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Left pleural effusion in a young woman with genital tuberculosis

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Abstract

Disseminated tuberculosis is a rare form of tuberculosis that can cause severe illness if diagnosed and treated late. We present the case of a young Senegalese woman who had a miscarriage due to a pelvic inflammatory disease, followed by the development of a left pleural effusion. Despite laparoscopic

findings and a salpinx biopsy that revealed necrotizing granulomas, only microbiological examinations of pleural biopsies revealed the final diagnosis of disseminated, drug-sensitive tuberculosis.

Introduction

Tuberculosis (TB) is one of the leading infectious disease and cause of death worldwide [1]. The optimal management of disease relies on a fast microbiological diagnosis and drug resistance detection with prompt initiation of an effective pharmacological treatment [2].

Disseminated TB, which is a rare form of disease due to hematogenous or lymphatic spread of *Mycobacterium tuberculosis complex* (MTB) from the primary site of infection, may be characterized, in high-income countries, by atypical or rare clinical pictures of extrapulmonary disease (e.g. genital TB) [3,4,5]. Poor knowledge of this form of disease may result in a delayed diagnosis and therapy with subsequent spread of MTB to multiple organs and potentially severe disease [3,4,5].

Case Report

A 27-year-old Senegalese woman, living in Italy for two years and with negative past medical history, was referred to our Pulmonology Department for a left pleural effusion.

One month before, following a miscarriage complicated by bilateral salpingitis, she underwent a laparoscopic left salpingectomy. During surgery, hyperemic and edematous salpingus, free abdominal effusion and several whitish, miliary-shaped peritoneal lesions, involving diaphragm and visceral serous, were detected. Abdominal fluid was sent for microbiological investigations, peritoneal and salpinx biopsies were collected only for histopathological analysis. All the microbiological investigations, including smear microscopy, culture and nucleic acid amplification tests (NAAT) for MTB were negative. Following the diagnosis of pelvic inflammatory disease (PID), oral antibiotic therapy with doxycycline and metronidazole were prescribed and the patient was discharged home without any symptom. Histopathological analysis showed chronic necrotizing granulomatous inflammation with multinucleated giant cells (Figure 1A); histochemical evaluation by Ziehl-Neelsen stain resulted negative.

One month after the discharge, due to the onset of exertional dyspnea, without cough, fever and malaise, the patient underwent chest X-ray and then computed tomography (CT) scan and was admitted to our Pulmonology Unit.

The CT scan showed a large left pleural effusion inducing dysventilation of the underlying lung parenchyma, associated with bilateral pleural thickenings and a minimal pericardial effusion. No lung parenchymal abnormalities were detected (Figure 2). Chest ultrasound confirmed the presence of left free pleural effusion. No homolateral mammary lymph node was detected. No previous thoracic radiological investigations were performed by the patient.

Blood tests showed increased C-reactive protein values (2.42 milligrams (mg)/dL; normal values: 0,03-0,5 mg/dL) without leukocytosis (white blood cells: 4450/uL, normal reference range: 3600-9200/uL). Human immunodeficiency virus (HIV) antibodies 1 and 2 were negative.

In the suspicion of tuberculosis, in the absence of sputum, and in the presence of a large pleural effusion that could have hidden abnormalities of the underlying lung parenchyma, a bronchoalveolar lavage (BAL) was performed; smear microscopy, XpertMTB/RIF and culture resulted negative. A medical thoracoscopy was then performed. The endoscopic pattern was characterized by markedly hyperemic visceral, parietal, diaphragmatic and pericardial pleura with diffuse and confluent whitish nodules (Figure 2). Microbiological investigations on aspirated pleural fluid (800 ml) were all negative; smear microscopy on pleural biopsies resulted positive and XpertMTB/RIF was positive for rifampicin-susceptible MTB, subsequently confirmed by liquid culture results. Drug susceptibility testing was performed and no drug resistances to the first-line anti-TB drugs were detected. Histopathological examinations showed necrotizing granulomas (Figure 1B-D). NAAT was then performed on salpinx biopsies and resulted positive. A diagnosis of disseminated tuberculosis was made.

The standardized regimen recommended by the World Health Organization (i.e., isoniazid 300 mg/day, rifampicin 600 mg/day, ethambutol 1600 mg/day, and pyrazinamide 1500 mg/day) was administered for a 2-month intensive therapy, which was followed by a 4-month continuation phase with isoniazid and rifampicin. Her clinical recovery was prompt and chest x-ray performed two months after did not detect any pulmonary abnormality and pleural effusion (Figure 3C).

Discussion

Tuberculosis (TB) is an important clinical and public health issue worldwide, causing 1.2 million TB deaths among HIV-negative people and an additional 208,000 deaths among HIV-positive people in 2020. It is estimated 10 million people were newly diagnosed with TB in 2019 [1].

As reported by World Health Organisation (WHO), Italy falls among the countries with low incidence of the disease (<20/100,000), with a clear prevalence of importation cases [6].

Disseminated TB is a rare form of the disease (1–5% of all TB cases) defined by MTB identified in blood or bone marrow samples, from liver biopsies, or from specimens collected from two or more non-contiguous organs [3,4,5]. Its pathogenesis, largely unknown, is determined by the hematogenous or lymphatic spread of MTB from the primary site of infection and affects predominantly immunocompromised patients, in most cases HIV-positive patients [3,4,5].

In the case presented here, related to an HIV-negative patient who moved to Italy two years before, we hypothesize that predisposing environmental and nutritional factors, related to the poor living conditions in which the patient lived, might have contributed to a state of immunological impairment which favored

mycobacterial haematogenous/lymphatic dissemination from the genital apparatus to the peritoneum and then the pleura [5].

Female genital tuberculosis accounts for 20-27% of cases of extra-pulmonary TB. It is a rare form of extrapulmonary TB in Europe, but a common cause of infertility in countries with a high incidence of disease. Salpinx and endometrium are the most frequently involved organs [7,8]. During the last years, intensified migration flows from Africa to Europe have raised the number of extrapulmonary TB cases, which may be characterized, in low TB incidence countries like Italy, by unusual clinical presentations [9].

Genital TB mostly spreads from the lung or other organs by haematogenous or lymphatic use but direct spread from near organ (i.e. bowel or abdominal lymph nodes) or by sexual transmission has been described [7,8]. Notably, in our case, despite endoscopic findings were suggestive of TB, salpinx biopsies were not sent for microbiological investigations. It significantly delayed the diagnosis of MTB infection and prompt treatment start, thus enhancing mycobacterial dissemination.

Pleural tuberculosis is one of the most common form of extrapulmonary TB worldwide [10]. It is typically paucibacillary being the genesis of pleural effusion mostly determined by a delayed hypersensitivity reaction rather than by the mycobacterial proliferation within the pleural cavity [10]. Indeed, the diagnostic performance of microbiological investigations on pleural fluid are suboptimal when compared to pleural biopsies [11,12].

Xpert MTB/RIF performed on pleural biopsies obtained by medical thoracoscopy provided rapid diagnosis and information on drug resistance, several days ahead of culture findings [13,14]. It allowed an immediate treatment start with a proper pharmacological regimen.

Medical thoracoscopy, a minimally invasive technique performed under local anesthesia and conscious sedation, has shown a good accuracy in the diagnosis of TB pleurisy [11,12]. It allows to select the most affected pleural areas where to obtain a large number of biopsies to be sent for histopathological and microbiological examinations. Furthermore, in advanced pleural infections it may have a key therapeutic role by mechanically disrupting pleural adhesions [15].

A recent study showed that assessment of internal mammary lymph node involvement (via CT scan and chest ultrasound) may be a key element to guide diagnostic work-up of patients with suspected tuberculous pleurisy [16]. Notably, we did not find internal mammary lymph adenopathies. However, the case described here represent a more complex case of disseminated tuberculosis.

Conclusions

In conclusion, disseminated TB is a rare and severe medical condition. Its knowledge by health-care workers in high-income country should be implemented. In cases of suspected disseminated TB, the

diagnostic work-up should be comprehensive and rapid to hamper the spread of MTB to multiple and/or vital organs that may result in life-threatening events [3,4]. Microbiological examinations of biopsies of the involved organs with drug-resistance information are key to prescribe a timely and appropriate treatment regimen.

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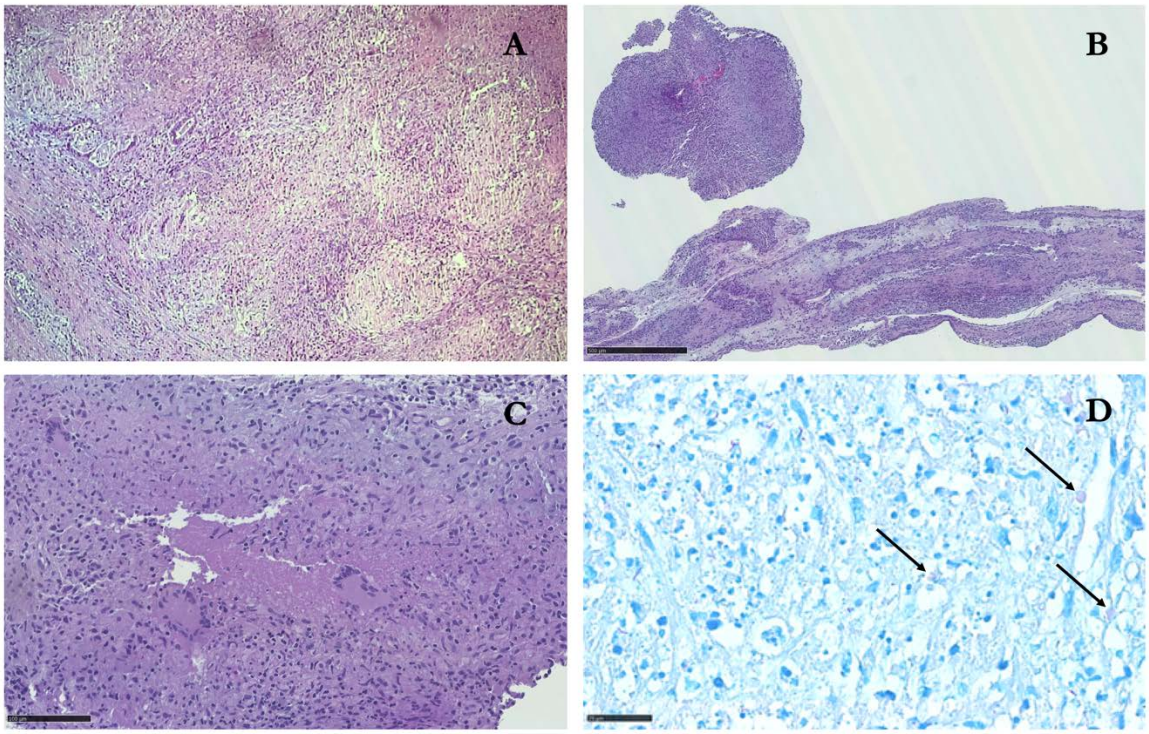

Figure 1. A: salpinx biopsy showing giant cells and granulomas (Haematoxylin & Eosin stain). B and C: pleural biopsies obtained by medical thoracoscopy showing necrotizing granulomas (Haematoxylin & Eosin stain). D: acid-fast bacilli (black arrows) detected on pleural biopsies (Ziehl-Neelsen stain).

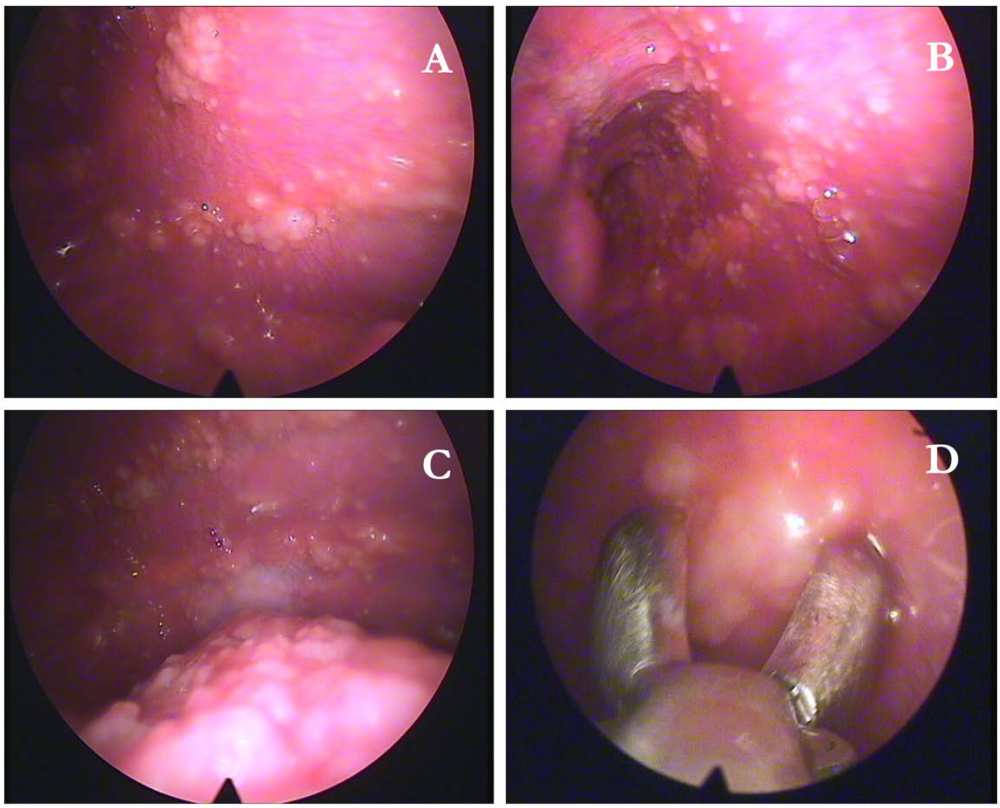

Figure 2. Medical thoracoscopy findings. White and confluent nodules on parietal pleura (A and B) with superior, posterolateral tent-shaped pleural adhesion (B). Diffuse white nodules on both visceral and parietal pleura (C). Thoracoscopic biopsy of a nodule of the parietal pleura (D).

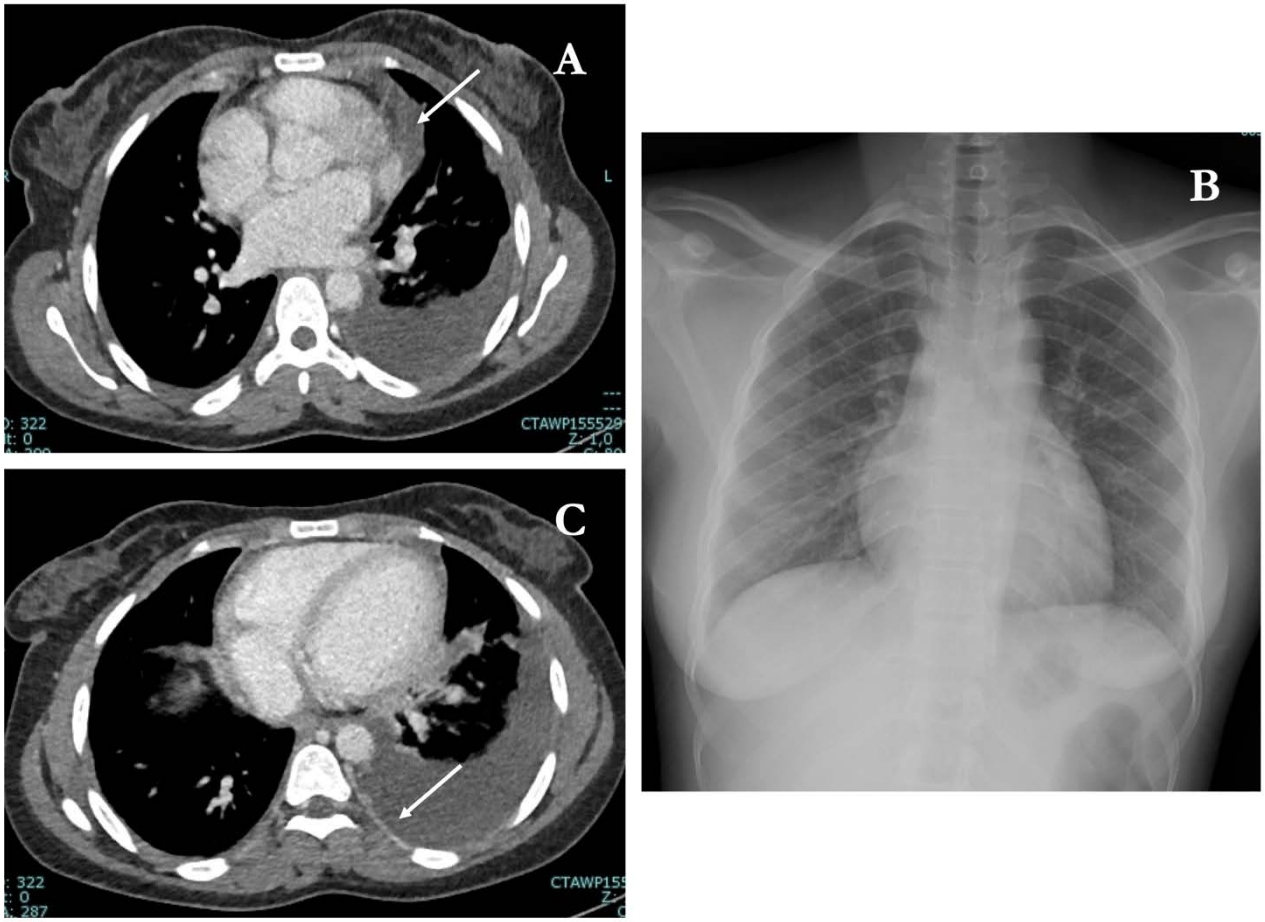

Figure 3. CT scan showing pericardial (arrow) and left pleural effusion (A), and parietal pleural thickening (arrow) in the left base (C). B: Chest X-ray performed two months after the treatment onset showing complete resolution of the pleural disease.