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Disseminated Tuberculosis in an immunocompetent patient

Research Article

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Abstract: A 53-year-old immigrant male patient presented with left scrotal swelling with a draining ulcer on the left hemiscrotum. Patient had intentional weight loss, fever and night sweats, cough, headaches, confusion and difficulty with ambulation. Imaging studies revealed innumerable pulmonary nodules, leptomeningeal enhancement of the brain and bilateral epididymo-orchitis. Acid fast bacilli (AFB) smear was positive from the surgical specimen of bilateral epididymis and left testes. Cerebrospinal fluid (CSF) analysis revealed neutrophilic predominant pleocytosis with low glucose and elevated protein. Polymerase chain reaction (PCR) test performed on the CSF and AFB smear of epididymis was positive for *Mycobacterium tuberculosis*. Though the CSF and sputum AFB smears were negative, cultures subsequently grew mycobacterium tuberculosis. Patient was diagnosed with disseminated tuberculosis. Human deficiency virus test was negative. Patient was successfully treated with anti-tuberculosis therapy. Steroid was used as adjuvant therapy due to presence of tuberculous meningitis.

Keywords: *Disseminated tuberculosis • Tuberculous meningitis • Urogenital tuberculosis*

1. Introduction

Immunocompetent host presenting with disseminated tuberculosis is uncommon [1,2]. Recognition of disseminated tuberculosis in countries with low endemic rates, especially in immigrant patients requires a high index of suspicion as they can be very challenging and potentially fatal. Our case describes a very complex presentation of disseminated tuberculosis with multiorgan involvement in an immunocompetent patient and the comprehensive diagnostic approach in our patient. Polymerase chain reaction (PCR) test played a significant role in rapid diagnosis of *Mycobacterium tuberculosis* with extrapulmonary focus as illustrated in our case.

2. Case report

A 53-year-old immigrant male patient presented with 2 month history of left scrotal swelling associated with spontaneous fluid drainage from the left hemiscrotum sinus wound for 2 weeks. He was experiencing malaise, unintentional weight loss of approximately 28 lb, dry cough and night sweats for past few weeks. One week prior to hospitalization he became overtly ill with intermittent low grade fever and chills, headaches, confusion, poor balance and with difficulty in ambulation. Patient appeared cachectic and was afebrile on initial presentation. Chest auscultation and cardiac exam was normal. Hepatosplenomegaly and lymphadenopathy were absent. Genitourinary examination revealed normal meatus, left testicle was enlarged with a sinus tract draining fluid on the lateral upper surface of the

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left hemiscrotum and bilateral epididymal fullness was present. Past medical history and surgical history was unremarkable. Patient denied prior exposure or diagnosis of active tuberculosis or latent tuberculosis. Patient denied smoking, alcohol and intravenous drug use. Patient immigrated to United States 14 years prior but he had travelled to Asian subcontinent during the previous one year. Family history was unremarkable.

The scrotal echography revealed heterogeneous appearance and hyperemia of the left testicle with associated enlargement of bilateral epididymis consistent with epididymo-orchitis. Computerized tomography (CT) of the chest revealed innumerable pulmonary nodules and mass like densities in both lungs and a large anterior mediastinal mass (Fig 1). Magnetic resonance imaging (MRI) of the brain with gadolinium showed diffuse nodular leptomeningeal enhancement (Fig 2).

Laboratory studies showed white cell count of 12.4 x10 ^{9} cells/L (normal, 4.8–10.8 x10 ^{9} cells/L), serum sodium of 123meq/l (normal, 136 – 145 mEq/L) and albumin of 2.9 gm/dL (normal, 3.4 – 4.6 gm/dL). Liver transaminases were normal. Carcinoembryonic antigen, alpha-feto protein and human chorionic gonadotropin level were normal. Rapid plasma reagin and human immunodeficiency virus test was negative. The absolute lymphocyte count was 728 (normal, 720-4320 mm^3); CD4 count of 425(normal, 223-2203) and CD4% of 58 (normal, 31 -51%).

Cerebrospinal fluid (CSF) examination revealed low Glucose -34 mg/dL (normal, 50- 80 mg/dL); elevated protein -142 mg/dL (normal, 15 -60 mg/dL); white blood cells- 313 mm^3 (normal, 0-5 mm^3); 86% segmented neutrophils (normal, 0-7%); 9% lymphocytes (normal 40 -80%) and 3 red blood cells; CSF for acid fast bacilli (AFB) smear, fungal smear and gram stains were negative. cytology was negative for malignant cells however, abundant acute inflammation was noted. The sputum AFB smear was negative but was positive from the left testis and bilateral epididymis. The real time PCR performed on the CSF and the perioperative genital specimen was positive for *Mycobacterium tuberculosis*. AFB cultures from sputum, cerebrospinal fluid and including the cultures from perioperative genital specimen all turned positive for *Mycobacterium tuberculosis* after 3 weeks. Drug resistance was absent. The blood cultures, CSF fungal and bacterial cultures were negative. Urinalysis revealed pyuria with sterile cultures. A CT guided core biopsy of the anterior mediastinal mass was consistent with benign thymic epithelial neoplasm of World health organization Type AB (mixed thymoma) and cultures for AFB were negative on thymoma specimen. Patient was initiated on therapy with rifampin, isoniazid, pyrazinamide and ethambutol at the first identification of

Figure 1. CT chest with multiple pulmonary nodules in both lungs, predominantly on the right with larger mass like consolidation on the bilateral lower lobes.

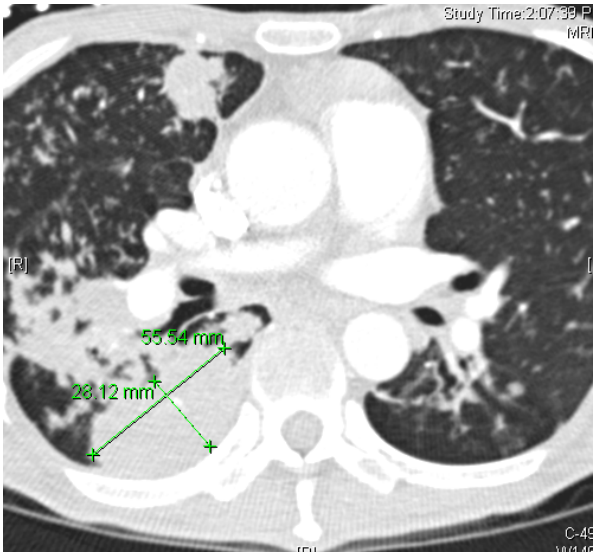

Figure 2. MRI brain, T1 signal showing diffuse nodular leptomeningeal enhancing foci with largest lesion with in the left sylvian fissure measuring 10 x 9 mm.

the positive AFB smear on the perioperative left testicular specimen. Dexamethasone was also administered for the initial part of the antituberculosis therapy due to leptomeningitis.

3. Discussion

In countries with low endemic rates such as United States of America, disseminated tuberculosis is mainly

encountered in foreign born patients, female sex, non-white population and immunocompromised host from human immunodeficiency virus infection, malignancy, use of steroids and immunomodulator drugs. Genetic defect in the interleukin -12 pathway or of gamma – interferon defect has been reported as predisposing factor for disseminated tuberculosis [2]. One should have a high index of suspicion for disseminated *Mycobacterium tuberculosis* in patients at risk, since these cases are potentially fatal and they are associated with high mortality. Not surprisingly these cases can be very challenging and misleading, leading to delayed diagnosis and treatment [3]. Here we described the central nervous system (CNS) and urogenital manifestation. Our patient presented with left scrotal swelling associated with an ulcer, low grade fever, headache, confusion, cough and malaise with progressive weight loss which made us suspect metastatic testicular cancer at the initial presentation. However, presence of leptomeningeal enhancement on the MRI of brain along with CSF analysis (presence of pleocytosis, hypoglycohrracia and high protein levels) pulmonary nodules with constellation of symptoms (cough, weight loss) and foreign birth were leading to the diagnosis of disseminated *Mycobacterium tuberculosis* infection with possible urogenital organ involvement. The AFB smear and Mycobacterium tuberculosis PCR on the epididymis and the CSF led to the definitive diagnosis of disseminated tuberculosis in our patient.

CNS involvement due to *Mycobacterium tuberculosis* is reported in 1% of the patients with tuberculosis. The CNS manifestations could be either as meningitis, tuberculoma, and abscess or as spinal arachnoiditis [4, 5]. Tuberculous meningitis, the most severe form of CNS tuberculosis although primarily seen in children is not uncommon in adults and more frequently results from reactivation of the dormant focus in the CNS [6]. Tuberculous meningitis constitutes 5 to 6% cases of extra pulmonary tuberculosis cases in hosts with preserved immune function [7,8]. Immunocompromised state increases the risk for tuberculous meningitis though clinical presentation of tuberculous meningitis can be similar to that seen in a normal host. Our patient was immunocompetent but he had tuberculous leptomeningitis with characteristic low glucose and elevated protein levels in the cerebrospinal fluid. Typically monocyte predominant pleocytosis is seen however, neutrophilic predominance can occur in early tuberculous meningitis similar to pyogenic bacterial meningitis. The diagnostic yield of positive AFB smear and culture increases upto 83% with 3 serial CSF examinations and also if at least 10 ml of CSF is obtained for testing [8]. In our patient single AFB smear on CSF was negative but the molecular method using PCR on the CSF helped in early diagnosis of *Mycobacterium tuberculosis* and timely initiation of appropriate therapy in our patient. The CSF cultures grew *Mycobacterium tuberculosis* at 3 weeks. CNS tuberculosis carries high morbidity and mortality despite treatment [7] due to complications that can occur in the course of the disease. Hydrocephalus, vasculitis, stroke from vasospasm, 6th and 7th cranial nerve dysfunction is noted with the basilar meningeal involvement resulting in significant morbidity. Hence early diagnosis and initiation of antituberculosis therapy is very crucial. Emperic therapy should be initiated when there is high suspicion for tuberculous meningitis while the work up or diagnosis in under progress [6]. Use of corticosteroids as adjuvant therapy for tuberculous meningitis in the initial part of therapy is widely accepted [6].

Urogenital tuberculosis constitutes 6.5% cases of extrapulmonary focus with 34% of cases occurring in patients above 60 years age [3]. It is the second most common extra pulmonary tuberculosis next to the lymphatic system [9]. Genitourinary tuberculosis cases occur from haematogenous spread of primary pulmonary infection and are associated with significant morbidity. One should have a high clinical suspicion for diagnosing the tuberculous epididymo-orchitis in men since these cases can mimic testicular malignancy. Genital tuberculosis can be easily mistaken to malignancy or other conditions especially in countries with low endemic rates of tuberculosis. Our patient had smear and culture positive bilateral tuberculous epididymo-orchitis and again the use of PCR test on the perioperative specimen of epididymis aided in rapid detection of *Mycobacterium tuberculosis*. Also noted in our patient was a sterile urine culture despite abundant white blood cells in the urine consistent with likelihood of involvement of renal system although urine for acid fast bacilli smear and culture was not performed.

In conclusion disseminated *Mycobacterium tuberculosis* is uncommon in immunocompetent individuals. Tuberculous meningitis by itself or urogenital tuberculosis by itself although not rare, but the combination of both leptomeningitis and urogenital tuberculosis occurring simultaneously in an immunocompetent host is a rare diagnosis making our case interesting.

Most of the time patients with disseminated tuberculosis or extrapulmonary tuberculosis have positive chest radiograph findings or exposure history as was the case in our patient who had pulmonary nodules and mass like consolidation of the lungs. Our case also depicts the complex nature of the disease manifestation posing a diagnostic challenge and emphasis for high index of clinical suspicion for disseminated tuberculosis in high risk patients especially in countries with low

incidence of tuberculosis. A PCR for rapid detection of *Mycobacterium tuberculosis* should also be used early especially when the index of suspicion is high however, the clinicians should remember that the negative PCR test should not exclude the diagnosis of tuberculosis especially in patients with high clinical suspicion.

Aknowledgements

None

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