

CASO CLÍNICO / CLINICAL CASE

# Tuberculose urinária em adolescente com cardiopatia congénita – Relato de caso

# Urogenital tuberculosis in a teenager with congenital heart disease – Case Report

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## / Resumo

Uma adolescente, migrante, de origem africana, com cardiopatia congénita complexa residente em Portugal há dois anos, apresentou-se com episódios recorrentes de hematúria macroscópica e piúria estéril com um mês de evolução. Foi diagnosticada tuberculose urinária com envolvimento extenso do parênquima renal e urotélio, condicionando necrose papilar, dilatação calicial com preenchimento caseoso, estenose ureteral e fibrose vesical. A tuberculose urinária é uma doença insidiosa e rara na idade pediátrica. De forma a diminuir a sua potencial morbidade, a tuberculose urinária deve ser considerada e excluída em doentes com sintomas urinários recorrentes, como a hematúria ou a piúria estéril, naturais de países com alta incidência para a doença.

**Palavras-chave:** Tuberculose urinária. Piúria estéril. Migrante

## / Abstract

*An african migrant teenage girl with complex congenital heart disease, living in Portugal for two years, presents with intermittent haematuria and sterile pyuria with one month of evolution. She was diagnosed with urinary tuberculosis with extensive renal and urothelium involvement, conditioning a papillary necrosis, challyx dilation with caseum filling, urethral stricture and bladder fibrosis. Urinary tuberculosis it is an insidious disease and a rare diagnosis in children. To reduce potential associated morbidity, urinary tuberculosis should be considered and excluded in patients with recurrent urinary symptoms, like haematuria and sterile pyuria, from countries with a high incidence.*

## / Introduction

Tuberculosis (TB) is primarily a pulmonary disease, but it can affect almost every organ. Extrapulmonary (EP) TB is more frequent in women, children (0-14 years), migrants and immunosuppressed patients<sup>(1)</sup>. Urogenital TB (UGTB) is the third most common form of EPTB in adults but is comparatively uncommon in children, owing to the long latency period (1-50 years).<sup>(2)</sup>

We report a case of UGTB in a migrant teenager. This case alerts for the UGTB non-specific symptoms and chronic and cryptic protean clinical manifestations, that can easily be overlooked, owing to a lack of clinician awareness.

## / Case report

Orphan teenage girl migrant from African country under an inter-governmental medical cooperation protocol for cardiomegaly investigation. She was diagnosed with moderate heart failure secondary to complex structural heart disease - superior-inferior abnormal atria and ventricular arrangement, discordant auriculo-ventricular connection, major interventricular communication, pulmonary obstruction - pulmonary hypertension and ventricular and supraventricular extrasystoles. The cardiopathy was deemed not surgically correctable. She started atenolol and kept follow-up appointments every three months. She remained stable, with intolerance to intense efforts.

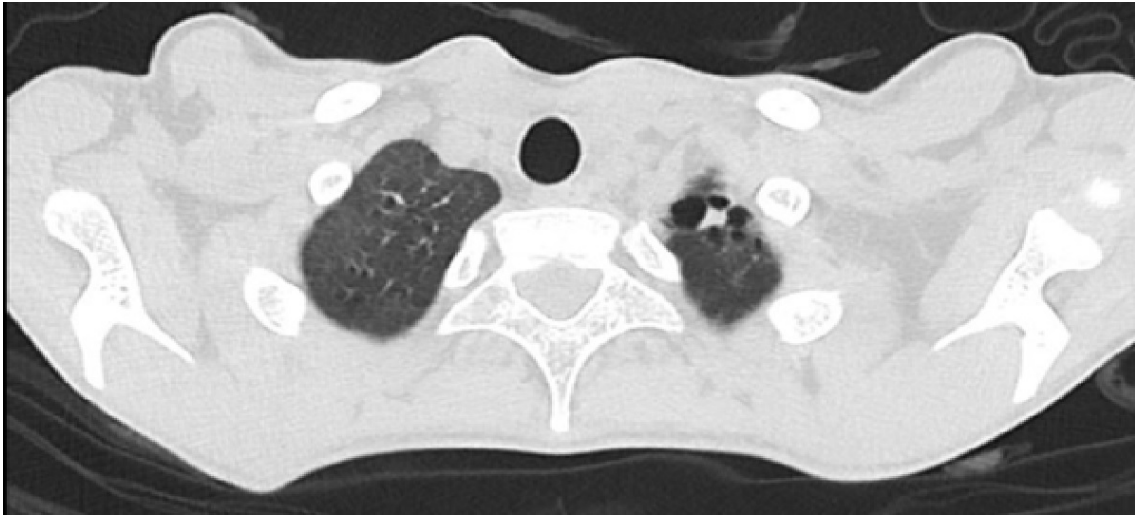
About two years after arrival, during a regular cardiology appointment, she complained of progressive asthenia, back pain, mild dyspnoea that worsened at school; and one-year evolution amenorrhoea. At the physical exam, she weighed 31,2 kg (BMI 12,49 kg/m<sup>2</sup>) - a weight loss of 1 kg in 4 months. The remaining exam was identical to priors, including peripheral oxygen saturation 86-90%, hyperdynamic precordium, holosystolic murmur intensity IV/VI and a palpable liver. She was admitted to the cardiology ward for investigation. Electrocardiogram,

transthoracic cardiac ultrasound and Holter monitoring excluded cardiac decompensation.

On the third day of admission to the cardiology department, an episode of gross haematuria was observed. Blood tests shown haemoglobin 12,8 g/dL, leucocytes 5050/μL and platelets 333000/μL with CRP 35.4 mg/L (URL 5.0 mg/L) and sedimentation rate 48 mm/h (URL 16 mm/H), creatinine 0.59 mg/dL, normal urea and ionogram. Urinalysis shown leukocyturia 2074 cells/μL (URL 25/μL) and haematuria 368 cells/μL (URL 22/μL), proteinuria 82.8 mg/dL, creatinuria 58.0 mg/dL. Seric uric acid, proteins, adenosine deaminase and liver transaminases were normal. HIV infection and schistosome disease were excluded. Three weeks prior, she had been observed at the emergency department for haematuria, dysuria and pollakiuria, without fever or other urinary symptoms. At the time, urinalysis shown proteinuria 100 mg/dL, leukocyturia 5130/μL and haematuria 184/μL without nitrates. A cystitis was assumed, and oral amoxicillin/clavulanic acid treatment started. Haematuria resolved after four days. The urine culture was negative after five days of incubation.

Considering the epidemiologic context *Ziel-Nielson's*-stained urine smear was requested and showed acid-fast bacilli (AFB), identified as *Mycobacterium tuberculosis* complex by TAAN. IGRA and cutaneous sensibility tests were positive. Later, the *Mycobacterium tuberculosis* strain was shown to be sensitive to all first line antibiatics.

Renal and bladder ultrasound described right kidney (RK) parenchyma with decreased thickness and poor differentiation, stenotic calyces with heterogeneous solid content filling and diffusely thickened bladder wall with a voiding volume of 312 mL. Abdominopelvic CT (Figure 2) showed asymmetric kidney dimension - RK 11,5 cm, left kidney (LK) 10,0cm with RK subacute/chronic nephropathy, stenotic calyx, papillary necrosis, and medial calyx dense filling and micronodular thickening of the urothelium and bladder. MAG3 renogram demonstrated asymmetric relative renal function (LK/RK: 63%/37% - normal range 50+/-5%), multiple cortical scars and pyelocaliceal dilatation.



**Figure 1** – Chest CT showing left lung vertex micronodular and fibrobulous lesions.



**Figure 2** – Abdominal CT showing semi-solid content of the middle caliceal groups of the right kidney.

Gynaecologic observation revealed previous mutilation. Ultrasound and pelvic CT were not suggestive of tuberculous gynaecologic involvement.

Baciliferous pulmonary TB was also diagnosed, with AFB detection in sputum. Thoracic - CT showed fibrobulous lesions of the left lung vertex (Figure 1).

She was started on isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) and pyridoxine supplementation with a progressive resolution of haematuria and urine and sputum smears becoming AFB negative after 14 days of therapy. Non-surgical management was decided, attending to cardiac comorbidity, and the preserved LK function. During the hospital stay, she remained

apyretic, normotensive, with persistent non-nephrotic proteinuria. Renal ultrasound showed a dwindling of the calyx filling.

The cohabitant aunt also had pulmonary TB.

During the following year, she gained 10 kg and recovered regular menses. Creatinine raised to 0.66 mg/dL. No secondary effects were documented. She completed 11 months of antibiatic treatment (2 months HRZE followed by 9 months HR). At treatment terminus, urinalysis showed no proteinuria, haematuria or leukocyturia; on ultrasound was described residual RK calyx dilation and normal urothelium and bladder wall. She transited to adult follow-up when aged 18, without further infectious, nephrological or cardiac complications.

## / Discussion

UGTB clinical presentation ranges from asymptomatic, through common urinary tract symptoms, obstructive uropathy or renal failure. Constitutional symptoms are commonly absent.<sup>(2)</sup> Urinalysis usually shows pyuria and microscopic or macroscopic haematuria with sterile cultures.<sup>(2)</sup>

The UGTB investigation should be considered in patients with urinary tract symptoms, and consistent urinalysis, refractory to antibiotic treatment, especially in those from high TB incidence environments or with epidemiological link<sup>(2,3)</sup>. Diagnosis is established by demonstration of AFB in the urine or tissue biopsy, mycobacteriology culture and molecular methods. Imaging and indirect methods supportive evidence of TB is also useful, once direct pathogen identification is infrequent.<sup>(2,3)</sup>

UGTB is an insidious disease, with symptoms only in advanced stages which leads to diagnostic delay and increases the risk of organ destruction at diagnoses time<sup>(2)</sup>. It has been associated with non-functioning unilateral kidney in 26.9% of cases and renal failure in 7.4%. Patients from developing countries are more likely to have a delayed diagnosis, renal failure, unilateral non-functioning kidney, contracted bladder and the need for ablative surgery.<sup>(4)</sup>

UGTB has many forms, with different clinical features, treatments and prognoses.<sup>(2)</sup> In uncomplicated drug-sensitive UGTB six to nine months of standard treatment regimens are recommended but might be prolonged to 12 months if there is extensive renal parenchyma involvement.<sup>(2,3,5)</sup>

Nephrectomy is necessary for a significant number of late-diagnosed and complicated cases<sup>(4,6)</sup>. It is indicated for extensive kidney involvement, severe upper UTI or kidney lithiasis, hypertension or renal cell carcinoma.<sup>(7)</sup>

We reported a case of an African teenage girl with a complex structural cardiac disease, migrator from a sub-Saharan Africa to a European country for medical assistance, that is diagnosed with urinary TB. The presenting clinical features included haematuria,

micturition and lumbar pain. The caseous lesions mainly affected the RK, ureter and bladder. On the MAG3 renogram, she had RK hypofunction, multiple cortical scars and pyelocaliceal dilatation. Initially, she had non-nephrotic proteinuria, which normalized after 11 months of anti-TBs. Even though creatine levels remained in the normal range, the glomerular filtration rate (GFR) was initially increased (160mL/min/1.73 m<sup>2</sup>), reflecting the extensive RK lesion and the consequent hyperfiltration of the remaining renal mass. GFR normalized to 97mL/min/1.73 m<sup>2</sup>, after five months of therapy. An improvement of the nutrition status was also obvious during treatment, with a significant weight gain and remitting secondary amenorrhea.

In our case, major cardiac comorbidities hindered surgical intervention, however conservative treatment with anti-TB had a positive response, supporting the idea that we still do not have sufficient information and objective parameters to predict the progression of UGTB and judicious patient selection must precede invasive procedures.<sup>(6)</sup>

Adolescence associates with increased susceptibility to TB.<sup>(6)</sup> EPTB and particularly UGTB in adolescents is probably an underestimated problem.<sup>(9)</sup> Attending to its concerning complications, progression to organ failure in late stages and the difficulties of early diagnosis, case reporting is crucial to raise attention to this problem.

Ködmön et al. in Eurosurveillance 2016 report, had already pointed-out migration as a major contributor to TB burden in Europe (especially to EPTB in young women) and suggested targeted prevention and control efforts and implementation of active case finding approaches to diagnose cases early, provide adequate treatment and support and reduce the burden of TB among migrants.<sup>(10)</sup>

Malnutrition in children is a global public health problem with wide implications. Latent TB with a coexistent low BMI is characterized by diminished protective cytokine responses and heightened regulatory cytokine responses, providing a potential biological mechanism for the increased risk of developing active TB<sup>(11)</sup>, and possibly favouring the risk of bacillaemia and EPTB<sup>(4)</sup>. Social and medical antecedents made our patient particularly prone to malnutrition, TB infection and progression. The complexity of basal cardiomyopathy might also have worked as an important distraction factor further delaying the diagnosis.

## / Conclusion

We would like to outline the importance of considering urinary TB patients with risk factors for TB with persistent urine tract symptoms, haematuria, and pyuria that do not respond to conventional antibiotic therapy for suspected UTI or that is associated with sterile conventional urine microbiological cultures. Our centre treasured this case as an important learning opportunity, not only as an example of a frequently missed

diagnosis but also as an indicator of the fragility of the TB surveillance protocols in tertiary hospitals where centralising medical care is a challenge.

We hope it can also alert others who assist migrant children to the delicateness of this issue.

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