A Case Report of Disseminated Tuberculosis With an Atypical Presentation

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Abstract

Here we report a 45-year-old male who presented to us with fever, loss of appetite, and painless bilateral testicular swellings. His routine chest X-ray revealed reticulo-nodular opacities in both lung fields. Ultra-sonogram of both testes revealed multiple fairly large space occupying lesions in both testes and epididymides. Initially thought to be a case of testicular tumor with lung metastases, the case later proved to be a case of chronic disseminated tuberculosis (TB), following fine needle aspiration and cytology of both testicular swellings and lung lesion. His sputum smear also revealed acid fast bacilli (2+). Interestingly, this patient had fever, loss of appetite, and cough 2 years ago, but remained well without specific anti-tubercular therapy in the intervening period. This case illustrates that common diseases can present in confusing and atypical ways. This cloaked appearance can misguide us to make a wrong diagnosis. Especially in a TB endemic zone such as ours, TB should not be excluded from the list of differential diagnoses, and should be actively searched.

Keywords: Disseminated tuberculosis; Diagnostic dilemma; Atypical presentation

Introduction

The infamous reputation “captain of all these men of death”, originally ascribed by Sir William Osler to pneumonia [1], has later been awarded to tuberculosis (TB) by many including clinicians to historians or even novelists [2-4]. TB has been a scourge of the humankind from time immemorial. Till date, no other disease in history matches the sheer magnitude of the misery inflicted by TB on the human race in terms of morbidity and mortality [5]. TB is caused by bacteria of the Mycobacterium tuberculosis complex and usually affects the lungs, although other organs are involved in up to one-third of cases [6]. In order of frequency, the extra-pulmonary sites most commonly involved in TB are the lymph nodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum and pericardium [6]. Disseminated TB refers to concurrent involvement of at least two non-contiguous organs of the body or involvement of the blood and bone marrow by TB process [7]. Disseminated TB is still uncommon, and unlike the rapid disseminating form, well known as military TB, chronic metastasizing form is less frequently recognized [8]. In healthy individuals, the dissemination is contained by a prompt immune response, particularly cell-mediated immunity and interferon gamma pathways, limiting the infection [9]. Therefore, clinical disseminated disease following primary or reactivation of established latent TB is more often in relatively or absolutely compromised hosts such as infants, patients with acquired immune deficiency syndrome (AIDS) or patients with latent infection placed on a tumor necrosis factor alpha blocker, compromising the regular immune surveillance [10-13]. Rarely, the dissemination occurs in healthy individuals with no known predisposing condition challenging our clinical suspicion to consider it as a differential diagnosis, and especially with very non-specific and atypical features, as is the case presented here.

Case Report

A 45-year-old Bengali male, day laborer, hailing from Satar-gul, Badda, Dhaka, presented to us with fever, loss of appetite and bilateral testicular swelling for 3 months. Fever was low-grade, intermittent associated with evening rise of temperature, night sweats, and chills and rigor. The highest recorded temperature was 100 °F. He had also lost his appetite during this course of time. Three months back, he had noticed swelling in his both testes, which were gradually increasing in size. The swellings were painless. On query, he mentioned occasional cough, but no sputum production and hemoptysis. He had no chest pain, respiratory distress, urinary problem, altered bowel habit, abdominal distension, abdominal pain, or joint pain, but he felt unusually fatigued, and at the time of admission, he was fatigued to such extent that he could not perform any heavy work. He had lost 15 kg of weight over the last 2 years. In fact, 2 years ago, he had suffered from fever, cough with purulent sputum production (but no hemoptysis), chest pain and loss
of appetite for 3 months. His past records showed that at 2 years before presenting to us, complete blood count (CBC), sputum smear for acid-fast bacilli (AFB), tuberculin skin test, bronchoscopy, and repeated chest X-rays were done. Except erythrocyte sedimentation rate (ESR), which had been 84 mm in first hour, all other parameters of CBC (done 2 years back in previous episode) had been normal. Sputum smear examination with Ziehl-Neelsen (Z-N) stain had revealed no AFB, and the tuberculin skin test had revealed induration of 5 mm in 72 h. Chest X-ray done 2 years back had shown ill defined, nodular and confluent opacities in all the zones of both lung fields suggestive of bilateral pulmonary TB or secondaries and also inhomogeneous opacities in both upper zones. Again at the same time, 2 years back, bronchoscopy also had been done and bronchial washing had been taken, which had revealed inflammatory lesion in the lungs. On clinical and radiological suspicion of pulmonary TB, he had been given anti-tubercular drugs, but due to serious hypersensitivity reactions, the drugs had been stopped after only 2 days. Then he had been prescribed only clarithromycin, and antihistamines. Since then, he had remained well, until 3 months back, when he again developed fever and loss of appetite. During this 2-year period, he had not followed his physicians’ advice and had not taken any antitubercular drugs. But this time, unlike previous occasion, he complained of bilateral painless testicular swellings, which was in fact, one of his main presenting complaints, this time. He was a non-smoker, non-hypertensive and non-diabetic. He had no history of contact with TB patient in the past and none of his family members were afflicted with this sort of illness. Apart from mild anemia, and swellings in the testes and epididymides, all other general and systemic examination findings were normal. Clinically multiple (3 - 4) swellings were palpable in both testes and epididymides. The largest one on right side measured about 7.5 × 6 cm and that on the left measured about 6 × 3 cm in size. The surface was smooth. They were firm in consistency, and non-tender. There was no erythema of the overlying skin, nor any local rise of temperature. CBC done during admission revealed Hb 10.1 g/dL (14 - 16 g/dL) and ESR 98 mm at first hour (< 20 mm at first hour); other parameters are within normal limits. Serum bilirubin, serum glutamic pyruvic transaminase (SGPT), and creatinine were normal. Serum albumin and prothrombin time were 2.7 g/dL (3.3 - 5.5 g/dL) and 16.2 s (11 - 14 s), respectively. A chest X-ray was done and it revealed reticulo-nodular opacities in both lung fields (Fig. 1), suggestive of bilateral pulmonary TB or secondaries. Sputum smear with Z-N stain revealed AFB (2+), which gave us the clue that the lung lesions were due to TB. A two-dimensional (2D) ultrasonography of both testes was done 2 days after admission and it showed: 1) enlarged right testis with multiple fairly large, hypoechoic space occupying lesions (SOLs), 2) mildly enlarged left testis, with multiple fairly large, hypoechoic SOLs, 3) grossly enlarged right epididymis, with multiple hypoechoic, fairly large SOLs, and 4) mildly enlarged left epididymis with multiple small SOLs.

Subsequently, fine needle aspiration (FNA) of both testicular swellings (epididymis) was done. Smears made from both epididymal swellings revealed many epithelioid cells, granulomas, giant cells, lymphocytes, histiocytes, small amount of caseation necrosis and cellular debris. No malignant cells were seen. All these features were suggestive of granulomatous inflammation compatible with TB.

**Discussion**

TB is an infectious disease caused by bacteria of the *M. tuberculosis* complex. TB infection almost always occurs through inhalation of aerosolized *M. tuberculosis* bacilli, which replicate in alveolar macrophages and typically form a Ghon focus [14]. The mycobacteria remain latent, presumably in lung granulomas or lymph nodes [15] until an alteration between the pathogen and the immune cells results in active disease. Following *M. tuberculosis* infection, 5-10% of people will develop the active disease while more than 90% of infections do not result in disease in an immunocompetent individual’s lifetime [15]. Primary disease occurs soon after the primary infection in the context of a naive immune system, and the bacilli multiply and spread [14]. The mycobacteria reach extrapulmonary organs by hematogenous dissemination and can then spread locally [14]. Post-primary disease occurs long after primary infection in the context of a sensitized immune system, either as reactivation of a latent infection or as result of re-infection with a new strain [9, 14]. Disseminated TB is defined as tuberculosis infection involving the blood stream, bone marrow, liver, or two or more non-contiguous sites, or military TB [16, 17]. Disseminated TB accounts for 1-2% of all cases.
of TB infection in immune competent individuals [18]. Our case presented to us with fever, loss of appetite, and bilateral testicular swellings. But the fact remains that he had also suffered from fever, cough, chest pain, and loss of appetite 2 years before this episode. Though there had been no microbiologic or histopathologic evidence of TB at that time, the clinical and radiologic features had been suggestive of TB. Though he had not received specific anti-tubercular therapy, he had received clarithromycin for some time, which has activity against M. tuberculosis. It is possible that after 2 years, the disease reactivated, and spread to involve the genital system. Some researchers have reported that genitourinary tuberculosis (GT) includes 8-15% of extra-pulmonary tuberculosis [19, 20], whereas some have mentioned a higher 30-40% of all extra-pulmonary cases [21]. But there is confusion concerning the accuracy of these numbers [22]. GT may occur during primary infection; however, it can expand late after a long latent period, even 20 - 30 years, following the primary localization [23, 24]. In this patient, the latent period spanned almost of 2 years. Genital TB in males most commonly involves the epididymis followed by the prostate [25]. The higher frequency of isolated epididymal TB lesions in children favors the possibility of hematologic spread of infection, whereas adults seem to develop tuberculous epididymo-orchitis caused by direct spread from the urinary tract [25, 26]. In 70% of patients, there is a previous history of TB [27]. Few cases have been reported where tubercular orchitis has been confused with malignancy, creating diagnostic dilemma such as this case [28-30]. Ultrasonography features of TB epididymo-orchitis include diffusely enlarged heterogeneously hypo-echoic, diffusely enlarged homogeneously hypo-echoic, and nodular enlarged heterogeneously hypo-echoic epididymis and testis as seen in this case [31, 32]. However, the sonographic pattern of TB epididymo-orchitis is non-specific and may be seen with non-TB infection, tumor or infarction [31, 32]. In the absence of histologic finding, it may be impossible to differentiate such a swelling from a testicular tumor [25]. Sensitivity and specificity of FNA biopsy in diagnosing tuberculous epididymitis has been determined as 87% and 93%, respectively [33]. Therefore, an FNA biopsy is very important as the primary examination in patients with epididymal lesions [33]. The presence of epididymal involvement with a testicular lesion supports an infection rather than a neoplastic cause [34].

**Conclusion and rationale**

Disseminated TB is uncommon, and more unthinkable is the combination of lung and genital lesions, sparing the other organ systems. The chronicity of disease in our case is also remarkable. Moreover, our case presented with painless bilateral swellings in the testes and epididymis, and on ultrasonography, there were multiple fairly large SOLs in both testes and epididymides, which were initially confused to be neoplastic in origin. To add to the confusion, chest X-ray also revealed reticulo-nodular opacities, mimicking secondaries. But all the mysteries were unearthed after getting the reports of FNAC from swellings and sputum smear for AFB. In the end, it turned out to be a case of disseminated TB. This case again illustrates the polymorphous presentation of the disease TB. It shows that common diseases can present in confusing and atypical ways. This cloaked appearance can misguide us to make a wrong diagnosis. Especially in a TB endemic zone such as ours, TB should not be excluded from the list of differential diagnoses, and should be actively searched.

**Competing Interests**

The authors declare that they have no competing interests.

**Author Contributions**

RS and PH contributed to writing, editing, literature review and overall preparation of this manuscript and in diagnosis of the patient, and AK contributed greatly in diagnosis and management of the patient.

**Abbreviations**

TB: tuberculosis; AIDS: acquired immune deficiency syndrome; Z-N: Ziehl-Neelsen stain; WBC: white blood cell; CBC: complete blood count; ESR: erythrocyte sedimentation rate; Hb: hemoglobin; SGPT: serum glutamic pyruvic transaminase; 2D: two-dimensional; SOL: space occupying lesion; FNA: fine needle aspiration; FNAC: fine needle aspiration and cytology; AFB: acid-fast bacilli

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