

RENAL TUBERCULOSIS – A CHALLENGE IN DIAGNOSTIC AND TREATMENT

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ABSTRACT:

TUBERCULOSIS IS CAUSED BY A BACTERIA CALLED MYCOBACTERIUM TUBERCULOSIS. THESE DISEASE STILL REMAINS A SERIOUS HEALTH ISSUE IN UNDEVELOPED COUNTRIES. IT USUALLY AFFECTS THE RESPIRATORY TRACT, BUT ALSO HAS EXTRAPULMONARY LOCATIONS. FROM THE EXTRAPULMONARY CASES, RENAL TUBERCULOSIS IS FOUND IN 27% OF THE CASES. EXTRAPULMONARY TUBERCULOSIS IS USUALLY DISCOVERED IN PATIENTS WITH DEPRESSED IMMUNE SYSTEM LIKE PATIENTS WITH HIV AND AFTER DIFFERENT ORGAN TRANSPLANTATION. THE INVOLVEMENT OF THE KIDNEY IN TUBERCULOSIS CAN BE PART OF A DISSEMINATED INFECTION OR A LOCALIZED GENITOURINARY DISEASE, AND IT REPRESENTS A CHALLENGE IN DIAGNOSTIC. THE PATIENTS WITH RENAL TUBERCULOSIS PRESENTS STERILE PYURIA. AS TREATMENT, THE FIRST LINE IS REPRESENTED BY ISONIAZIDE, RIFAMPICIN, PIRAZINAMIDE, ETHAMBUTOL, AND STREPTOMYCIN, BUT NOT IN FEW CASES SURGICAL INTERVENTION IS REQUIRED BECAUSE IF LEFT UNTREATED CAN LEAD TO RENAL DESTRUCTION, OR A SMALL AND UNEXTENDABLE BLADDER.

KEY WORDS: TUBERCULOSIS, TREATMENT, SURGERY, KIDNEY

INTRODUCTION

Urinary tract tuberculosis is mainly asymptomatic, which can easily be misdiagnosed and therefore appears a risk of renal function loss or general complications¹¹. Symptoms in renal tuberculosis (TB) usually include flank pain, haematuria, and other factors must be included: hydronephrosis of unknown causes discovered on ultrasound exam, small bladder capacity, nonvisualized kidney on intravenous urography, or impaired renal function on radionuclide renogram¹².

¹¹Zhukova II, Kulchavenia EV, Kholobin DP, Brizhatiuk EV, Khomiakov VT, et al. *Urogenital tuberculosis today*. Urologia 2013; 1: 13–6; Diaconu CC, Stănescu AMA, Pantea Stoian A, Tincu RC, Cobilinschi C, Dragomirescu RIF, Socea B, Spînu DA, Marcu D, Socea LI, Bratu OG. *Hyperkalemia and cardiovascular diseases: new molecules for the treatment*. Rev Chim (Bucharest) 2018, 69(6):1367-1370; Manea M, Marcu D, Pantea Stoian A, Gaman MA, Gaman AM, Socea B, Neagu TP, Stănescu AM, Bratu O, Diaconu C. *Heart failure with preserved ejection fraction and atrial fibrillation. A review*, Revista de chimie, 2018, 69(11): 4180-4184; Diaconu CC, Manea M., Iancu MA, Stănescu AMA, Socea B, Spînu DA, Marcu D, Bratu OG. *Hiponatremia in patients with heart failure: a prognostic marker*. Revista de Chimie. 2018. 69; 5:1071-1074; Diaconu CC, Dragoi CM, Bratu OG, Neagu TP, Pantea Stoian A, Cobelinschi PC, Nicolae AC, Iancu MA, Hainarosie R, Stănescu AMA, Socea B. *New approaches and perspectives for the pharmacological treatment of arterial hypertension*. Farmacia 2018, 66(3):408-415

¹²Niculăe A, Peride I, Vinereanu V, Rădulescu D, Bratu O, Geavlete B, Checheriță IA. *Nephrotic syndrome secondary to amyloidosis in a patient with monoclonal gammopathy with renal significance (MGRS)*. Rom J Morphol Embriol 2017;58(3): 1065-1068; Mititelu R, Bratu O. *Radionuclide Imaging. An Update on the Use of Dynamic Renal Scintigraphy*. Modern Medicine, 2017, 24(4), p. 199-203; Constantinoiu S, Bărlă R, Iosif C, Cociu L, Gîndea C, Hoară P, Bratu O, Rușitoru L. *Difficulties in diagnosis and surgical treatment of a giant retroperitoneal lipoma*. Chirurgia 2009;104(3): 363-367; Diaconescu D, Stoian Pantea A, Socea L, Stănescu AM, Iancu M, Socea B, Pituru S, Bratu O, Diaconu C. *Hepatorenal Syndrome: A Review*. Archives of the Balkan Medical Union, 2018, 53(2), pag. 239-245

MAIN TEXT

Extrapulmonary TB tends to appear in patients infected with HIV. They have 20–37 times greater risk of developing renal TB than normal people¹³, and it is the most frequent opportunistic infection in patients with HIV. TB can appear on any of the phases of the HIV infection. Renal biopsy in these type of patients shows a severe interstitial inflammation and mild-to-moderate mesangial proliferation. Studies show that TB contributes to proteinuria in HIV-infected patients and after treatment for TB the renal function returns to normal and the proteinuria decreases to normal¹⁴.

Patients with history of tuberculosis and that had undergone kidney transplantations and have received immunosuppressive drugs tend to develop renal TB. A study performed by Matuck et al showed that 4,5% of patients with renal transplant tend to develop renal TB¹⁵.

Other cases of urogenital TB have been reported in patients with bladder tumors that have been endoscopically resected, and after the resection they have received instillations with BCG¹⁶.

A renal lesion caused by the infection with *Mycobacterium tuberculosis* can disseminate through the renal capsule and mimic a neoplastic lesion. When the ureter is involved in the dissemination process stenosis and dilatation occur, leading to obstruction and reflux¹⁷.

FIZIOPATHOLOGY IN RENAL TUBERCULOSIS

Renal tuberculosis is usually a part of a disseminated infection from the respiratory tract or a localized genitourinary disease. Pulmonary infection is the most important. The renal system is mostly affected by miliary TB. The miliary lesions are usually found in renal tissue because of the hematogenous dissemination. It is specially located in the cortical region. Some patients can present renal failure without evidence of typical localized lesions in the renal parenchyma¹⁸.

The hematogenous dissemination is caused by a vessel erosion, the most commonly a vein in the lung. From here the emboli containing the microorganisms get into systemic circulation. From here the bacillus arrives in organs where it has conditions to proliferate, like the kidney, epididymis, encephalus, bone marrow, and the testis tubes. In the kidneys, the preferred place for colonization by *M. tuberculosis* is the medullary region, where granulomatous lesions can occur, with caseous necrosis, which leads to local tissue destruction. When the disease progresses, it appears a bigger area of papillary necrosis that can cause the apparition of cavities that destroy the renal parenchyma. After the caseum cavity appears the next step in the evolution of the disease if it is still left untreated is the migration into the collecting system of the bacillus. Papillary necrosis usually appears when vascular insufficiency appears in the renal papillae. When the infection reaches the pelvis it causes a tuberculous pyelonephritis, after that it can evolve to pyonephrosis,

¹³World Health Organization. *Tuberculosis and HIV*. Available at: <http://www.who.int/hiv/topics/tb/en/>. Accessed September 10, 2012

¹⁴Nourse PJ, Cotton MF, Bates WD. *Renal manifestations in children co-infected with HIV and disseminated tuberculosis*. *Pediatr Nephrol*, 2010, 25: 1759–1763

¹⁵Matuck TA, Brasil P, Alvarenga MF, Morgado L, Rels MD, da Costa AC, Araujo M, Rodrigues ME, de Carvalho Dde B. *Tuberculosis in renal transplants in Rio de Janeiro*. *Transplant Proc*, 2004, 36: 905–906

¹⁶Eastwood JB, Dilly SA, Grange JM. *Tuberculosis, leprosy and other mycobacterial diseases*. Cattell WR, ed. *Infections of the Kidney and Urinary Tract*. Oxford, UK: Oxford University Press, 1996, 291–318

¹⁷Eastwood JB, Corbishley CM, Grange JM. *Tuberculosis and the kidney*. *J Am Soc Nephrol*, 2001, 12: 1307–1314

¹⁸Eastwood JB, Corbishley CM, Grange JM. *Tuberculosis and the kidney*. *J Am Soc Nephrol*, 2001, 12: 1307–1314

which in the end causes renal insufficiency where the only treatment is represented by nephrectomy¹⁹.

Min-Bo Yan et al performed a study on a lot of 53 males and 30 females with a mean age of 36 that had been diagnosed by symptoms, a urinary tuberculosis test, cystoscopy and computed tomographic urography with pulmonary tuberculosis. 72 of these patients also had renal tuberculosis. In all cases renal tuberculosis was presented on one side only, with normal renal function on contralateral side. Because the affected side showed severely impaired renal function, nephrectomy was necessary. Prior to surgery all patients underwent antituberculosis chemotherapy, for one and a half to six months. All the operations were performed successfully using laparoscopic retroperitoneal technique. After the surgery 75 patients were followed-up, the symptoms of urinary frequency and urgency disappeared, and no active tuberculosis lesions were observed at the ESR level. Also no tuberculosis bacilli were detected postoperational in urine sample²⁰.

Another study was performed by Vinayak Gorakhanath Wagaskar et al on a lot of 31 patients with renal tuberculosis with the purpose to analyse challenges in reconstruction of the urinary tract in patients with urinary tuberculosis and renal failure. The majority of the patients were male 18 of 31. The symptoms included flank pain, dysuria and frequency, fever, renal failure, haematuria, even scrotal pain. A total of 11 patients presented simultaneous kidney, ureter and bladder involvement or bilateral disease. From the imaging point of view on a plain X-ray film of abdomen or on CT image it can appear: distortion, scarring, hydronephrosis or hydroureteronephrosis, calcifications, fistula when contrast substance is used, ureteric strictures, vesico-ureteral reflux, reduced capacity of the bladder and irregularities of the bladder.

All the patients received anti-tuberculosis therapy. A total of 11 patients with an advanced disease in the form of multiple calyceal involvement or simultaneous kidney, ureter and urinary bladder involvement, with a creatinine level of 2-3 after external drainage required a surgical procedure: four patients underwent ureterocalicostomy procedure and three out of them had single functioning kidney. The surgery failed in all 4 patients. Four patients required bladder augmentation with ureteral reimplantation²¹.

The reconstruction procedures, such as uretero-ureteral anastomosis, pyelo-ureteral anastomosis, caliceal reconstruction, uretero-caliceal anastomosis, and ureter substitution by ileus are performed in 40% of the cases²².

Sometimes the renal infestation is manifested late in the evolution of the disease like the case presented by *S. Toccaceli et al*, where a 67 year old male presented himself to the emergency room in Rome with abdominal pain, constipation by 36 hours. The clinical examination revealed the presence in the entire left abdomen of a fixed mass with irregular margins of about 30 cm. After a

¹⁹Yarger WE, 1991. *Urinary tract obstructive*. Brenner BM, Rector FC, eds. The Kidney. Fourth edition. Saunders: Philadelphia/ London: W.B. Saunders, 1768–1808

²⁰Min-Bo Yan, Jing Lu, Xiao-Feng Li, Zhen-Yu Guo. *Clinical analysis of retroperitoneoscopic nephroureterectomy for renal tuberculosis*. Chronic Diseases and Translational Medicine, 2015, 1, 217e220

²¹Vinayak Gorakhanath Wagaskar, Rahul Arun Chirmade, Vidyasagar Hansraj Baheti, Harshwardhan Vedpalsingh Tanwa, Sujata Kiran Patwardhan, Ganesh Gopalakrishnan. *Urinary Tuberculosis with Renal Failure: Challenges in Management* DOI: 10.7860/JCDR/2016/16409.7017

²²Mochalova TP, Starikova IY. *Reconstructive surgery for treatment of urogenital tuberculosis: 30 years of observation*. World J Surg, 1997, 21: 511–515

ultrasonography and a CT was performed who revealed presence of a retroperitoneal mass of renal origin completely filling the left retroperitoneal space, from the subdiaphragmatic area to the iliac fossa. The mass displaced the spleen and the descending colon. The optimal line of treatment for the patient was nephrectomy. The HP result proved the tumor to be a huge post-tuberculosis chalk kidney. Postoperative course was with no significant events and the patient was discharged on 8th day. The treatment at home was a therapy based on isoniazid 250 mg twice a day²³.

DISCUSSIONS

Since the late 1980s, the incidence of tuberculosis increased in the US and Europe while the disease was virtually eradicated by the BCG vaccine. This can be explained by the apparition of the HIV and the immunosuppression it creates, by the emergence of bacterial strains resistant to usual treatments²⁴. Renal localization of tuberculosis is usually the result of hematogenous spread of mycobacteria from a pulmonary focus. The renal infection with this bacillus appears in 8 to 10% of cases of primary pulmonary infection. The pulmonary infection is the gateway from where the infection spreads.

There were a few cases, less than 50, of tuberculous kidney cancer reported²⁵. In the literature, the conventional cell adenocarcinoma is the most frequent histological type of renal cancer. The combination of a tuberculous lesion to other tumor histological types such as transitional cell carcinoma has rarely been described²⁶.

Nephrectomy via the peritoneal and the retroperitoneal approach are the two main procedures performed when the TB infection destroys the renal parenchima, and a surgical treatment must be performed. Also reconstructive procedures like pielloplasty or partial nephrectomy, classical, laparoscopic or robotic assisted, are performed. The retroperitoneal approach can avoid dissemination of the tuberculosis bacterium and can reduce interference to the abdominal organs, but sometimes it can be difficult to be performed in particular when the TB infection causes a perinephritic reaction and inflammation which proves a real challenge when the kidney dissection is performed²⁷. In laparoscopic nephrectomy procedures for tuberculous nonfunctioning kidneys, the main reasons for conversion to open surgery are perinephric adhesions and intraoperative major hemorrhages. It is extremely important not to spill caseous materials from the kidney when the kidney dissection is performed, because there is a high risk to contaminate other vicinity organs²⁸.

Laboratory examinations are important means of diagnosis of renal TB. The correct line of approach is that the patients should stop anti-TB and antibacterial drugs 1 week before the urine smear for acid fast bacilli, which should be performed 3 times in a row to improve the positive testing rate.

²³ S. Toccaceli, L. Perisco Stella, M. Diana, A. Taccone, G. Giulliani, L. de Paola, M. Valvano. *Renal tuberculosis: a case report*. G Chir, 2015, 36(2), p. 76

²⁴ Miller WT. *Tuberculosis in the 1990's*. Radiol Clin North Am. 1994;32:649e661

²⁵ Neibling HA, Walters W. *Adenocarcinoma and tuberculosis of the same kidney: review of the literature and report of seven cases*. J Urol. 1948;59:1022e1026

²⁶ Conde Redondo C, Estebanez Zarranz J, Rodriguez Toves A, et al. *Tuberculosis and renal cancer*. Actas Urol Esp. 1999;23:617e620

²⁷ Zhang X, Zheng T, Ma X, et al. *Comparison of retroperitoneoscopic nephrectomy versus open approaches to non-functioning tuberculous kidneys: a report of 44 cases*. J Urol. 2005;173: 1586e1589

²⁸ Chibber PJ, Shah HN, Jain P. *Laparoscopic nephroureterectomy for tuberculous nonfunctioning kidneys compared with laparoscopic nephroureterectomy for other diseases*. J Laparoendosc Adv Surg Tech A. 2005 Jun;15(3):308e311

CONCLUSION

Tuberculosis has a high incidence in developing countries. There is a worrisome underdiagnosis of renal TB, which leads to development of renal insufficiency, chronic kidney disease, and ESRD. If the patient presents ureterohydronephrosis with the event loss of kidney function, nephrectomy is to be performed via classical or laparoscopic approach. New research is needed to trace the main forms of clinical presentations of renal TB, as well as to develop new more efficacious diagnostic methods and less toxic anti-TB drugs.

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