoms. CT scan with contrast of the chest should be done to exclude PTE in disseminated tuberculosis.

Keywords: Pulmonary thromboembolism; disseminated tuberculosis, spinal tuberculosis (Pott's disease)

TUBERKULOZI I DISEMINUAR (SËMUNDJA POTT DHE VERSAMENT PLEURAL BILATERL TUBERKULAR) SHOQËRUAR ME TROMBEMBOLI PULMONARE

Abstrakt

Hyrje. Tuberkulozi spinal, i njohur gjithashtu si sëmundja e Pott-it diagnostikohet përgjithësisht në bazë të shenjave klinike dhe radiografike. Ka raportime të rralla në mbarë botën të shoqërimit të sëmundjes Pott me Trombembolinë Pulmonare.

Metodologjia. Për pacientin e paraqitur në këtë studim u përballëm me vështirësinë e diagnozës të sëmundja e Pott. Për të konfirmuar diagnozën u përdorën disa egzaminime si: tomografia e kompjuterizuar (CT scan) me kontrast të rregjionit torakal dhe abdominal për të zbuluar trombembolinë pulmonare, destruksionin kockor të trupave vertebralë, versamentin pleural bilateral; egzaminimi i likidi pleural për vendosjen e diagnozës se likidit pleural. Gjithashtu u konsultua literatura shkencore për të përcaktuar diagnozën e pacientit.

Raportim rasti. Ne po paraqesim një rast me sëmundjen Pott's me versament pleural bilateral tuberkular në një pacient 55 vjec i cili u paraqit me dhimbje kraharori, kollë, temperaturë persistente, rënie në peshë, djersitje natën për një periudhë 2 mujore. Ai kishte gjithashtu dhimbje progresive në pjesën e poshtme të shpinës dhe deformim klasik i kifozës së shtyllës kurrizore dorsale, dobësi të këmbëve me ndryshime në posturë dhe ecje për më shumë se 2 vjet. Ai u diagnostikua gabimisht me kancer të shtyllës kurrizore me destruksion të L1, L2. Analiza e çlirimit të interferon-γ QuantiFERON®-TB Gold dhe testi i lëkurës së tuberkulinës ishte negativ. Likidi pleural ishte eksudat me limfocite 80%, adenosinë deaminasë 83.50 U/L, Xpert MTB/RIF pozitive. CT torakal dhe abdominal me kontrast tregoi Trombemboli pulmonare në arterien pulmonare të djathtë, likid pleural bilateral, destruksion kockor të trupave vertebrale T12-L1-L2. Pasi përjashtuam të gjithë shkaqet e tjera të trombozës, arritëm në përfundimin se TB i disiminuar ka shkaktur Trombembolinë pulmonare në këtë rast.

Konkluzioni. Sëmundja e Pott duhet të dyshohet në diagnozën e dhimbjes kurrizore në pacientët me prani të të dhënave si një histori e zgjatur e dhimbjes progresive të shpinës, simptomat konstitucionale. CT scan me kontrast duhet të bëhet për të përjashtuar PTE në tuberkulozin e diseminuar.

Fjalë kyçe. Embolia pulmonare, tuberkuloz i diseminuar, tuberkulozi spinal (sëmundja Pott)

Introduction

Spinal tuberculosis, also known as Pott's disease or tuberculous spondylitis, results from the hematogenous spread of Mycobacterium Tuberculosis (MT) bacteria from an extra-spinal focus to the spine or through lymphatic channels from the paravertebral lymph nodes or pleural space (1,2,3). Tuberculous spondylitis is the most dangerous type of skeletal tuberculosis, as it can lead to deformity of the spine and cause neurological deficits or

pulmonary insufficiency (4). The diagnosis of Pott disease is generally based on clinical and radiographic signs (5).

TB is considered a risk factor for Pulmonary thromboembolism (PTE) and there are rare reports of TB with PTE worldwide. Which TB patients are more susceptible to PTE is still not clear. As a chronic infectious disease, TB is also associated with PTE. Further studies showed that pulmonary TB induced a systemic hypercoagulable state (1).

Case presentation

We report a case of tuberculosis spondylitis (Pott's disease) with bilateral pleural effusion in a 55-year-old male who presented with chest pain, dyspnea, cough, persistent fever, weight loss, night sweats, and anorexia over approximately 2 months. He also had progressive lower back pain with local tenderness, the classical kyphosis deformity of the dorsal spine, and leg weakness with changes in posture and gait for more than 2 years. He was mistakenly diagnosed with cancer of the spine with destruction of L1, L2 and surgical intervention was recommended two years ago. He was a non-smoker. Cardiovascular and neurological examinations were clinically normal. He was normotensive and not tachypneic or tachycardic. On auscultation of the chest, there were decreased breath sounds in bilateral basal regions. The pulse oximeter reading was 96% on air. Pulmonary X-Ray imaging showed bilateral pleural effusion and cultures of sputum were negative for tuberculosis.

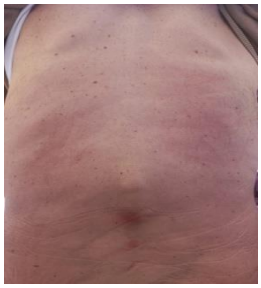

Figure 1. Spinal deformity, a significant feature of spinal tuberculosis.

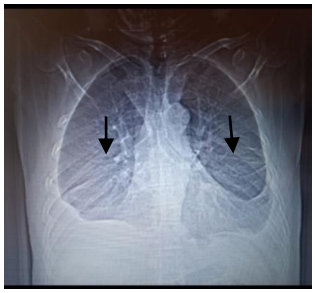

Figure 2. Chest x-ray PA view shows bilateral pleural effusions.

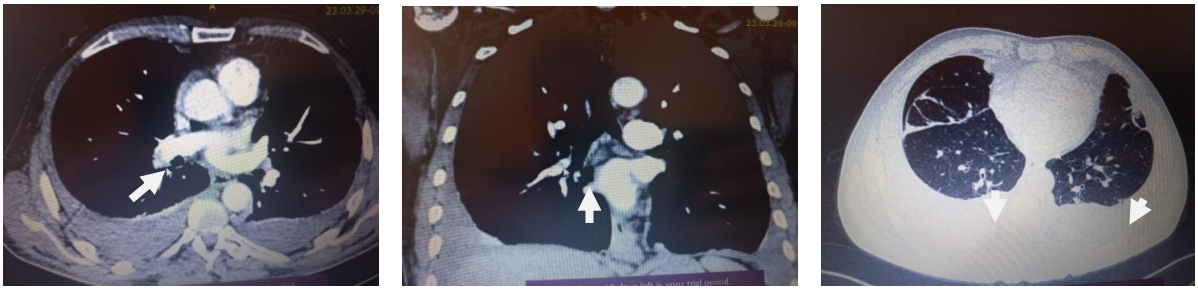

Figure 3. A CT scan with contrast of the chest and lumbar region: thromboembolism of bifurcation of right pulmonary artery with bilateral pleural effusion.

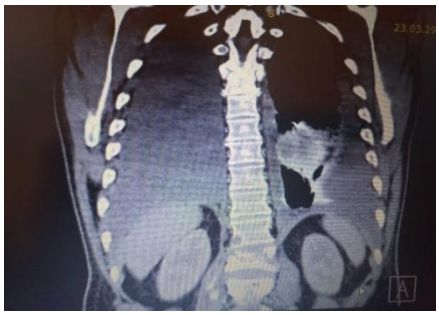

Figure 4.Computed tomography coronal view of the thoracic spine from the initial visit shows significant worsening bony destruction of the T12-L1-L2 vertebral bodies with paravertebral soft tissue extension and a stenosis of the intervertebral disc space.

Laboratory studies showed markedly increased inflammatory activity (CRP 8.5 mg/dL), but a normal white blood count of 8,700/μL. HIV serology was negative. Remarkably, the interferon-γ release assay QuantiFERON®-TB Gold In-Tube was negative (IFN 0.17 IU/mL) and the tuberculin skin test (TST) was negative (0 mm). The initial diagnosis was tuberculosis pleuritis. The pleural effusion was investigated by thoracentesis. The fluid was an exudate with a clear predominance of lymphocytes (80%), and an adenosine deaminase (ADA) value of 83.50 U/L, Xpert MTB/RIF positive. A Computed Tomography (CT) scan with contrast of the chest, lumbar, and spine region was obtained which showed thromboembolism of bifurcation of the right pulmonary artery with bilateral pleural effusion, significant worsening bony destruction of the T12-L1-L2 vertebral bodies with paravertebral soft tissue extension and stenosis of the intervertebral disc space (spondylodiscitis). The patient was a poor surgical candidate for an open biopsy of the lesion.

D-dimer was 13.17 mg/L. Serum protein C, protein S, antithrombin, and factor V levels were normal, and Antinuclear Antibodies (ANA) and antiphospholipid antibodies APLA profile were negative, also. The bilateral limb and lower limb color Doppler scan were negative for any thrombus. After ruling out all the other thrombosis causes, we concluded that disseminated TB led to PTE in this case.

Neurosurgery declined operative medicine due to the patient was without advanced neurological deficits. The patient was initiated on anti-coagulation and weight-based anti-

tubercular therapy (ATT). The patient was started on a four-drug antitubercular treatment regimen of oral rifampin 600 mg/day, isoniazid 300 mg/day, pyrazinamide 500 mg thrice/day, and ethambutol 1200 mg/day (RIPE). Therefore, LMWH was prescribed as anticoagulant.

Discussion

Although it is well known that MT can be pathologic to any organ system, its manifestations can be so variable that sometimes it becomes a challenge for the clinician to identify or even consider it as the cause of the patient's symptomatology (6).

Extra pulmonary tuberculosis (EPTB), defined when the tuberculosis mycobacterium invades areas outside the pulmonary parenchyma, has nonspecific clinical findings developing insidiously mimicking other noninfectious conditions. It requires a high clinical suspicion and carries a long period from the initial symptoms to the final diagnosis. Clinical presentation will vary according to the organ system involved and more than one organ could be involved at the same time. The initial step in early identification is having knowledge of its findings in the proper clinical setting and including them within the differential diagnosis (6).

The diagnosis and treatment of EPTB are challenging. Most cases show constitutive symptoms such as fever, weight loss, night sweats, or malaise with specific systemic symptoms based on the organ affected (7). The sensitivity and specificity of various tests used to diagnose EPTB are highly variable; in most cases, clinical disease presentation should be considered in choosing and interpreting a specific diagnostic test (7).

The initial diagnosis was tuberculosis pleuritis. Diagnosis involves a combination of clinical, radiological, microbiological, and molecular testing (7). Fluid analysis in PLTB is exudate characterized by lymphocytic predominance. It usually presents with more than 80% of lymphocytic predominance (8). Biochemical parameter, ADA levels is monitored in pleural fluid, and elevated level of this marker help pleural tuberculosis diagnosis in high-prevalence or endemic countries. In endemic countries, pleural ADA levels of >40 IU/L have a positive predictive value of 98% (9). In a high prevalence population, an elevated ADA level (>40 U/L) is considered confirmatory with a clear indication for therapy (8). Xpert MTB/RIF can be used as an initial test for adults with EP-TB indications using a pleural fluid sample. The Xpert MTB/RIF and Xpert Ultra sensitivities are 50% and 71% over MRS with 99% and 71% specificity, respectively, for adult pleural fluid (10). The fluid analysis of our patient was an exudate with a clear predominance of lymphocytes (80%), and adenosine deaminase (ADA) levels of 83.50 U/L, Xpert MTB/RIF positive.

Tuberculosis spondylitis (Pott's disease) is an ancient human disease. Because it is rare in high-income, tuberculosis (TB) low-incidence countries, misdiagnoses occur as sufficient clinical experience is lacking (11). Most spinal infections typically come from a pulmonary focus or extra-pulmonary foci (12). Tubercle bacilli reach the spine either hematogenous or through lymphatic channels from the paravertebral lymph nodes or pleural space (3). Reports suggest that most tuberculosis empyema and patients with vertebral bone involvement (Pott's disease) develop after the transport of tubercle bacilli from the pleural spaces to the parasternal and the para-aortic lymph nodes and the breakdown of caseous foci in these nodes (13). Diagnosis of spinal tuberculosis is multifaceted and includes components of clinical history, laboratory results, and imaging findings (7). The diagnosis of Pott's disease is

generally based on clinical and radiographic signs (5). Pott's disease should be considered when patients present with neurological findings suggesting spinal cord compression and spinal deformity (14). Results in pain and stillness early on, then muscle spasms and restriction of spinal movement, local tenderness, and varying degrees of deformity. The pain may be restricted to the affected region or it may radiate in the distribution of the affected segment (3). In advanced stages of the disease, large areas of bone destruction, associated with the collapse of the vertebrae and kyphoscoliosis deformity of the spine constitute the familiar radiological picture. The classical deformity especially in the lesion of the dorsal spine is the (Gibbus) or (Kyphosis) (3). Chronic back pain is sometimes accompanied by muscle spasms and changes in posture and gait. MT infection often presents with constitutional symptoms such as weight loss, fever, and night sweats (especially if disseminated MT is present) (2).

Our patient showed a combination of alarm signals: chest pain, dyspnea, cough, persistent fever, weight loss, night sweats, anorexia over approximately 2 months, progressive lower back pain with local tenderness, the classical kyphosis deformity of the dorsal spine, leg weakness with changes in posture and gait for more than two years, which encouraged us to do further work-up to establish a definite diagnosis. Due to the subtle nature of symptoms, diagnostic evaluations are often not initiated until the process is advanced. However, establishing the correct diagnosis is challenging and misdiagnoses may occur in up to 41% of cases (15).

The CT scan appearance can be highly suggestive of tuberculosis spondylitis (3). CT scan of the spine is considerably more sensitive and should be obtained whenever an infectious process is suspected (16). The disease is located in the vertebral column, and more specifically, in about 3/4 of the cases, in some part of the column between the sixth dorsal and the third lumbar vertebrae, the ninth dorsal vertebra seems to be the one most frequently involved (3). Two types of lesions can be seen: Vertebral, cavity in a vertebral body, erosion of one or more vertebral surface with or without compression and cuneiform, aspect Disk damage with compression and disappearance of the intervertebral space (5). CT with contrast of the chest, abdominal and the spine region of our patient showed thromboembolism of bifurcation of right pulmonary artery with bilateral pleural effusion, significant worsening bony destruction of the T12-L1-L2 vertebral bodies with paravertebral soft tissue extension and a stenosis of the intervertebral disc space (spondylodiscitis).

Fine Needle Aspiration is a valuable method because it reveals tissue fragments for histopathology and culture, leading to diagnosis. It is usually done when the diagnosis is in doubt or when the patient has received medical treatment for a long period enough to show a clinical response (3). Our patient was a poor surgical candidate for an open biopsy of the lesion.

Treatment regimens do not differ from pulmonary and extrapulmonary tuberculosis (3). Occasionally, surgical intervention is recommended, mainly when organ damage is debilitating to the patient (7). Neurosurgery declined operative medicine because our patient was without advanced neurological deficits. The occurrence of thrombosis in TB patients was associated with the severity of TB itself. It’s known that the three major factors causing thrombosis in TB patients are local lesion invasion, venous compression, and hypercoagulability. MT can directly cause vascular endothelial damage and release

chemoattractant such as complement C3a C5a, plasma enzyme activator and kinin releasing enzyme (kallikrein), which can further promote coagulation and thrombosis. Venous compression caused by lymph node tuberculosis could also lead to thrombosis. Hypercoagulability was due to elevated blood fibrinogen with impaired fibrinolysis, reduced thrombin III, protein C binding to thrombin, and platelet aggregation (1). D-dimer was 13.17 mg/L. We ruled out all the other causes of thrombosis and concluded that disseminated TB led to PTE in this case. The patient was initiated on anti-coagulation and weight-based anti-tubercular therapy (ATT).

Conclusion

Pott's disease should be suspicioned in the diagnosis of spinal pain in patients with significant risk factors and the presence of signals like a prolonged history of progressive back pain and constitutional symptoms. PTE should be suspected and investigated with imaging tests whenever serum D-dimer levels are elevated, particularly in those with severe pulmonary or disseminated tuberculosis. A chest CT scan with contrast should be done to exclude PTE in disseminated tuberculosis. Prophylactic use of anticoagulants should be indicated for patients with severe or hematogenous disseminated tuberculosis.

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