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Clinical case

Malacoplakia of the urinary bladder: case report and systematic review

Malacoplaquia de la vejiga urinaria: reporte de caso y revisión sistemática

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Abstract

Introduction: Malacoplakia is a rare chronic inflammatory disease that commonly affects the urinary bladder, and it is characterized by the presence of large cells containing vacuoles known as Michaelis-Gutmann bodies.

Case report: A 79-year-old woman was admitted to the emergency department a poorly defined with symptoms of fever, dysuria, hematuria, and pain and swelling in her right knee. Microbiological studies indicated the presence of Escherichia coli in blood cultures, urine cultures, and synovial fluid cultures of the right knee. A computed tomography scan revealed nonspecific bladder thickening, which was further confirmed by a cystoscopy. A poorly defined lesion in the trigone was resected, and subsequent pathological examination revealed the presence of malacoplakia without evidence of malignancy. The patient was treated with antibiotic therapy, and the hematuria eventually resolved.

Systematic review: We conducted a comprehensive search in the Medline, EMBASE, and WoS databases from January 1, 1993, to January 1, 2023, for articles that focused on Malacoplakia, involved human subjects. Were included 32 articles reporting on 35 cases of urinary bladder malacoplakia. The majority of those diagnosed with bladder malacoplakia were women under the age of 50, with recurrent urinary tract infections and immunosuppressive conditions as frequent comorbidities. Positive cultures showed Escherichia coli (E. coli) in 72% of cases. Successful outcomes were achieved in 26 cases (74.3%).

Discussion: Malacoplakia is triggered by an inadequate immune system response to lower urinary tract infections. Diagnosis requires prior biopsies before resection or more aggressive treatments. Appropriate treatment of urinary tract infections with antibiotics targeted at gram-negative bacteria is essential for treating malacoplakia.

Keywords:
Malacoplakia;
Escherichia coli;
Urinary Bladder;
Systematic Review;
Case Report

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Resumen

Introducción: La malacoplaquia es una enfermedad inflamatoria crónica poco común que afecta comúnmente a la vejiga urinaria y se caracteriza por la presencia de células de gran tamaño que contienen vacuolas conocidas como cuerpos de Michaelis-Gutmann.

Reporte de caso: Mujer de 79 años ingresó al servicio de urgencias con síntomas de fiebre, disuria, hematuria y dolor e hinchazón en rodilla derecha. Los estudios microbiológicos indicaron la presencia de *Escherichia coli* en hemocultivos, urocultivos y cultivos de líquido sinovial de la rodilla derecha. Una tomografía computarizada reveló un engrosamiento inespecífico de la vejiga, que se confirmó mediante una cistoscopia. Se resecó una lesión mal definida en el trígono y el examen patológico posterior reveló la presencia de malacoplaquia sin evidencia de malignidad. El paciente fue tratado con terapia antibiótica y la hematuria finalmente se resolvió.

Revisión sistemática: Se realizó una búsqueda exhaustiva en las bases de datos Medline, EMBASE y WoS desde el 1 de enero de 1993 hasta el 1 de enero de 2023 de artículos centrados en la malacoplaquia en humanos. Se incluyeron 32 artículos que informaban sobre 35 casos de malacoplasia de la vejiga urinaria. La mayoría de los diagnosticados con malacoplaquia vesical eran mujeres menores de 50 años, con infecciones recurrentes del tracto urinario y condiciones inmunosupresoras como comorbilidades frecuentes. Los cultivos positivos mostraron *Escherichia coli* (*E. coli*) en el 72% de los casos. Se lograron resultados exitosos en 26 casos (74,3%).

Discusión: La malacoplaquia se desencadena por una respuesta inadecuada del sistema inmunológico a las infecciones del tracto urinario inferior. El diagnóstico requiere biopsias previas antes de la resección o tratamientos más agresivos. El tratamiento adecuado de las infecciones del tracto urinario con antibióticos dirigidos a bacterias gramnegativas es esencial para tratar la malacoplaquia.

Palabras clave:
Malacoplasia, *Escherichia coli*, vejiga urinaria, revisión sistemática, reporte de un caso

Introduction

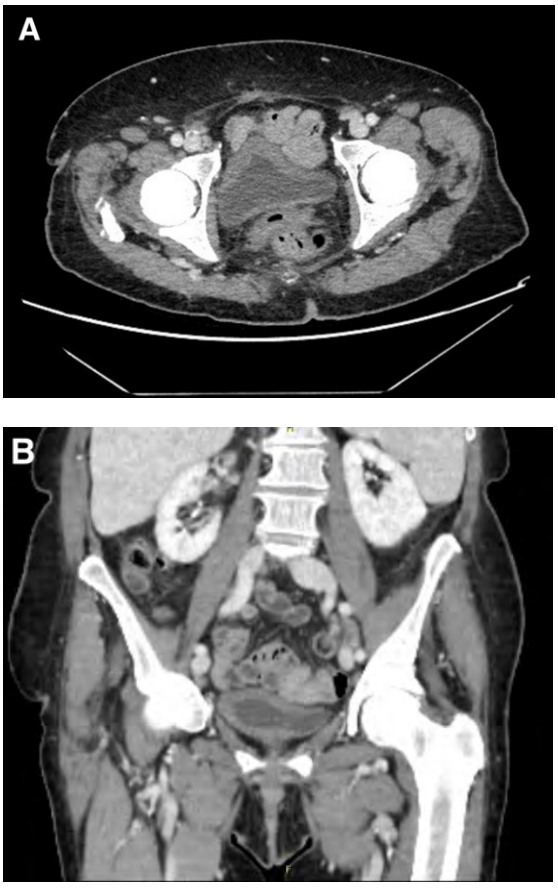
Malacoplakia is a chronic granulomatous inflammatory disease, first discovered by Michaelis and Guamas in 1902 and later described by v. Hansmann.[1] While malacoplakia can affect various systems including gastrointestinal, respiratory, nervous, endocrine, and musculoskeletal, the urinary tract is the most commonly affected location, with a prevalence of 40% of cases occurring in the urinary bladder.[2–4] Despite being a benign and self-limited process, malacoplakia often mimics malignancy and is associated with high morbidity and mortality.[5] In this paper, we present a clinical case report and conduct a systematic review of the literature on malakoplakia of the urinary bladder.

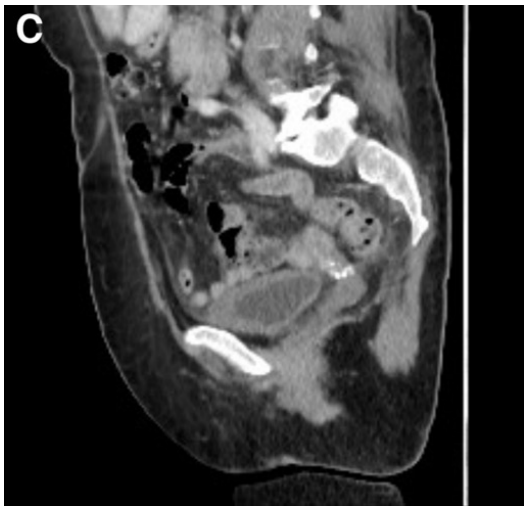
Case report

A 79-year-old woman presented to the emergency department with a 5-day history of fever, dysuria, and hematuria, along with pain and swelling in her right knee. Her medical history included a myeloproliferative syndrome with myelofibrosis, treated with prednisone 40mg once a day. She had no history of recurrent urinary tract infections or other urological pathology.

A physical examination and blood tests were performed, which showed chronic anemia and elevated acute phase reactants, while all other parameters were normal. Microbiological studies showed the growth of *Escherichia coli* in blood cultures, urine cultures, and synovial fluid cultures of the right knee. The patient was admitted to *hospital* and started on intravenous treatment with ceftriaxone. Despite the disappearance of the infectious symptoms, the patient continued to have persistent hematuria, which led to an ultrasound and subsequently a computed tomography (Figure 1). These tests showed nonspecific bladder thickening without extramural bladder involvement, no dilation of the urinary tract, and normal-sized and shaped kidneys.

Figure 1. CT scan of patient with bladder malacoplakia of the urinary bladder

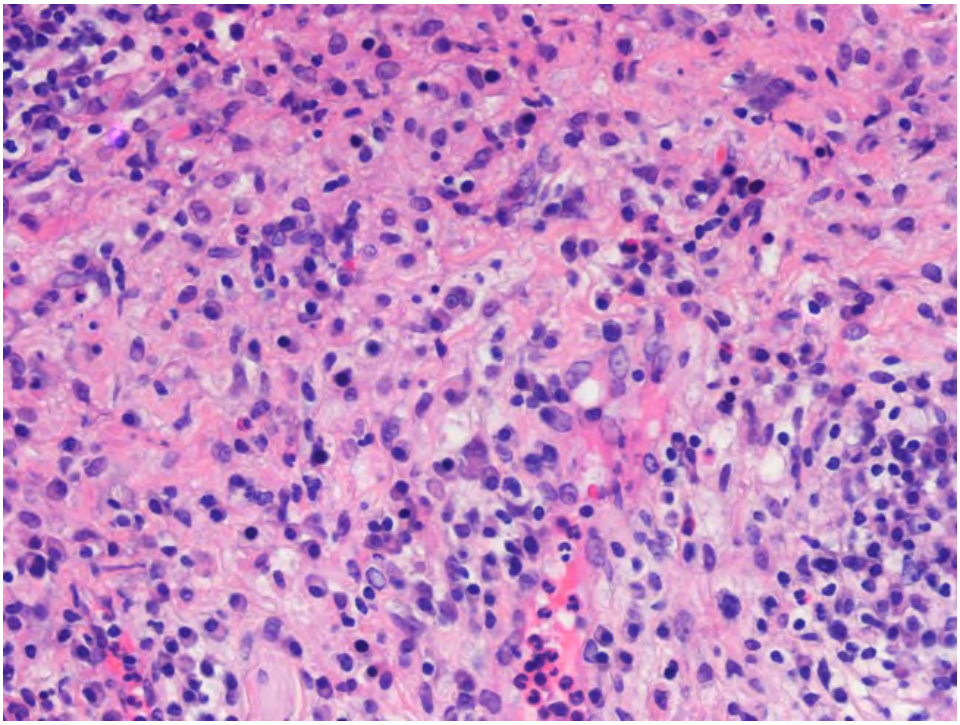




(A) transverse plane, (B) sagittal plane, (C) coronal plane.

To investigate the high suspicion of malignancy, a cystoscopy was performed which revealed numerous vascular nests in the mucosa and a poorly defined lesion in the trigone. After transurethral resection and antibiotic therapy, the hematuria resolved. Pathological examination revealed changes in the lamina propria, with aggregates of histiocytes with broad, microvacuolated cytoplasm and positivity for CD-68, as well as an inflammatory infiltrate of lymphoplasmacytic type. No evidence of malignancy was found (Figure 2).

Figure 2. Histological findings



Bladder wall fragments with intense inflammatory infiltrate consisting of uniform histiocytes (IHC: CD68+) with broad, granular eosinophilic cytoplasm (von Hansemann cells) were identified, with round and basophilic intracytoplasmic inclusions corresponding to Michaelis-Gutmann bodies

During follow-up, no recurrence of the disease was observed. However, the patient died 3 months after the intervention due to progression of her myeloproliferative syndrome.

Systematic review

Materials and methods

This systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations.[6] The review was registered with a protocol registration number in The International Prospective Register of Systematic Reviews (PROSPERO): CRD42023404140

Search y selection strategy

We searched for relevant articles published in English or Spanish in the Medline, EMBASE, and WoS databases from January 1, 1993, to January 1, 2023. The search terms included (Malacoplakia) AND (Bladder OR bladder).

The inclusion criteria were: 1) articles with Malacoplakia as the central theme; 2) studies involving human subjects; 3) full-text available in English or Spanish. Full texts of potentially relevant articles were obtained and assessed for eligibility.

Exclusion criteria were: 1) studies that presented Malacoplakia of organs other than the urinary bladder; 2) studies that are not case reports or case series studies.

Two independent reviewers (O.B. and G.M.) assessed the articles for eligibility, and disagreements were resolved through discussion. In cases where a consensus could not be reached, a third reviewer (M.B.) made the final decision. A PRISMA flow diagram was used to report the results of the selection process.[6]

Data extraction

The data were extracted and cross-checked by two authors (O.B. and G.M.). The following information was extracted from each article: title, first author's name, year of publication, patient age, patient sex, relevant medical history, renal function (creatinine level, if reported), microbiological urine culture, antibiotics used, treatment, and clinical outcomes. The articles were not evaluated for the risk of bias.

Data synthesis and statistical analysis

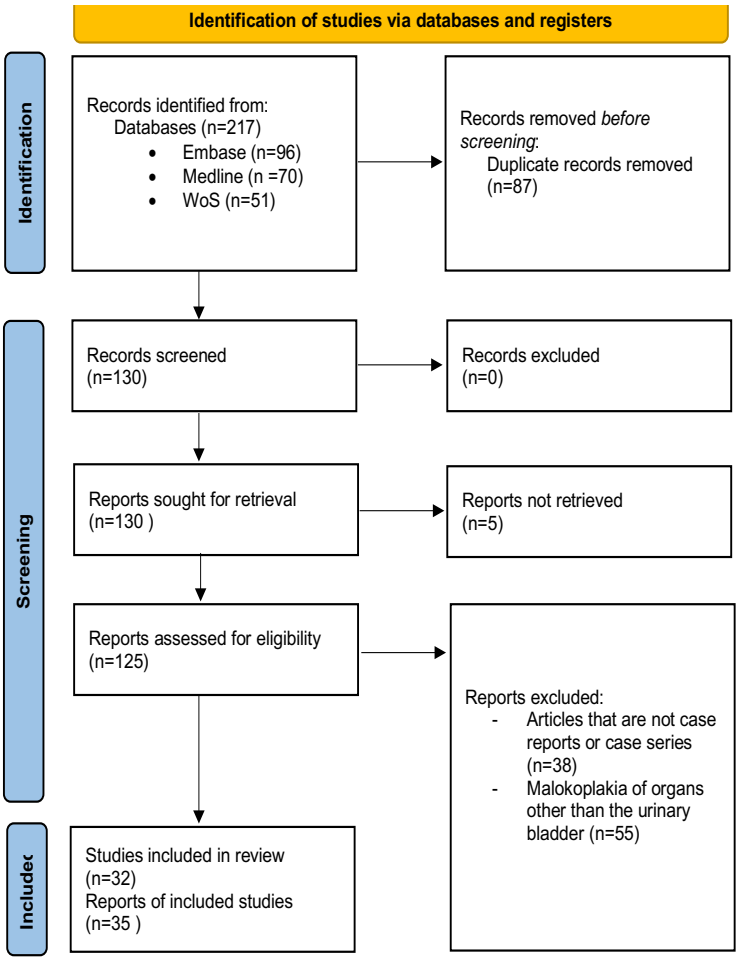
For qualitative analysis, the main findings of the selected studies were combined narratively. For quantitative analysis, we used descriptive statistics. The data were analyzed using JASP 0.17 (GNU Affero GPL v3 license).[7]

Results

Study selection

We conducted an initial search of Medline, EMBASE, and WoS, identifying 217 studies. After removing duplicates, we screened 130 articles and assessed 125 of them for eligibility. Based on the exclusion criteria, we excluded 93 papers, of which 55 were cases of malacoplakia affecting organs other than the urinary bladder, and 38 articles that were not case reports or case series. Ultimately, we included 32 articles reporting on 35 cases of urinary bladder malacoplakia for data analysis (Figure 3).

Figure 3. PRISMA 2020 flow diagram for studies on malakoplakia of the urinary bladder



Study characteristics

The mean age of the patients was 50 years (SD 23.3), and the majority of those diagnosed with bladder malacoplakia were women (74.3%). The most common comorbidity was recurrent urinary tract infections (40.0%), followed by immunosuppressive conditions (20.0%), DM (11.4%), and other urinary system disorders (11.4%). Only 5 patients (14.3%) had no relevant medical history.

A urine culture test was positive in 22 cases (62.8%) and negative in 3 cases (8.6%); in the remaining 10 cases (28.6%), it was not reported. E. coli was detected in 72% of positive cultures. Antibiotics were administered to more than 70% of the patients, with fluoroquinolones being the most frequently used group, followed by trimethoprim/sulfamethoxazole and piperacillin/tazobactam. In 3 cases (8.6%), antibiotic therapy was not used.

The diagnosis was confirmed by biopsy in 15 cases (42.8%), while treatment with TUR was given to 20 patients (37.1%), cystectomy to 4 patients (11.4%), and fulguration with holmium laser to 1 patient (2.8%). Of the 4 cases of cystectomy, 2 were performed due to suspected extension of colon cancer, 1 due to severe hematuria, and 1 without a clear cause.

The bladder lesion was most frequently observed on the lateral wall (31.4%), posterior wall (11.4%), and anterior wall (11.4%). The ureteral orifices and trigone were affected in 11.4% and 8.6% of the cases, respectively. The location of the malacoplakia was not specified in 16 cases (45.7%). During the course of malacoplakia, 42.8% of the patients developed renal failure.

Of the 35 cases, only 2 patients developed recurrence, and 1 had persistent malacoplakia. Six patients (17.1%) died during the first 9 months after diagnosis, but malacoplakia was not documented as the cause of death. Recovery was achieved in 26 cases (74.3%) (Table 1).

Table 1. Summary of studies of urinary bladder malakoplakia

N	Reference	Year	Age	Sex	Medical history	Renal failure	Microbiology	Antibiotic	Location	Procedure	Outcome
1	Berney.[8]*	1996	72	F	No reported	N/a	Negativ	N/a	N/a	Cystectomy	Died 3 monte after
2	Berney.[8]*	1996	57	M	N/a	Renal failure	Corynebacterium urealyticum	N/a	N/a	Cystectomy and nephrostomy	Died 1 monte after
3	Berney.[8]*	1996	13	F	Linfoblast leukemia	N/a	Negativ	N/a	N/a	Biopsy	Recovery
4	Sawamura.[9]*	1996	69	F	No reported	N/a	E. coli	Trimethoprim/ sulfamethoxazole	Right lateral wall	Biopsy	Recovery
5	Castillo Gimeno.[10]*	1998	61	M	rUTI	N/a	N/a	Trimethoprim/ sulfamethoxazole	N/a	TUR	Recovery
6	Castillo Gimeno.[10]*	1998	72	F	rUTI	N/a	N/a	Trimethoprim/ sulfamethoxazole	N/a	TUR	Recovery
7	Fariña Pérez. [11]*	1999	69	M	*Chronic glucocorticoid therapy*	N/a	Corynebacterium urealyticum	Teicoplanina	Posterior and lateral walls	TUR	Died 1 monte after
8	Kogulan.[12]*	2001	29	F	*No reported*	N/a	E. coli	Ciprofloxacin	Perforation of the left wall.	TUR	Recovery
9	Matter.[13]*	2001	65	M	*Chronic glucocorticoid therapy*	N/a	N/a	N/a	N/a	A partial cystectomy with a low anterior resection	Recovery
10	Darvishian.[14]*	2001	75	F	N/a	N/a	Negativ	N/a	Lateral wall	TUR (low-grade papillary urothelial carcinoma)	Recovery
11	García-Cosío.[15]*	2003	76	F	N/a	N/a	N/a	Ciprofloxacin	Fundus and bladder roof	TUR	Died 15 days after
12	Steele.[16]*	2003	16	F	Chronic renal failure owing to reflux nephropathy.	2.8 mg/dl	E. coli	N/a	N/a	TUR	Recovery

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13	Minor.[17]*	2003	16	F	No reported	3.0 mg/dl	N/a	Flouroquinolone	N/a	Biopsy	Recovery
14	Shah.[18]*	2005	11	M	Megaloureter/rUTI		E. coli	N/a	Posterior and left lateral walls	Biopsy	Recurrence
15	Bylund.[19]*	2008	51	F	rUTI	3.4 mg/dl	E. coli	Ciprofloxacin	N/a	TUR	Recovery
16	Sánchez.[20]*	2009	48	F	rUTI	16 mg/dl	E. coli	Ciprofloxacin	Walls and ureteral orifices	Biopsy	Recovery
17	Krauel.[21]*	2009	12	F	rUTI	N/a	E. coli	Fluoroquinolones	Blader/ Gatrointestinal	Biopsy	Recovery
18	Rafailidis.[22]*	2009	66	F	Urinary problems	N/a	N/a	N/a		Resection en bloc along with part of the urinary bladder, small intestine	Recovery
19	Patnayak.[23]*	2009	18	M	No reported	1.6 mg/dl	E. Coli	Yes	Trigonal area and bladder neck	Biopsy	Recovery
20	Ristić-Petrović.[24]*	2013	53	F	rUTI	N/a	E. coli,	N/a	Trigonal area, left ureteric orifice, posterior wall and bladder roof	TUR	Recovery
21	Matsuda.[25]*	2014	78	F	rUTI	1.89 mg/dl	E. coli	N/a	Right wall	Biopsy (MALT lymphoma)	Recovery
22	Graves.[26]*	2014	56	F	Kidney transplant/ rUTI	N/a	Klebsiella pneumoniae/ story r-UTI by Esherichia coli	Piperacillinta/ tazobactam		Biopsy	Recovery
23	Stamatiou.[27]*	2014	72	M	DM/rUTI	21mg/dl	Negative	Fluoroquinolones	Trigonal area, left uréter orifice, posterior wall, bladder roof.	Biopsy	Died 8 months after (renal failure, cardiovascular system complication)
24	Sharma.[28]*	2015	9	F	N/a	1.8 mg/dl	N/a	Cefixime		Biopsy	Recovery
25	Lee.[29]*	2015	74	F	DM	1.14 mg/dl	N/a (Reported urinary sepsis)	Ceftriaxone		TUR (urothelial carcinoma)	Recovery

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26	Sachanas.[30]*	2016	69	F	Chronic lymphocytic leukemia	N/a	E. coli	Antibiotics with intravenous immunoglobulin replacement	Anterior wall	Biopsy	Recovery
27	Nieto-Ríos.[2]*	2017	45	F	Kidney transplant/ rUTI	2.8 mg/dl	E. coli	Trimethoprim/ sulfamethoxazole	Bladder/Kidney	Biopsy	Persistent
28	Bullock.[31]*	2017	62	F	N/a	Renal failure	E. coli	Ciprofloxacino	Anterior wall	Biopsy	Died 9 months after
29	Cavallone.[32]*	2018	65	F	DM/rUTI	9.3 mg/dl	E. coli	Ciprofloxacin	Anterior and left walls.	TUR	Recovery
30	Sirithanapho.[33]*	2018	66	F	Systemic sclerosis (chronic immunosuppressive therapy)	No reported	N/a	Ciprofloxacin	N/a	Biopsy	Recovery
31	Hina.[34]*	2019	55	F	DM	1.13 mg/dl	E. coli, sensitive to quinolones.	Fluoroquinolone	Around right ureteric orifice	Fulguration with holmium laser	Recovery
32	Rabani.[35]*	2019	20 meses	F	rUTI	N/a	E. coli	Trimethoprim/ sulfamethoxazole	Anterior part of the right wall	Partial cystectomy	Recovery
33	Xiao.[36]*	2020	64	F	No reported	2.35 mg/dl	Klebsiella pneumonia.	Piperacillin/ tazobactam	Right wall and left ureteral orifice	TUR	Recovery
34	Gao.[37]*	2021	48	M	DM	1.39 mg/dl	Escherichia coli macrolides, quinolones, and most penicillins	Piperacillin/ tazobactam	Right wall	TUR	Recurrence
35	Chaudhry.[38]*	2022	56	F	Kidney disease	Renal failure	E. coli	N/a	N/a	Biopsy	Recovery

Abbreviations: rUTI = recurrent urinary tract infection; M = male; F = female; n/a = not aplicable; E. coli = Escherichia col; TUR = transurethral resection.

Discussion

Malacoplakia (from greek malako "soft" + plako "plaque") is condition that characterized by the presence of large cells containing vacuoles known as Michaelis-Gutmann bodies.[1,39] The role of gram-negative bacteria in the development of malacoplakia is well-established, with urine culture detection of E. coli being reported in 92-96% of patients with urinary bladder malacoplakia.[40,41] Recent ultrastructural analysis have confirmed that these bodies are partially digested E. coli that have been captured by phagosomes or lysosomes within the cell.[42] Consistent with these findings, our study also showed that the majority of patients had a positive urine culture for gram-negative bacteria, with E. coli being the most commonly detected organism.

In our review, the majority of patients diagnosed with malacoplakia were women, which is consistent with previous studies on malacoplakia of the urinary system.[41] However, a review of malacoplakia cases involving the gastrointestinal tract did not observe a gender predominance, and cutaneous malacoplakia was more common in males.[43] This gender trend in urinary system malacoplakia may be due to the higher prevalence of uncomplicated urinary tract infections in women, which can contribute to the development of this condition.

Malacoplakia primarily affects patients over the age of 50, particularly those with comorbidities such as organ transplants, systemic disorders, oncological diseases, HIV, and those receiving immunosuppressive treatment.[4,40] In a study analyzing 40 cases of malacoplakia in kidney transplant patients, is concluded that the reduction of immunosuppression is crucial in the treatment of malakoplakia.[2]

It is likely that both age and comorbidities increase the risk of developing lower urinary tract infections, which in turn increases the risk of developing malacoplakia.

Malacoplakia usually presents as a bladder mass or yellow soft plaques in different parts of the mucosa. In a review by Polisini *et al.*, the most frequent location was the vesicoureteral junction (42.31%). This location was correlated with hydronephrosis, which almost always led to renal failure.[41] In our review, no area was found to be more susceptible to malacoplakia. Ureteral involvement was observed in only 11% of cases, however, renal failure was reported in approximately half of the patients. Therefore, the cause of renal failure is not clear and requires further study.

The diagnosis of malacoplakia typically requires a biopsy with an anatomopathological study. However, as these lesions can often resemble malignant lesions, many patients are treated with more aggressive therapies, involving partial or complete resection of affected organs, such as the colon, urinary bladder, prostate, or testicles.[5,44–46] In our study, half of the patients underwent TUR, laser therapy, or cystectomy. However, anatomopathological analysis confirmed malignancy in only four cases. It is important to consider the possibility of malakoplakia when there is a suspicion of massive malignant involvement of the urinary bladder, particularly in the context of a UTI. Performing a biopsy before resection is recommended to avoid potential complications from aggressive treatments.

Conservative management is often effective in treating lower urinary tract malacoplakia, and recurrence is uncommon in most patients.[5] Treatment with antibiotics that are active against gram-negative bacteria typically results in complete resolution of the condition. While

studies report relatively high mortality rates after diagnosis, malacoplakia was not identified as the primary cause of death in any cases.[5,41] Among the cases in our review, mortality during the first year reached up to 17.1%. This rate may be partly explained by the presence of comorbidities and the age of affected patients. Further investigation is needed to better understand the relationship between malacoplakia and mortality.

Conclusion

Malacoplakia is a condition triggered by an inadequate immune system response to lower urinary tract infection. For its diagnosis, prior biopsies before resection or more aggressive treatments are recommended. Appropriate treatment of urinary tract infections with antibiotics targeted at gram-negative bacteria is essential for preventing and treating malacoplakia.

CRediT taxonomy

Oleksandr Boiko: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing - original draft.
Giselle Hirwa Mutsinzi Mukarukaka: Conceptualization, Data curation, Investigation, Methodology, Writing - review & editing.
Miren Imaz Murga: Visualization, Data curation, Writing - original draft.
Eva Dominguez: Visualization, Data curation, Writing - original draft.
Mykola Boiko: Writing - review & editing, final approval of the version to be submitted.
Andrea Carlevaris Fernández: Writing - review & editing, final approval of the version to be submitted.
Antonio Arruza Echevarria: Writing - review & editing, final approval of the version to be submitted.

Conflict of interest

None of the authors have any conflicts of interest or financial ties to disclose.

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Ethics statement

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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