Navigating the diagnostic maze of renal tuberculosis in advanced chronic kidney disease: A case report

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Abstract. Renal tuberculosis (TB) is a rare extrapulmonary manifestation of *Mycobacterium tuberculosis*, often leading to irreversible renal damage due to delays in diagnosis. The present study reports the case of a 72-year-old male patient with pre-existing type II diabetes mellitus, hypertension, and stage G3bA0 chronic kidney disease (CKD), who manifested with a sub-acute deterioration of renal function necessitating renal replacement therapy. The initial workup for uropathies, including repeated urine cultures, was negative despite the clinical suspicion, presenting the hallmark sign of sterile pyuria. The QuantiFERON-TB Gold test revealed a highly positive value, confirmed in two measurements, followed by contrast-enhancing computed tomography, which revealed a subtle hypodense area consistent with early granulomatous inflammation, supporting the diagnosis of renal TB as the sole site of infection. The case described herein underscores the critical need to prioritize renal TB in the differential diagnosis for high-risk patients with CKD with unexplained subacute renal function decline and sterile pyuria. The present case report highlights the robust diagnostic utility of the QuantiFERON test over conventional methods such as the tuberculin skin test in immunocompromised settings (e.g. advanced CKD), advocating for its earlier and routine deployment to prevent irreversible renal failure.

Introduction

Renal tuberculosis (TB) is a rare, yet critical extrapulmonary manifestation of *Mycobacterium tuberculosis* infection, often resulting from hematogenous dissemination from a primary, sometimes subclinical, pulmonary focus (1). Due to its progression through granulomatous inflammation and fibrosis, diagnosis is often delayed and is often made after the irreversible renal parenchymal destruction is manifested (2).

A characteristic diagnostic challenge in renal TB is the presentation of sterile pyuria with a subacute decrease in kidney function, mostly where invasive tests are not available.

Case report

The present study describes the case of a 72-year-old male patient affected by type II diabetes mellitus, arterial hypertension and a positive history for NSTEMI in 2006 and for the aneurysmal dilation of the left anterior descending artery in 2018. The first indication of CKD was found in 2021, staged G3bA0. A worsening of CKD was found in May, 2024, when an estimated glomerular filtration rate (eGFR) of 20 ml/min/1.73 m^2 was detected. This impairment of renal function had been related to new therapy with the SGLT2 inhibitor (dapaglifozin at 10 mg/die), which commenced in February, 2024. Subsequently, he developed prostatitis and a further deterioration of renal function with an eGFR of 16 ml/min/1.73 m^2.

He was admitted to the ward of Nephrology and Dialysis of the Hospital Umberto I (Enna, Itlay) in December, 2024 following 7 days of diarrhea and vomiting, followed by hypovolemia and oliguria. Laboratory tests revealed non-anion gap metabolic acidosis with a Delta/Delta ratio <1, a creatinine level of 9.4 mg/dl and a blood urea nitrogen level of 254 mg/dl. Urine analysis and a chest X-ray yielded negative results. Volume status was corrected, and high-dose sodium bicarbonate (1.4% 1,000 cc) and furosemide (from 100 mg to 250 mg/die) were administered, without an improvement in renal function until renal replacement therapy was required.

An ultrasound evaluation suggested chronic pyelonephritis, which added to the history of prostatitis and a decrease in eGFR advised for bacterial uropathies. The QuantiFERON-TB Gold test was performed when repeated negative microbiological urine tests were negative, which revealed a positive values >64 IU/ml. Moreover, an extensive diagnostic workup, including serological tests for autoimmune diseases, granulomatosis diseases, vasculitis, amyloidosis and sarcoidosis, was

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performed, and all were negative, further limiting the differential diagnosis to renal TB. A confirmatory QuantiFERON test was performed 1 month thereafter, which was also positive, but revealed lower values compared to the initial result. With the suspicion of renal TB, a computed tomography scan of the abdomen with contrast was performed, documenting the presence of a 'small hypodense area plausibly related to an initial stage of granulomatous inflammation' (Fig. 1). The presence of granulomas may explain the negative Ziehl-Neelsen staining, which is often negative in the chronic phase of the disease (3-5). Ziehl-Neelsen microscopic Urine Bk Detection was performed as follows: Centrifugation of 10-15 ml of fresh urine for 15 min at 3,000 x g/min at room temperature. The supernatant was discarded and the sediment was used for the smear (3 micron) and placed in a uniform layer onto a slide. This was then air-dried and heat-fixed (2-3 quick passes over a flame), The slide was coated with 0.4% fuchsin (Liofilchem) and left for ~10 min, followed by rinsing with water, This was followed by destaining with acid-alcohol for 2-3 min, and rinsing with water. The slide was then coated with blue 0.3% methylene (Liofilchem) for 1 min and rinsed with water and air-dried. The section was observed under a microscope with a 100X objective and oil immersion. All staining was performed at room temperature. Note that as no bacteria were detected, no images were saved.

The patient is currently receiving anti-TB therapy and received mono-weekly hemodialysis treatment for 9 months. Treatment commenced without a histopathological confirmation due to the refusal of the patient to undergo an invasive procedure, but with the necessity to admission to the transplantation program. The progression of renal failure was definitively halted, with a mild improvement of the eGFR from 5 ml/min/1.73 mq to 9 ml/min/1.73 m^2, terminating dialysis and starting with a conservative and low-protein-added to ketoanalogues management of the disease for 3 weeks, with a weekly monitor of the laboratory findings.

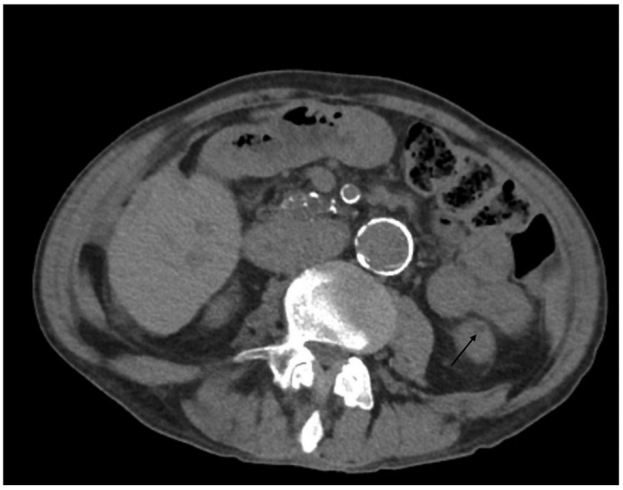

Figure 1. Contrast-enhanced computed topography scan: Small hypodense area plausibly related to an initial stage of granulomatous inflammation in the upper left pole.

Discussion

The present study describes a rare case of renal TB, where the renal localization of the micobacterium was the only site of disease, without pulmonary or other organ diseases. Renal TB is notorious for presenting with sterile pyuria, a hallmark that, if overlooked, invariably leads to delays in diagnosis (2). This delay is particularly detrimental in renal TB, which progresses insidiously through granulomatous inflammation and fibrosis, often culminating in irreversible renal parenchymal destruction requiring dialysis treatment.

The QuantiFERON test detects T-cell-mediated immune response to *Mycobacterium tuberculosis*-specific antigens, providing a substantial advantage over the traditional tuberculin skin test (TST) in immunocompromised hosts, which includes patients with advanced CKD and those undergoing hemodialysis (6). Indeed, research consistently indicates that the uremic environment impairs cellular immunity, leading to a higher proportion of false negatives at the TST in a significant proportion of recipients of renal replacement therapy (7). Conversely, the QuantiFERON test generally maintains a higher specificity and sensitivity even in patients with severe immunosuppression.

In keeping with this characteristic, it can be pivotal and is accessible in any center for the diagnosis of tuberculosis pathologies. Herein, the serial monitoring aspect, with a positive, but lower confirmatory value 1 month later, is a noteworthy feature. While some studies have investigated the utility of serial QuantiFERON to monitor the treatment response in active TB, the fluctuation observed herein may reflect the dynamic interplay of the active disease burden (8-10).

Limiting the diagnostic workup to the more conventional microbiological and imaging investigations, typically used to investigate the presence of infectious diseases, while precluding the use of the QuantiFERON test and the serial monitoring of this value (9), can lead to an incomplete clinical image, consequently delaying the diagnosis and worsening the outcome of the patient. Radiological findings range from early non-specific changes to classical manifestations, such as papillary necrosis and calyceal destruction, ureteral strictures, or a non-functioning, calcified 'autonephrectomized' kidney. The absence of cavitary lesions suggests that the renal involvement, while causing severe functional decline, was relatively at an early chronic phase, where the granulomatous interstitial nephritis can precede the visible, destructive radiological sequelae (11).

In the present case report, even though the initiation of appropriate anti-TB therapy, as granulomas represent chronic disease, was not sufficient to markedly improve the residual kidney function, it is necessary for a prospective transplantation hypothesis (12).

Although the lack of the gold standard histopathological or microbiological confirmation represents an important limit, the slight response after 3 months of therapy can present a compelling *ex juvantibus* argument in support of the diagnosis.

In conclusion, the critical take-home message supported by the present case report is a reminder that renal RB needs to be a prioritized differential diagnosis in any patient with subacute kidney function decline, particularly when conventional infectious workups, including urine cultures, are negative. Although rare, TB presenting solely with renal manifestation must be considered in patients with a

subacute decline in renal function when a comprehensive differential diagnosis has been ruled out and the gold standard confirmation is unfeasible. The limitations of relying solely on conventional diagnostic tools in immunocompromised cohorts can lead to a critical diagnostic inertia. The successful diagnosis hinged upon the decisive utilization of the QuantiFERON test, demonstrating its robust capability to detect active TB observed in the setting of advanced renal failure. This suggests a clinical update to advocate for the earlier and routine deployment of QuantiFERON in high-risk patients with CKD presenting with unexplained renal function deterioration. Future research is required to focus on refining the interpretation of QuantiFERON values as a potentially prognostic tool in patients and establishing clinical protocols for managing highly probable renal TB in the absence of a confirmatory biopsy.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MRS and VC Conceptualized the study. VC and GR were involved in reporting the methodology described in the text. VC, MRS and SG were involved in the writing and preparation of the original draft of the manuscript. AR, VF and EB were involved in obtaining the medical history and laboratory data of the patient, including the results of the Ziehl-Neelsen test. SG and EB were involved in the writing, reviewing and editing of the manuscript. All authors have read and agreed to the published version of the manuscript. MRS and VC confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Written informed consent was obtained from the patient described in the present study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Declaration of Helsinki 1964 and its later amendments or comparable ethical standards.

Patient consent for publication

Written informed consent was obtained from the patient described in the present study for the publication of the present case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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