

TB epididymo-orchitis: A rare entity reveals the cause of a falsely diagnosed "COPD disease progression"

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ABSTRACT

A 57-year-old male, diagnosed with chronic obstructive pulmonary disease (COPD) at the age of 49, with rapid disease progression over the last six months, presented with a palpable nodule in his right testicle which progressed to abscess not responding to common antibiotics and was finally submitted to right orchiectomy. The histology of the resected tissue revealed caseating granulomas that set the diagnosis of Tuberculosis (TB) and the patient was re-evaluated for the deterioration of his COPD. *Mycobacterium tuberculosis* was isolated in his sputum and he was treated successfully with six months of anti-tuberculous treatment. TB is included in the differential diagnosis of both testicular nodules and deteriorating COPD. Had TB been suspected in the patient's initial evaluation, he would have avoided a severe deterioration of his respiratory function, a high-risk surgery and an unnecessary orchiectomy. *Pneumon 2020, 33(2):1-6.*

INTRODUCTION

Tuberculosis (TB) is considered by World Health Organization (WHO) a global epidemic estimated as one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS))¹. Apart from pulmonary disease, TB can most commonly involve pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, and meninges, with or without concomitant pulmonary disease^{2,3}. However,

Abbreviations:

ABG: arterial blood gas, COPD: chronic obstructive pulmonary disease, CRP: c-reactive protein, CT: computed tomography, DLCO: diffusion capacity for Carbon Monoxide, FEV1: forced expiratory volume in 1 second, HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome, LTOT: long-term oxygen therapy, mMRC: modified medical research council, MRI: magnetic resonance imaging, NTM: non-tuberculous mycobacteria, RV: residual volume, TB: Tuberculosis, WBC: white blood cells, WHO: world health organization

epididymo-orchitis is an uncommon localization of TB and its diagnosis prior to that of pulmonary disease is rare and can be particularly challenging. Although it is rather infrequent in the developed world, TB can also be a cause of deterioration of chronic obstructive pulmonary disease (COPD)⁴. We present the case of a middle-aged man with right granulomatous epididymo-orchitis that evolved to abscess, the cause of which was diagnosed only after its resection. The patient was subsequently re-evaluated for his deteriorating COPD and was found to have concurrent pulmonary TB and received a six-month regimen of anti-TB treatment which resulted in significant improvement of his respiratory function.

CASE PRESENTATION

A 57-year-old male presented to the out-patient urology clinic with a testicular nodule, painful at palpitation, and low fever for a week. Clinical examination also revealed redness and swelling in the region. The patient's urination was not affected, while he did not have any sexual activity during this period. From his history, he was an ex-smoker (80 packyears) who was diagnosed with COPD eight years ago with slow decline of his lung function, treated with inhaled aclidinium bromide/formoterol fumarate twice a day, without need for supplemental long-term oxygen therapy (LTOT).

Six months prior to his visit he was evaluated for his COPD, which had deteriorated rapidly, with worsening dyspnea (modified medical research council (mMRC)=4 from 2), increased sputum production and hypoxia. He also had a weight loss of 8Kg. At that time, the patient had performed spirometry which had revealed significant forced expiratory volume in 1 second (FEV1) decrease (780ml (25% of predicted) from 1564ml (50% of predicted)) since his previous visit. Static lung volumes and diffusion capacity for Carbon Monoxide (DLCO) had revealed severe gas trapping with a residual volume (RV) at 3587ml (158% of predicted) plus an impaired DLCO at 31% of predicted. His arterial blood gas (ABG) analysis had showed type I respiratory failure with a pO₂ at 53mmHg and LTOT was initiated. His chest computed tomography (CT) had revealed central bronchiectasis, panlobular emphysema and incipient fibrosis bilaterally and mass-like infiltrations in the upper left lobe and in the middle and lower right lobe (figure 1a – d). The patient had been subjected in bronchoscopy and the results of his biopsy and cytology came back negative for malignancy. Since no cause was identified, his deterioration was characterised as “disease

progression". His history was otherwise unremarkable.

At presentation, the patient's white blood cells (WBC) were slightly elevated (10.670/ μ L (68.0% neutrophils, 22.2% lymphocytes)) and his c-reactive protein (CRP) was also elevated (7.48mg/dl). His scrotum ultrasound revealed a multispaced cystic lesion of the right testicle. A scrotum magnetic resonance imaging (MRI) was ordered and showed an enlarged right testis with heterogeneity seen on coronal T1 fat sat images and low signal intensity intratesticular lesions along with severe enlargement of the right epididymis seen on axial T2 fat sat images. After contrast material administration, an enhancement of the testicular lesions and peripheral enhancement of the epididymis were observed on axial and coronal T1 fat sat images. Right hydrocele was also visible (figures 2a – d).

Based on his scrotum imaging along with the compatible clinical findings, the patient was diagnosed with epididymo-orchitis and was treated with Ciprofloxacin which later changed to Piperacillin/Tazobactam plus Daptomycin although without success. His infection worsened and progressed to abscess formation, thus he was subjected to right orchiectomy, the histology of which revealed caseating granulomatous inflammation by lymphocytes, histiocytes and multinucleated giant cells (Langhans type).

With the histological diagnosis of testicular TB, he presented at the TB out-patient clinic where standard quadruple anti-TB treatment with Isoniazid, Rifampicin, Pyrazinamide and Ethambutol was initiated. Interestingly his sputum culture grew positive for *Mycobacterium tuberculosis* sensitive to all first-line drugs. Thus the patient received 6 months of treatment (2RHEZ/4RE).

His sputum culture reversed to negative after 40 days of treatment and his sputum production decreased. At the end of treatment his dyspnea improved significantly (mMRC = 2) and he had regained 6Kg. A significant improvement in his pulmonary function was observed (FEV1=1387ml, 44% predicted from 780ml, 25% predicted, RV=2882ml, 127% predicted from 3587ml, 158% predicted) and his chest CT infiltrations dissolved, while his pO₂ increased from 53mmHg to 73mmHg at room air. LTOT was discontinued.

DISCUSSION

The differential diagnosis of scrotal masses includes a wide variety of possible causes, the most common of which at our patient's age are infection and malignancy⁵. The initial diagnosis of epididymo-orchitis was based on

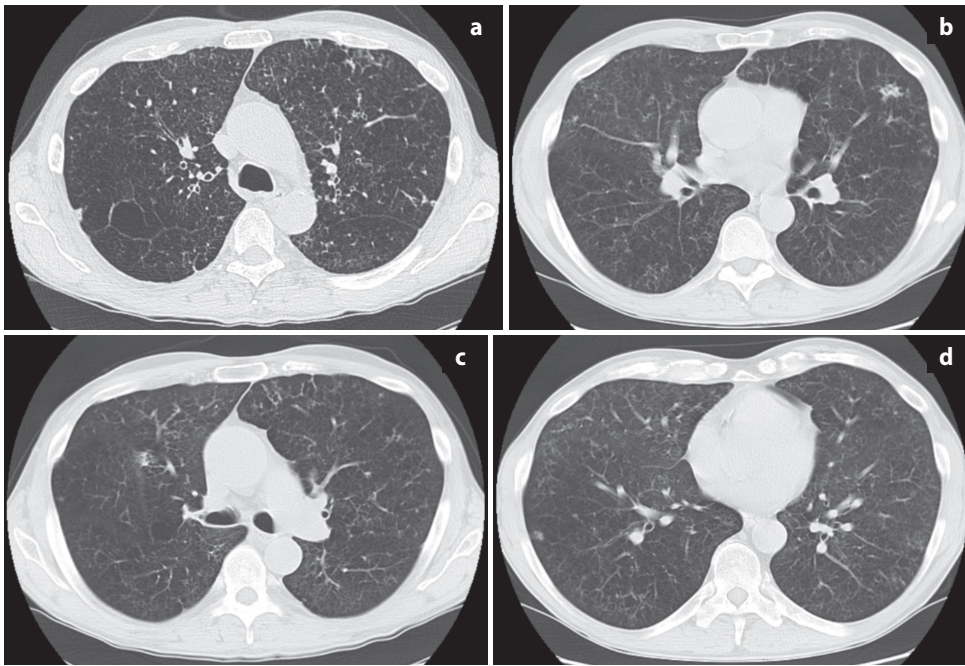


FIGURE 1. a-d. Chest CT revealing central bronchiectasis, panlobular emphysema and incipient fibrosis bilaterally (a) and mass-like infiltrations in the upper left lobe (b) and in the middle (c) and lower right lobe (d).

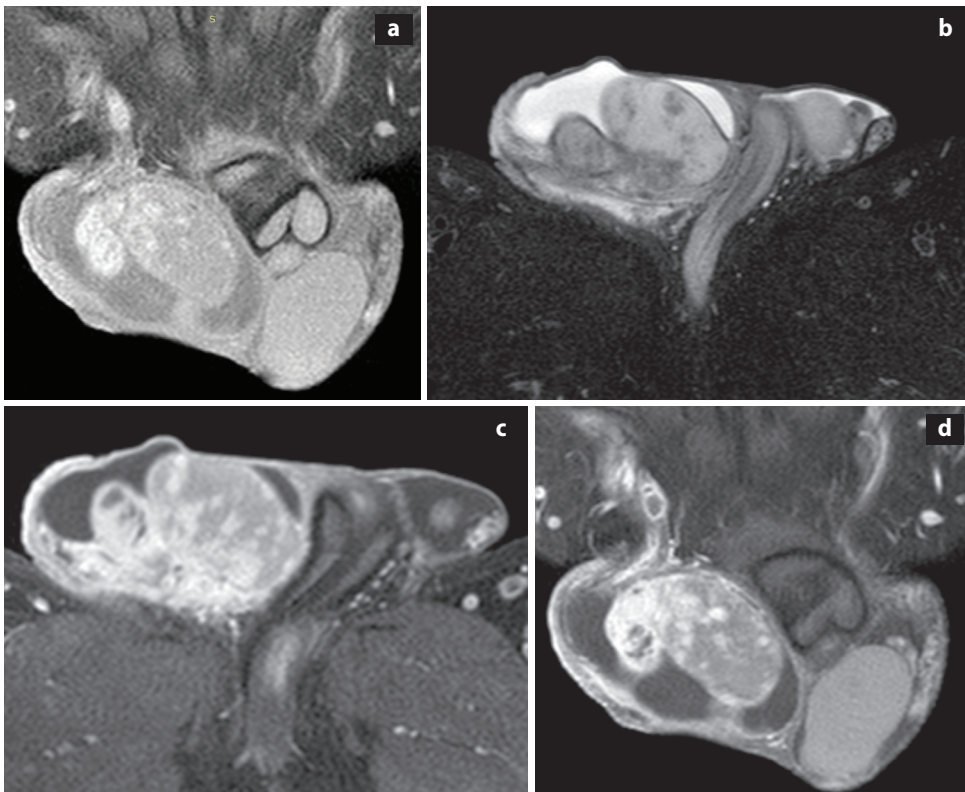


FIGURE 2. a-d. Enlarged right testis with heterogeneity seen on coronal T1 fat sat images (a) and low signal intensity intratesticular lesions along with severe enlargement of the right epididymis seen on axial T2 fat sat images (b). After contrast material administration enhancement of the testicular lesions and peripheral enhancement of the epididymis are observed on axial (c) and coronal (d) T1 fat sat images. Right hydrocele.

clinical findings and duration of symptoms. However, the patient's scrotal nodule could have been of malignant origin without causing any symptoms until its contamina-

tion. This clinical scenario could have been investigated if a biopsy was taken from the lesion for microbiological, cytological and/or histological examination, but unfor-

Unfortunately was not. This was particularly relevant after the antibiotic treatment failure in order to identify the responsible pathogen and to guide treatment.

The emergence of the patient's scrotal mass along with the worsening of his COPD could have also raised concerns about a common causative factor and TB should have been included in the differential diagnosis. However, the patient's increased sputum production was initially attributed to the presence of bronchiectasis and his weight loss was attributed to a possible malignancy. Moreover, other specific symptoms or signs of TB, such as low fever, night sweats or hemoptysis, were lacking from the patient's history at his initial respiratory evaluation. Unfortunately culture for common bacteria, TB and non-tuberculous mycobacteria (NTM) was not performed. Patients with severe emphysema are often colonized with common bacteria and suffer from exacerbations, especially when they also have bronchiectasis⁶⁻⁷. Emphysema and bronchiectasis are also predispositional factors for TB and NTM infections⁸⁻⁹. Furthermore it is very likely that worsening of COPD was initially considered independently from the epididymo-orchitis and the two different physicians (respiratory physician and urologist) followed separate diagnostics paths. Indeed, testis is a rather uncommon localization of TB¹⁰⁻¹¹. Nonetheless, half of the patients with genitourinary TB, also present pulmonary TB¹⁰. In a review of genitourinary TB, out of 3109 patients treated for TB in a medical center during an 11-year period, only 28 (0.9%) had testicular or epididymal TB, while more recently, testicular TB was calculated at about 11.5% of all genitourinary TB cases, with exact prevalence varying, depending on the area and the time period¹⁰⁻¹¹.

Testicular abscesses most commonly share the same pathogens with epididymo-orchitis¹². Thus, it is not unusual for patients with testicular TB to initiate treatment with common antibiotics before the diagnosis of TB¹³. The imaging tools for the diagnosis of testicular TB include ultrasonography and MRI¹³⁻¹⁵. However, MRI is more preferable, since ultrasonography may potentially miss testicular pathology¹⁵. The diagnosis of testicular TB is confirmed with the isolation of the *Mycobacterium tuberculosis* or the finding of caseating granulomas in the

materials obtained from the affected area¹³⁻¹⁴.

The first line of treatment in testicular TB is pharmacotherapy according to current guidelines for TB treatment¹⁶. Surgery is the second line of treatment when pharmacotherapy fails or the first choice in cases of abscesses and cutaneous fistulas or extensive involvement of the epididymis and testis¹⁴. The preferred time of surgery is 4-6 weeks after the initiation of pharmacotherapy¹⁷. It has been reported in some cases that surgery was performed due to difficulty in differential diagnosis between abscess and malignancy¹⁴. In the case described here, surgery was performed after the treatment failure with common antibiotics and the incipient necrosis so that sepsis would be avoided.

The diagnosis of TB was confirmed after the surgery based on the compatible clinical and histological findings, since the isolation of the *Mycobacterium tuberculosis* was not attempted. Nevertheless, the diagnosis of the testicular disease led to the suspicion of pulmonary TB, which was later confirmed with the isolation of the *Mycobacterium tuberculosis* from a sputum culture according to current guidelines¹⁸. Although uncommon, there are cases in the literature, in which pulmonary TB was confirmed after the diagnosis of testicular disease¹⁹. Regarding the treatment, in this case the patient received quadruple anti-TB treatment for two months (intensive phase) and Isoniazid plus Rifampicin alone for another four months (continuation phase) according to current guidelines for the treatment of microbiologically confirmed pulmonary TB and of genitourinary TB, by drug-susceptible Mycobacteria¹⁶.

In conclusion, poor differential diagnostic effort, along with the confusion caused by the two independent diagnostic approaches led to an undesirable outcome. Had TB been suspected in his initial evaluations, the patient could have avoided a high-risk surgery and an unnecessary orchiectomy.

CONFLICT OF INTEREST

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

ΠΕΡΙΛΗΨΗ

Φυματιώδης ορχεοεπιδυμίτιδα: μία σπάνια οντότητα οδηγεί στην αποκάλυψη λανθασμένης διάγνωσης «επιδείνωσης ΧΑΠ»

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Ασθενής 57 ετών με χρόνια αποφρακτική πνευμονοπάθεια (ΧΑΠ) διαγνωσθείσα από 8ετίας και ταχέως επιδεινούμενη από εξαμήνου, προσήλθε με ψηλαφητό μόρφωμα δεξιού όρχεως, που εξελίχθηκε σε απόστημα. Λόγω μη ανταπόκρισης σε κοινά αντιβιοτικά διενεργήθηκε ορχεκτομή, η οποία αποκάλυψε νεκρωτικά κοκκιώματα. Στο πλαίσιο αυτό τέθηκε η διάγνωση της φυματιώδους ορχεοεπιδυμίτιδας και επανεκτιμήθηκε η επιδείνωση της ΧΑΠ. Στα πτύελα απομονώθηκε *M. tuberculosis*, και ο ασθενής έλαβε τετραπλή εξαμηνια αντιφυματική αγωγή, στην οποία ανταποκρίθηκε επιτυχώς. Η φυματίωση συμπεριλαμβάνεται στη διαφορική διάγνωση τόσο των μορφωμάτων του όρχεως όσο και της επιδείνωσης της ΧΑΠ. Αν η υπόνοια της φυματίωσης είχε τεθεί εξαρχής, ο ασθενής πιθανώς να είχε αποφύγει την επιδείνωση της ΧΑΠ αλλά και μία άχρηστη ορχεκτομή.

Πνεύμων 2020, 33(2):1-6.

Λέξεις - Κλειδιά: Φυματίωση, Ορχεοεπιδυμίτιδα, ΧΑΠ, Πρόσδος νόσου

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