

Incapacitating pollakiuria affecting daily life. A case report of tuberculosis of the bladder. Tuberculosis remains on the list of the differential diagnoses for most diseases

Polaciúria incapacitante para a vida usual. Relato de tuberculose da bexiga. A tuberculose permanece no rol do diagnóstico diferencial da maioria das doenças

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ABSTRACT

Tuberculosis (TB) is among the most serious human health concerns and is associated with poverty, limited availability of health care services and bad management, all of which negatively affect the possibility of reducing socially-determined diseases, such as HIV/AIDS epidemics and multidrug resistant *M. tuberculosis*. Extrapulmonary involvement occurs in 15% of TB cases and can develop with the same overall symptomatology of exclusively pulmonary involvement, with smaller variations depending on location and severity. This report presents a patient with hematuria and pollakiuria with incapacitating effects on social life, initially thought of as a malignancy and later identified as genitourinary TB. Diagnosis was based on histopathology of clinical specimens from the bladder. Time elapsed between onset and diagnosis led to considerable sequelae. This report aims at raising awareness of TB as a permanent concern in Brazil and of the need to always consider it as a differential diagnosis of pulmonary or extrapulmonary disease.

Key words: Tuberculosis; *Mycobacterium tuberculosis*; Tuberculosis, Male Genital/diagnosis; Tuberculosis, Male Genital/therapy.

RESUMO

A tuberculose (TB) é dos mais graves problemas de saúde humano e associa-se a pobreza, incipiência do sistema de saúde, deficiência de gestão que dificulta a diminuição de doenças de determinismo social, epidemia do vírus da imunodeficiência humana e imunodeficiência adquirida e multirresistência do M. tuberculosis. O acometimento extrapulmonar ocorre em 15% dos casos de TB e pode evoluir com a mesma sintomatologia geral do acometimento pulmonar, com variações na dependência de sua localização e gravidade. Este relato apresenta paciente com hematúria e polaciúria incapacitante para a vida social, associada inicialmente à neoplasia, e determinada pela TB geniturinária, com diagnóstico após histopatologia de espécime clínico obtido da bexiga, em que o tempo longo para o diagnóstico foi determinante para grave seqüela. Objetiva alertar para a TB como doença permanente no Brasil e a necessidade de ser considerada sempre como diagnóstico diferencial de doenças pulmonares ou extrapulmonares.

Palavras-chave: Tuberculose; *Mycobacterium tuberculosis*; Tuberculose dos Genitais Masculinos/diagnóstico; Tuberculose dos Genitais Masculinos/terapia.

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INTRODUCTION

Tuberculosis (TB) is one of the most serious human health problems, caused by the *Mycobacterium tuberculosis* (*M. tuberculosis*). The *Mycobacterium tuberculosis* complex comprises the *M. bovis*, *M. africanum*, *M. microti* (non-pathogenic in humans), *M. tuberculosis* subsp. *Canetti* (isolated in Africa and Europe) and the *M. tuberculosis* subsp. *caprae* (mainly isolated from goats).

All species of the genus *Mycobacterium* are unable to move, alcohol and acid-resistant bacilli (AFB), strictly aerobic, and non-spore forming. The non-tuberculous mycobacteria (NTM) have low prevalence in Brazil, differ from the *Mycobacterium tuberculosis* complex, and can be pathogenic in men (mycobacteriosis). Clinical presentation is similar to TB and is associated, in general, with sequelar lesions, silicosis, and acquired immunodeficiency (AIDS).¹⁻³

The severity of TB in Brazil is associated with poverty, the health system's incipience, management deficiencies which hinder reduction of socially-determined diseases, the epidemic of the human immunodeficiency virus (HIV) and AIDS, and *M. tuberculosis* multi-drug resistance. Brazil ranks 19th among 22 countries accounting for 80% of the total cases of TB in the world, with incidence of 38/100,000 cases/inhabitants, approximately 50 million infected, 72,194 new cases and 4,500 deaths annually, and distribution of 85 and 15%, respectively, among people below and above the age of 15. For these two age groups, respectively, it progresses to pulmonary in 90 and 75% of cases. Treatment is associated with 72.2, 11.7 and 7% of discharge by cure, abandonment, and death, respectively.^{2,4,5}

The probability of the TB/HIV co-infection progressing from the infection state into the disease state, with or without immunodeficiency, occurs in around 8 to 10% per year or 10% throughout life, respectively.^{2,6,7}

The bacilli's resistance to drugs is a growing problem after the *Programa de Controle da Tuberculose* (Tuberculosis Control Program), with acquired resistance at 21.0% and primary resistance at 8.5%. These changes led to the addition of Ethambutol to the first phase of the treatment in 2009 due to increased primary resistance to Isoniazid (4.4 to 6.0%). The initial primary resistance to multi-drug resistant TB (MDR-TB) is 1.1%.^{1,8-10}

The likelihood of contracting TB depends on exposure to the source of infection, the host's resistance, the bacillus' virulence, and the amount of bacilli that reach the host. Some diseases can alter immunity, such as: diabetes mellitus, neoplasms, malnutrition, alcohol-

ism, senility, immunosuppressive therapy; others constitute predisposing conditions, such as: silicosis and gastric resection. Resistance may be lower during the first two years of life, adolescence, and postpartum.^{10,11}

Extrapulmonary involvement (cutaneous, endobronchial, peripheral lymph node, gastrointestinal, genitourinary, laryngeal, miliary, neurological, ocular, musculoskeletal, pericardial, and pleural) occurs in about 15% of cases of TB and can evolve with the same general symptoms of pulmonary involvement, with variations depending on location and severity.¹¹⁻¹⁶

TB is therefore a particularly important problem in Brazil and should always be present in the differential diagnosis of various diseases due to its ability to provoke and dissemble varied pathophysiological involvements.

This report presents the progress of a patient with hematuria and polyuria with incapacitating effects in social life, initially associated with neoplasia and determined by genitourinary TB, confirmed only after histopathology of a specimen obtained from the bladder, and whose delayed diagnosis was determinant to the serious sequelae that ensued. We aim to raise awareness of TB as a permanent disease in Brazil and of the permanent need of considering it as differential diagnosis, whether of lung or extrapulmonary diseases.¹⁴⁻¹⁶

CASE REPORT

HEB, 41 years of age, male, mixed-race, mason, single, born and residing in Itabirito (Minas Gerais), three years previous had noticed a hard nodule in the right scrotum, which was thought to have been caused by testicular growth. The nodulation progressed after a short time, showing increased volume and simultaneous macroscopic hematuria and pollakiuria. The pollakiuria rendered the patient unable to perform his social activities because of the number of times he had to urinate, which reached more than 30 times a day, in addition to breaking his nightly sleep more than 10 times, thus restraining him to the confines of the home.

Six years previously he had had prolonged contact with a neighbor who was a pulmonary TB carrier.

He did not look for medical attention immediately and was only submitted to propedeutics one year ago. The initial clinical examination suggested a nodular lesion in the right scrotum, which was hardened, mobile, and painless. After the biopsy of the lesion was done, pathological analysis revealed a fibrotic lump on the right testicle. The computed tomography (CT) of the entire ab-

domen made at that time showed gallbladder with halos compatible with kidney stone, left kidney with dilated calyces and delayed elimination of contrast. The left ureter had an important reduction of its caliber in the distal end and the prostate had poorly-defined cranial contours and no evidence of expansive lesions (Figure 1).

Six months ago a renal scintigraphy was made and revealed the left kidney to be normal and the right to be markedly hypoperfused (Figure 2); non-reactive HVII and 2 antibodies; urine culture (negative) and urine (for general characteristics, abnormal elements, sediments) with 20 red blood cells/field and positive bacterioscopy for acid-fast bacilli in one and negative in two tests. The tuberculin test (TT) carried out at that time showed 23 mm in diameter, with intensely erythe-

ma nodosum area. The cystoscopy showed a patent urethra in all its extension; mild increase of the prostatic lobes not in contact with the median lobe; lateralization of the urethral meatus and a golf hole showing diffuse desmoplastic reaction extending to the side of the bladder wall; lithiasis to the left of the interureteric bar, a distortion on the vesical trigone and whitish mucosa also to the left; usual vascularization; absence of vegetative lesions or foreign bodies. The pathological analysis of bladder fragments highlighted a diffusely ulcerated surface covered by fibrinopurulent exudate; chorion and muscular layers with various granulomas consisting of giant histiocytes and multinucleated cells; dense inflammatory linphoplasmocitary infiltrate, with frequent associated eosinophils.

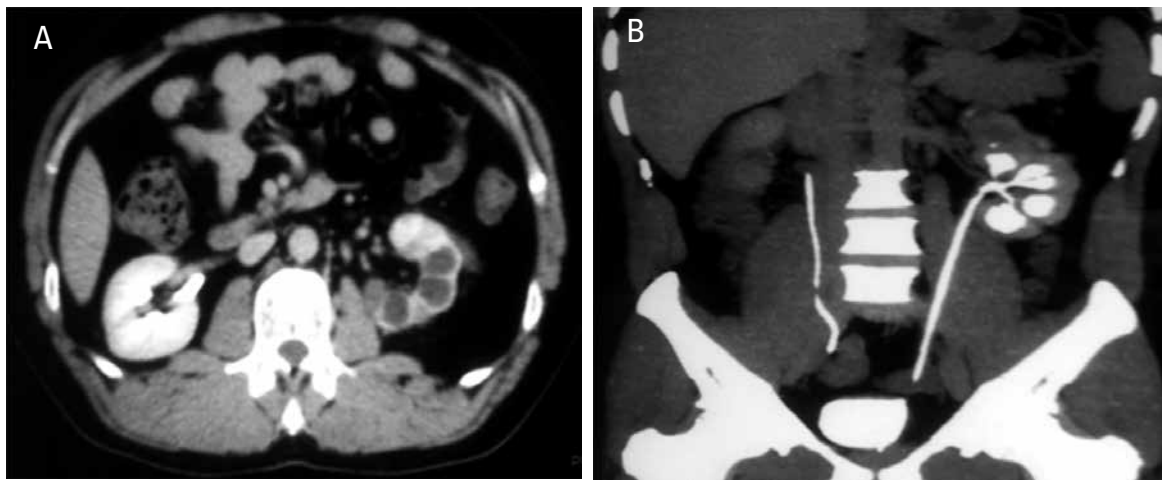


Figure 1 A and B - Computed tomography of the entire abdomen shows calyceal dilation on the left kidney and delayed contrast elimination, left ureter with major caliber reduction in distal end, prostate with ill-defined cranial contours and no evidence of expansive lesions.

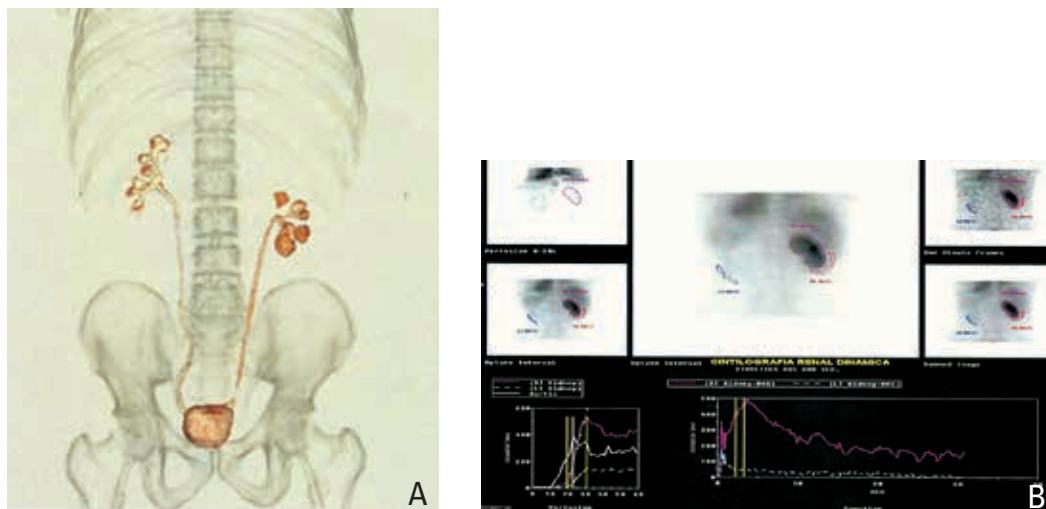


Figure 2 A and B - Renal scintigraphy shows a normal left kidney and a sharply hypoperfused right kidney

The treatment for genitourinary TB was started by administering Rifampin, Pyrazinamide, Isoniazid, and Ethambutol.

The patient presented, after three months of treatment, decreased urination from 30 to 15 times per day, less disturbance at night and remission of hematuria.

DISCUSSION

This study describes an adult male patient in close contact with pulmonary TB for more than three years, with fibrotic nodulation in the right testicle, pollakiuria (40 times in 24 hours) incapacitating him for his working and social life, hematuria, renal imaginologic changes on the left (dilated calyces with delayed elimination of contrast, ureter with gauge reduction in distal end; and severe hypoperfusion), sterile urine culture with positive AFB, 23 mm TT; and endoscopic examinations, revealing pathological fibrotic lump on right testicle, granulomatous lesion of the bladder. The chronic progression with no significant involvement of the general condition, the absence of expansive lesions around the genitourinary tract, and the tuberculin test guided the anti tuberculosis treatment with significant clinical improvement.

Humans acquire *M. tuberculosis* from particles expelled by a patient with pulmonary TB during coughing, sneezing, or speaking. These particles are very small and contain a few bacilli units that, when eliminated, are quickly dried out and held in suspension in the atmosphere, in which condition they can be inhaled. When it overcomes the host's physical and nonspecific barriers, the bacillus is destroyed by mature alveolar macrophages, depending on these macrophages' inhibitory capacity, the virulence of the bacillus and on the infection load. Activation of the host's specific defense mechanisms, at this moment, determines inflammation and nonspecific bronchopneumonia. Immature macrophages, when invaded by *M. tuberculosis*, however, do not prevent their multiplication, which becomes logarithmic. As a result, the initial tubercular lesion appears. The number of bacilli stops growing because their multiplication is inhibited by the cellular immune response, which results in the formation of a tuberculosis focus, with a solid cheese-like texture center that prevents the extracellular multiplication of the bacillus. The epithelioid cells around the necrotic center inhibit multiplication of the *M. tuberculosis* and destroy it.

TB progression depends on the relation between the numbers of mature and/or immature macrophages (which allow the multiplication of the bacillus). An increase of the bacillary population at its inoculation site originates initial pulmonary lesion(s) (inoculation chancre or Ghon focus). From this inoculum the bacilli spread by lymphatic and hematogenous routes, respectively, to drainage lymph nodes and extrathoracic organs.

The *M. tuberculosis* in the hilar and mediastinal lymph nodes cause the same pulmonary inflammatory reactions, constituting an inoculation chancre, lymphangitis, and lymphadenopathy - Ranke complex. The development of cellular immunity determines the emergence of a nodular lesion, the tuber, which is associated with the turn of the TT. At the moment of hematogenous dissemination, the development of acquired immunity prevents TB disease from setting in 95% of cases, thus ending primary infection. The liquefaction of the cheese-like material and the evasion of the bacillus are related to large-scale extracellular bacillary multiplication, their expectoration, preservation, and transmission to another host - situation in which the host's defense mechanisms are unable to control the infection.^{4,6,16}

Primary infection rarely occurs by the digestive route and exceptionally by the skin or mucous membranes, such as the ocular conjunctiva. The lesions caused by primary infection (primary complex) progress in 5% of cases, resulting in primary TB, in general within five years after the initial inoculum. The lesion may present a pneumonic aspect, extend to the pleura or dig in, thus creating the primary cave. Satellite lymphadenomegaly can compress bronchi and, by entirely or partially blocking its light, determine atelectasis or pulmonary insufflation with valvular mechanism, respectively. Perforation of the lymph nodes into the bronchial lumen causes tuberculous bronchitis, which can manifest as uncontrollable coughing. At this stage, very small granulomatous lesions can spread to the lungs and other organs, the miliary form being one of the most serious kinds of TB.^{6,14,16}

The primary infection bacilli can remain viable in the organism for many years or a lifetime, without initially causing primary TB. Immunosuppression favors the multiplication of quiescent bacilli and may originate reactivation TB in any organ, especially in the lungs, or extrapulmonarily (bones, kidneys, eyes) or where the bacillus lodged previously. In regions of low or high prevalence of TB, endogenous reactivation predominates in elderly or young adults, respectively.¹⁶

TB generally presents in chronic form, with low fever, night sweats, weight loss; initially non-productive cough and later with expectoration for more than three weeks; and, when advanced, with hemoptoics and hemoptysis, chest pain and dyspnea.^{10,14,16}

The extrapulmonary form occurs in approximately 15% of cases of TB and can present the same general symptoms observed in pulmonary involvement, besides varying according to the affected organ and its severity. TT is found in extrapulmonary form, generally in at least 10 mm. The most prevalent form among immunocompetent patients is the pleural form. Genitourinary TB manifests itself asymptotically in many patients; and when it is symptomatic, it is characterized especially by dysuria and lumbago. Bladder involvement is associated with pollakiuria and pain and, especially, by (sterile) non-bacterial pyuria. Hematuria is not common. Involvement of the male genitalia affects the prostate, seminal vesicles, epididymis, and testicle, and more often it leads to edema and scrotal fistulas. Female genital TB affects the fallopian tubes, endometrium, and ovaries and is accompanied by infertility, pelvic inflammatory disease, amenorrhea, or increased menstrual flow. The diagnosis is made through mycobacteriology and histopathological examinations. The TT is positive for most patients.

Urine smear can be positive. However, due to NTM present in the genitourinary tract, the diagnosis should be made by culture. Imaging tests such as excretory urography may reveal ureteral stenosis and loss of flexibility, calyceal clubbing with hydronephrosis, renal parenchymal calcification, decreased bladder volume and bladder distension when intensely affected; and the ultrasound shows the renal parenchyma in more detail (microcalcifications). Cystoscopy is important for biopsy of bladder lesions.

The changes described here, resulting from severe tuberculous involvement of the bladder, emphasize the need for attention to the multiple manifestations associated with *M. tuberculosis* and the need to include it in differential diagnoses, especially in places it is endemic, as is the case of Brazil. TT is found in 70 to 80% of TB patients with erythematous induration of at least 10 mm. While a positive result evidences mycobacterial infection and not necessarily disease, in some situations it can help the diagnosis of TB and allow no further delay in treatment, preventing what happened in this case, which led to the development of serious

and disabling sequelae. Delay in seeking medical attention and the difficulty in obtaining the diagnosis in this case allowed a serious lesion to develop, greatly reducing bladder volume and compromising the patient's ability to store urine, which determined its functional incapacity. TB continues to be an issue with a significant impact on life and on the functions of organs and systems, and it always needs to be considered as in the diagnostic spectrum in areas where this millennial entity remains present.

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