



RENAL MALAKOPLAKIA. A CASE REPORT

Malacoplaquia renal. Presentación de caso

Federico Guillermo Lubinus Badillo¹

Isabel Bolívar Aguilera²

Catherine Sánchez Prada³

Laura Vanessa Ramírez Pedroza⁴

Juan David Santander Landazábal⁴



Palabras clave (DeCS)

Malacoplaquia
Enfermedades renales
Enfermedad
granulomatosa crónica
Escherichia Coli

Key words (MeSH)

Malacoplakia
Kidney diseases
Granulomatous disease,
chronic
Escherichia coli

Summary

Introduction: Malakoplakia is a chronic multisystemic granulomatous disease characterized by the presence of one or multiple white plaques in various organs of the body, preceded by some chronic bacterial infection. In most reported cases it is found that *E. coli* contributes in approximately 80% of cases. **Objective:** The objective of this article is to show a case report of this disease and its characteristics through a review of the subject. We present a case of renal Malakoplakia in a 65-year-old woman with multiple comorbidities associated with this entity. We emphasize on the use of the diagnostic methods, as well as the outcome. **Discussion:** Malakoplakia is a pathology that is usually found in the urinary tissue, although it may develop in other organs. Its cause has not been fully explained and it is assumed to be due to a defect in phagolysosome activity, apparently by alteration in the concentration of intracellular cyclic guanosine monophosphate (Cgmp) in macrophages and monocytes. Patients with this pathology may be asymptomatic or have non-specific symptoms. **Conclusion:** Malakoplakia is an entity that although rare in the general population should be taken into account when there is uni or multifocal involvement of the renal parenchyma in patients with the potential risk where the role of imaging is to provide a first work-up of the extension, with the final work-up taking place through histopathological studies, giving patients the opportunity to receive timely treatment with excellent results.

Resumen

Introducción: La malacoplaquia es una enfermedad granulomatosa multisistémica crónica caracterizada por una o múltiples placas blancas en varios órganos del cuerpo, precedida por alguna infección crónica bacteriana. En la mayoría de los casos estudiados se encuentra que la *E. Coli* contribuye en aproximadamente el 80 % de ellos. **Objetivo:** Dar a conocer la existencia de esta enfermedad y sus características mediante una revisión de tema, y exponer un caso de malacoplaquia renal en una mujer de 65 años de edad con múltiples comorbilidades asociadas a dicha entidad; se describe la utilización de los métodos diagnósticos, así como su desenlace. **Discusión:** La malacoplaquia es una patología que se encuentra frecuentemente en el tejido urinario, a pesar de que puede desarrollarse en otros órganos. Su etiopatología no ha sido totalmente explicada; sin embargo, se asume que se da por un defecto en la actividad fagolisosomal, al parecer por alteración en la concentración de guanósín monofosfato cíclico intracelular (cGMP) en macrófagos y monocitos. Los pacientes que cursan con esta patología pueden ser asintomáticos o presentar síntomas



¹Radiologist, Foscal. Bucaramanga, Colombia.

²Pathologist, Foscal. Bucaramanga, Colombia.

³Resident Radiology Physician, Foscal. Bucaramanga, Colombia.

⁴Medical Student, Unab. Bucaramanga, Colombia.

inespecíficos. **Conclusión:** La malacoplaquia es una entidad que, aunque poco frecuente en la población general, debe tenerse en cuenta cuando existe compromiso uni o multifocal del parénquima renal en pacientes con factores de riesgo. Las imágenes pueden no ser concluyentes y hacer sospechar patología tumoral; sin embargo, el estudio histopatológico de la muestra permite un diagnóstico definitivo, lo cual les da la oportunidad a los pacientes de recibir manejo oportuno con excelentes resultados.

Case Presentation

A 65-year-old female patient with a history of nonsteroidal anti-inflammatory nephropathy (NSAID), who underwent cadaveric kidney transplantation and was subsequently hospitalized multiple times for bacteremia secondary to urinary tract infection by *E. Coli* β -lactamases with extended spectrum (EABL) negative resistant to ciprofloxacin with in-hospital management. In the last hospitalization she was admitted to the emergency department for pain in the lower left hemiabdomen at the height of the transplanted kidney, with in-hospital diagnosis of mixed-origin sepsis, positive urine culture for multidrug resistant *Klebsiella Pneumoniae* (MDR) (1) and positive peripheral blood cultures for *E. Coli* EABL positive. A renal ultrasound study was performed that showed nodular lesions of the upper and lower poles of the transplanted kidney, with extracapsular extension towards the wall of the abdomen and infiltrating obstructive compromise of the skin-ureteral junction of the transplanted kidney and secondary hydronephrosis compatible with expansive lesion of neoplastic type. A simple abdomen tomography was performed with the discovery of multiple rounded, high signal, heterogeneous, well defined border masses in the transplanted kidney (2), which bulge the contour of the renal silhouette, located in the lower pole and middle third of the transplanted kidney (Figures 1-4). A biopsy was performed that resulted in the definitive diagnosis of malakoplakia, evidenced by renal parenchyma replaced by a collection of macrophages with granular eosinophilic cytoplasm with cellular detritus and concentric basophilic inclusions morphologically compatible with Michaelis-Gutmann bodies, as well as stromal fibroblast proliferation and inflammatory infiltrate (Figures 5-7).

Discussion

Malakoplakia originates from the Greek *malakos* (plaque) and *pakos* (soft) (1,2). Malakoplakia is defined as a chronic multisystemic granulomatous disease characterized by one or multiple white plaques in various organs of the body (3,4), mainly in the bladder, but could be found in other organs not involving urinary tissue (1). Although its cause has not been fully explained, it is assumed to be due to a defect in phagolysosomal activity, apparently due to alteration in the concentration of cyclic intracellular guanosine monophosphate (cyclic GMP) in macrophages and monocytes, which phagocytize bacteria, as in the case of chronic *E. Coli* infections (5), but they are not fully digested, so that when they accumulate in the cytoplasm they generate a granulomatous reaction of the immune cells (3). In addition to this microorganism, other possible ones are described, such as *Klebsiella*, *Proteus*, *Mycobacterium*, *Staphylococcus* and fungi, which release cytokines and produce inflammation and kidney damage (6).

On May 14, 1901, Professor von Hansemann observed it and gave it the name malakoplakia; later, Michaelis and Gutmann made the official

publication in 1902, describing the microscopic findings that characterize the disease (4,6-8).

The prevalence is unknown; however, more than 700 cases have been studied so far. It occurs predominantly in the female sex, with a ratio of 4:1 with respect to the male sex (1, 9) and the average age of diagnosis is at 50 years, it does not occur in paediatric ages, although some authors affirm its occasional appearance (1). It has also been shown that *E. Coli* contributes to approximately 80% of cases (2,6,10,11).

As far as risk factors are concerned, this pathology is more related to immunosuppressed patients, 40 % of the cases, which include transplant clinical history, as in the case described here, due to immunosuppressive drugs such as tacrolimus and mycophenolate (10) as they act by inhibiting enzymes such as calcineurin and blocking the activation of N-terminal kinase, as well as cascades linked to the T-cell receptor, making their effect more specific to lymphocytes (12). Other risk factors are HIV/AIDS, lymphoma, poorly controlled diabetes, steroid therapy or alcoholism (1-3,13). With regard to urinary tract involvement, in 64% of cases the disease will affect both kidneys (4).

Patients with this pathology may be asymptomatic or show non-specific symptoms, such as fever (14), pain and others that vary according to the organ involved (3); for example, formation of plaques or papules, ulceration and pruritus when there is skin alteration (6), recurrent diarrhoea, dyspepsia, abdominal pain and haemorrhage when there is gastrointestinal alteration, which represents 15 % of cases (1,3), and finally, in 60 to 80 % of cases, there is alteration at the level of the urinary tract (bladder), and urethra) and precisely when there is renal malakoplakia, as evidenced in the clinical case presented in this article, it will manifest with bilateral or unilateral multifocal lesions (2) and symptoms such as flank pain, hematuria, recurrent urinary tract infections, increased white and red cells in urine and may or may not have renal dysfunction (6). Lesions caused by malakoplakia in most patients are identified in studies that are performed for other reasons, which include: hematuria, renal failure, persistent urinary tract infection despite antibiotic treatment, which happened in the case studied.

Imaging findings range from diffuse unilateral augmentation of the size of the affected kidney to bilateral involvement that is infrequent and presents as an infiltrative lesion that compromises the renal cortex and is difficult to differentiate from a neoplasm. When renal compromise is suspected, the best examination for its evaluation is renal and urinary tract ultrasound, in which loss of differentiation of the parenchymal cortex by focal or multifocal compromise is observed, the latter is the most frequent pattern 75% (15), with multiple focal lesions, well defined, with a tendency to coalesce in variable diameters that can reach up to 4 cm, and reach beyond the cortical margin, resulting in irregularity of the contour of the renal silhouette; In some cases the involvement of perirenal fat is evident (15).



Figure 1. Sagittal cut, transplanted left iliac fossa kidney: multiple rounded lesions of high signal, heterogeneous, well-defined edges in the anterior aspect and lower pole that alter the contour of the renal silhouette.



Figure 4. Simple abdomen tomography. Axial section: high-signal, heterogeneous, well-defined-edged lesions in the cortex of the upper pole of the transplanted kidney.



Figure 2. Single abdomen tomography, Coronal cut. High-signal, heterogeneous, well-defined-edged lesions in the cortex of the upper and lower poles of the transplanted kidney.

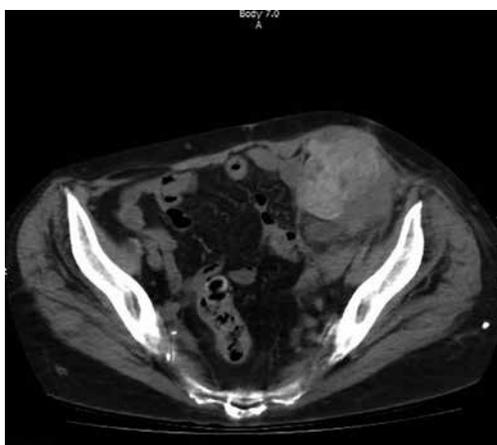


Figure 3. Simple abdomen tomography. Axial cut. High signal images, heterogeneous, that bulge the contour of the renal silhouette, in the anterior aspect of the cortical of the transplanted kidney.

These plates can be located anywhere in the urinary tract and cause dilation of the urinary tract; in the bladder there may be polypoid lesions of variable diameter. Calcifications are rare.

In excretory urography, filling defects can be observed in the collecting system. In computed tomography images, masses with heterogeneous enhancement of the contrast medium could be observed, which make it difficult to differentiate between acute infectious processes. And plaques may coexist in the urinary system, which makes this pathology suspicious (4). However, it is more common for the diagnosis of these patients to be incidental due to non-specific symptoms; however, when performing an endoscopy, yellowish (3,7) polyposis plaques or nodules could be observed, or nodules known in the literature as white, with a nodular shape on the surface of the mucosa, vascularized and the diagnosis of malacoplakia would be confirmed by histopathological study; this lesion could also be confused with a carcinoma due to two specific characteristics: central ulceration of the lesion and/or extensive vascularisation, already mentioned (1, 16). Renal biopsy is the gold standard for diagnosis (17), by means of which a microscopic study is carried out and thus aggregates of histiocytes known as von Hansemann histiocytes (histiocytes with small nuclei and granular acidophilus cytoplasm) with pathognomonic inclusions called Michaelis-Gutmann bodies (calcified inclusions with positive staining for Schiff's periodic acid, von Kossa and Pearls), findings consisting of mineralized bacterial components that were not digested, trapped in lysozyme. The urothelium, which may be present, is superimposed, benign, and may be hyperplastic, metaplastic, or ulcerated, but is usually intact (1,3,5,13,18,19).

The disease represents a rare granulomatous response to urinary tract infections, usually; such response could be confused with malignancy, radiologically or endoscopically, and therefore in the literature this pathology is also known as pseudotumor (1).

Differential diagnoses in radiological studies include local abscesses, granuloma, xanthogranulomatous pyelonephritis, lymphoma, and multifocal primary or metastatic tumors (7).

The definitive diagnosis is made by means of a histopathological study that proves the existence of histiocytes with abundant eosinophilic, granular cytoplasm and intracytoplasmic laminated round inclusions (19).

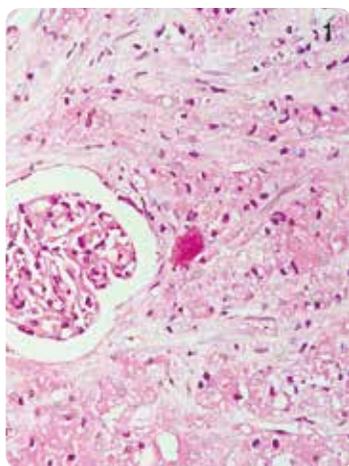


Figure 5. A 4X, hematoxylin eosin staining shows renal parenchyma with a preserved glomerulus. The interstitium is replaced by a collection of macrophages with granular pink cytoplasm.

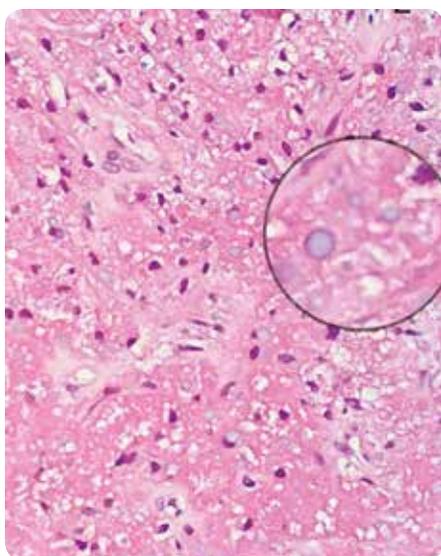


Figure 6. At 10X, hematoxylin eosin staining, some of these macrophages show round intracytoplasmic basophilic inclusions (circle content) corresponding to the bodies of Michaelis-Guttman.

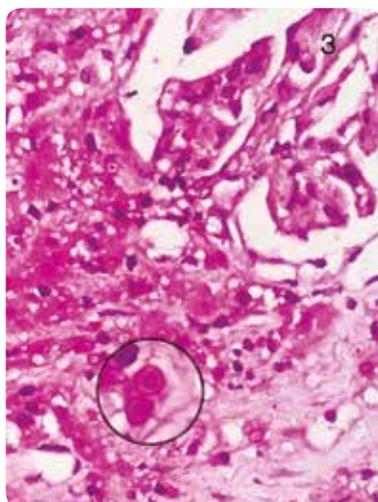


Figure 7. A 40X, PAS (periodic acid-Schiff) coloration highlights the intracytoplasmic inclusions (circle contents). Demonstrates a point surrounded by halo that corresponds to an early lesion.

The differential diagnoses to be considered are primary or metastatic malignancies such as renal cell carcinoma (9), polycystic kidney disease (19), inflammatory diseases (sarcoidosis, Crohn's disease), infectious diseases (tuberculosis), Whipple's disease, multifocal bacterial nephritis (19), cutaneous or renal fungal infections (17), leprosy, reticulated cell sarcoma, *Mycobacterium avium-intracellulare* infection (3,5), local abscesses, xanthogranulomatous pyelonephritis and lymphomas (2, 16). All its characteristics make malacoplakia to be considered in the differential diagnosis of chronic inflammatory renal lesions, even when the infiltrate is predominantly neutrophilic (19).

The treatment of malacoplakia focuses mainly on controlling the infection, avoiding complications such as abscess or some obstruction (1). The use of fluoroquinolones is preferred for approximately 2 months (10) due to their easy access through the cell wall of the macrophage and histiocyte to reach high intracytoplasmic concentrations, however, are also described other drugs such as rifampicin, trimetoprim-sulfamethoxazole and gentamicin (4). At present, the duration of therapy is not standardized (3), but long-term and low-dose use is recommended to prevent recurrence (18). In pseudotumoural cases or severe haemorrhage that does not subside with endoscopic therapy, surgical removal of the lesions is required (3,5); however, in some cases described, patients have had unnecessary nephrectomy, as adequate clinical management may prevent it (2), and in patients on immunosuppressive treatment, it is advised to discontinue it during the malacoplakia treatment period (4,8).

Some outstanding antibiotics include quinolones, as well as cotrimoxazole, rifampicin, doxycycline, trimethoprim and vancomycin, which have been shown to be effective and which, roughly speaking, enter the phagocytes and assist in the intracellular killing of bacteria. However, the use of these, as well as other possible drugs, could affect the functionality and integrity of the kidney, damaging it (20-22). In patients without comorbidities, recurrences and complications may occur over the years, such as renal failure, in the case of urinary tract involvement and, depending on the presentation, may be of variable severity (2,3,5).

About 40% of patients have some form of immunosuppression, including solid organ transplants, autoimmune diseases requiring the use of steroids or chemotherapy, chronic systemic diseases, malignancy, alcohol abuse and poorly controlled diabetes mellitus.

Twenty years ago their morbidity and mortality was up to 50% and the estimated survival in patients transplanted with renal graft involvement was approximately 6 months (10, 23); however, with the development of quinolones this percentage has improved (13), it is a disease with a good prognosis and its degree of involvement varies when associated with underlying diseases such as immunosuppression and malnutrition (9).

References

1. Blair J, MacLennan GT. Malacoplakia. *J Urol.* 2005;173:986.
2. Abolhasani M, Jafari AM, Asgari M, Salimi H. Renal malacoplakia presenting as a renal mass in a 55-year-old man: a case report. *J Med.* 2012;6:379.
3. Greek. Malacoplakia. Portal de información de enfermedades raras y medicamentos huérfanos [internet]. 2011 [citado 2018 abr. 15]. Disponible en: [www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=ES&data_id=3392&Disease\(s\)/group%20of%20diseases=Malacoplakia&title=Malacoplakia&search=Disease_Search_Simple](http://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=ES&data_id=3392&Disease(s)/group%20of%20diseases=Malacoplakia&title=Malacoplakia&search=Disease_Search_Simple).

4. Velásquez JG, Vélez A, Uribe JF. Malacoplaquia en urología. *Rev Urolog Colomb*. 2006;(15):1.
5. Rozman C, Cardellach F. Otras enfermedades intestinales. En: *Medicina interna*. Elsevier; 2016. Capítulo 23.
6. Wang GQ, Xu XG, Chen YP, Cheng H. Renal parenchymal malakoplakia presenting as acute renal failure in a young woman department of nephrology Beijing: Anzhen Hospital; 2017.
7. Stamatou K, Chelioti E, Aikaterini T, Kalliroi K, Papalexandrou A, Efthymiou E, Tsilivigkou M, Vasilakaki T. Renal failure caused by malakoplakia lesions of the urinary bladder. *Nephro Urol Mon*. 2014;6(4):e18522.
8. Honsova E, Lodererova A, Slatinska J, Boucek P. Cured malakoplakia of the renal allograft followed by long-term good function: A case report. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*. 2012;156(2):180-2.
9. Lusco M, Fogo A, Najafian B, Alpers Ch. Atlas of renal pathology: Malakoplakia. *Am J Kidney Dis*. 2016;68(4):e27-e28.
10. Graves AL, Texler M, Manning L, Kulkarni H. Successful treatment of renal allograft and bladder malakoplakia with minimization of immunosuppression and prolonged antibiotic therapy. *Nephrology*. 2014;19:18-21.
11. Augusto JF, Sayegh J, Croue A, Subra JF, Onno C. Renal transplant malakoplakia: case report and review of the literature. *NDT Plus*. 2008;1(5):340-3.
12. Leão CA, Duarte MI, Gamba C, Ramos JF, Rossi F, Galvão MM, et al. Malakoplakia after renal transplantation in the current era of immunosuppressive therapy: case report and literature review. *Transpl Infect Dis*. 2012;14(6):E137-41.
13. Rubin E, Reiser H. *Essentials of Rubin's pathology*. 6^o ed. Philadelphia: Lippincott Williams; 2014.
14. Chandrankunnel J, Cunha BA, Petelin A, Katz D. Fever of unknown origin (FUO) and a renal mass: renal cell carcinoma, renal tuberculosis, renal malakoplakia, or xanthogranulomatous pyelonephritis? *Heart Lung*. 2012;41(6):606-9.
15. Hartman DS, Davis CJ Jr, Lichtenstein JE, Goldman SM. Renal parenchymal malacoplakia. *Radiology*. 1980;136:33-42.
16. Abolhasani M, Jafari AM, Asgari M, Salimi H. Renal malakoplakia presenting as a renal mass in a 55-year-old man: a case report. *J Med Case Rep*. 2012;6(6):379.
17. Puerto IM, Mojarrieta JC, Martínez IB, Navarro S. Renal malakoplakia as a pseudotumoral lesion in a renal transplant patient: A case report. *Int J Urol*. 2007;14(7):655-7.
18. Dong H, Dawes S, Phillip S, Chaudhri S, Subramonian K. Malakoplakia of the urogenital tract. *Urol Case Rep*. 2015;3(1):6-8.
19. Gupta M, Venkatesh S, Kumar A, Pandey R. Fine-needle aspiration cytology of bilateral renal malakoplakia. *Diagnostic Cytopathology*. 2004;31(2).
20. Ayllon J, Verkarre V, Scotté F, Fournier L, Corréas JM, Mejean A, Teghom C, Oudard S. Renal malacoplakia: Case report of a differential diagnosis for renal cell carcinoma. *Am J Case Rep*. 2012;13:28-40.
21. Muttarak M, Peh WCG, Thamprasert K. Case quiz. *Australian Radiology*. 1999;43:405-7.
22. Vincent B, Michaël Z, Pierre M, Laurence B, Solange M. Malakoplakie rénale: une cause rare d'infiltration rénale pseudotumorale. Elsevier Masson; 2011.
23. Reinout C, Jo C, Andre AM, Van der Ven K, Jacques A, et al. Functional and morphological monocyte abnormalities in a patient with malakoplakia. *Am J Med*. 1998;105.

Correspondence

Catherine Sánchez Prada
Médica Residente de Radiología
Foscal
Universidad Autónoma de Bucaramanga
Av. 42 # 48-11
Bucaramanga, Santander
kasapra_0611@hotmail.com

Received for assessment: May 2, 2018

Accepted for publication: June 20, 2018