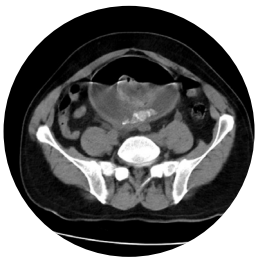

Squamous cell carcinoma of the urinary bladder. A case report

Carcinoma escamocelular de vejiga. Reporte de un caso

Claudia Isabel Cabarcas Herrera[1]
Julio Goenaga Pareja[1]
Juan Fernando Salcedo Brand[2]
Dolcey Márquez Florián[2]
Sindy Claudina Vergara Severiche[3]
María José Herrera Bedoya[4]

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Summary

Bladder cancer is the most common cause of malignancy involving the urinary system. Within its clinical spectrum it can manifest as painless hematuria, irritative voiding symptoms (pollakiuria, urgency, dysuria) and urinary obstruction, findings that can delay the diagnosis due to similarity of these symptoms to those of other benign pathologies (UTI, prostatitis, lithiasis, benign prostatic hyperplasia). Squamous-cell carcinoma, of all bladder malignancies, is responsible for the 3-5% of bladder tumors in North America and Europe, the most common being the transitional cell cancer with 95%. (1) We present a case of a 53 years-old man with abdominal pain and irritative voiding symptoms, in whom imaging studies established the diagnosis of bladder tumor. He underwent transurethral cystoscopy and specimens were collected for histopathologic evaluation. The histopathological study with histochemical staining confirmed the finding of a squamous-cell carcinoma of the bladder.

Resumen

El cáncer de vejiga es la causa más común de malignidad del sistema urinario. Dentro de su espectro clínico se puede manifestar como hematuria no dolorosa, síntomas urinarios irritativos (polaquiuria, urgencia, disuria) y obstrucción urinaria, hallazgos que pueden retrasar el diagnóstico debido a sus similares características con otras patologías benignas (infección de tracto urinario, prostatitis, litiasis, hiperplasia prostática benigna). De todas las neoplasias de la vejiga, el carcinoma escamocelular corresponde del 3 al 5 % en Norte América y Europa; el más común es el carcinoma de células transicionales con una frecuencia del 95 %. Se presenta el caso de un hombre de 53 años de edad con dolor abdominal y síntomas urinarios irritativos, en quien los estudios de imagen establecieron el diagnóstico de tumor de vejiga. Se le practicó una cistoscopia transuretral y se recolectaron especímenes para valoración por patología. El estudio histopatológico con análisis histoquímico confirmó el hallazgo de un carcinoma escamocelular de vejiga.

Introduction

Bladder cancer is the most common malignant tumor of the urinary system. Its estimated annual prevalence in the United States is approximately 77,000 cases and 16,000 deaths (1). Between 90 % and 95 % of bladder carcinomas are transitional cell carcinomas; however, there are other variants with a lower incidence, such as squamous cell carcinoma, which accounts for 2-5 %. Other less frequent types of bladder carcinomas are adenocarcinoma (0.5-2 %) and small cell carcinoma (<1 %). Squamous cell carcinoma can be of two types: not associated with schistosomiasis (NAS) and associated with schistosomiasis (AS). Within the NAS subtype there is a clinical relationship between squamous cell carcinoma, chronic bladder inflammation and urinary retention. Unfortunately, this type of carcinoma is usually diagnosed in advanced stages, with poor prognosis and low survival rates. Radical cystectomy is the treatment of choice, but there is discussion about the benefit of neoadjuvant or adjuvant therapy (2).

Case Report

A 53 year old male patient with a history of renal lithiasis and multiple admissions to the emergency department for left renal colic and recurrent urinary tract infections. He has images from 2014 showing bilateral renal lithiasis and large intravesical lithiasis, so he underwent open cystolithotomy with release of adhesions in the bladder. On admission she reported clinical symptoms of three days of evolution, characterized by colicky pain in the hypogastrium radiating to the bilateral lumbar region, associated with episodes of urinary retention, pollakiuria and hematuria. Physical

[1]Radiology Resident, Universidad del Norte. Barranquilla, Colombia.

[2]Radiologist, Hospital Universidad del Norte. Professor, Universidad del Norte. Barranquilla, Colombia.

[3]Radiologist, Radiology Department, Ayudas Diagnosticas Sura. Barranquilla, Colombia.

[4]Pathologist, Hospital Universidad del Norte. Professor, Universidad del Norte. Barranquilla, Colombia.

examination revealed a distended abdomen, positive peristalsis, painful bladder balloon on palpation, with no signs of peritoneal irritation. Due to the findings, bladder catheterization and paraclinical examinations were performed, the results of which were: elevated serum creatinine values of 2.0 mg/dL, pathological urine partial with pyuria, uncountable red blood cells, Gram-negative bacilli (3+ bacteria). Due to the clinical and paraclinical findings, as well as the patient's history, urinary tract ultrasonography was performed.

Imaging

Urinary tract ultrasound showed an enlarged bladder with an irregular solid mass with lobulated margins and heterogeneous echogenicity depending on the right inferolateral wall of the bladder, projecting into the lumen, with loss of the mural cleavage planes. The lesion was approximately 16 × 10 × 10 cm in size (L × AP × T) (Figure 1), with color Doppler flow enhancement, with monophasic waves of low resistance to spectral analysis (Figure 2). In addition, bilateral dilatation of the urinary tract with decreased size and parenchymal thickness of the right kidney was observed. Because of the ultrasound findings, tomography urography (CT) with contrast medium was indicated. The CT showed an irregular mass, with a wide base, with partially defined margins, lobulated, depending on the right inferolateral wall of the bladder, with extension towards the bladder base and neck, obstructing both ureterovesical junctions; in addition, loss of mural cleavage planes, heterogeneous enhancement after the administration of contrast medium, areas of low central density related to necrosis, with probable transmural extension (Figure 3). Likewise, a 2.8 cm diverticulum was found at the bladder base (figure 3), a 4.4 cm intravesical lithiasis (figure 4) and adenopathies in the bilateral internal iliac chain, with dominance in the left one of 1.3 cm in short axis. The prostate gland was displaced towards the bladder floor and minimally deviated to the left. Renal lithiasis associated with large bilateral hydronephrosis with right renal atrophy was also found (Figures 4 and 5). Cystoscopy was performed, which showed abundant sediment in the bladder, which prevented an adequate evaluation of its walls; bladder lavage was performed with an evacuator, in order to collect samples for pathological anatomy study.

Histopathology

The histopathological study identified necrotic material intermixed with fibrin, blood and mixed inflammatory infiltrate with foci of abscessation; minimal viable component of anaplastic cells of squamous aspect, atypical mitoses, apoptotic cells with evidence of keratization and formation of "horny pearls".

Immunohistochemistry confirmed its squamous epithelial lineage; in addition, the second biopsy showed infiltration of the bladder muscle layer, without lymphovascular or perineural invasion in the material examined.

Morphological and immunohistochemical analysis confirmed the diagnosis of poorly differentiated infiltrating squamous cell carcinoma (Figure 6).

Discussion

Bladder cancer is the most common cause of malignancy in the urinary tract, with approximately 77,000 new cases and 16,000 deaths per year in the United States (1). In Colombia it is the fourth leading cause of cancer in men with an incidence of 863 cases per 100,000 inhabitants (3). Bladder cancer refers to a wide spectrum of neoplasms, among which squamous cell carcinoma is an infrequent histopathological variant, and corresponds to 2-3 % of cases; compared to urothelial carcinoma, the most common variant, which corresponds to 90-95 % of cases (1).

The association between chronic bladder irritation and squamous cell carcinoma has been postulated in multiple articles, considering that chronic inflammation creates an environment conducive to squamous metaplasia and cancer development, given by the abundant growth factors and cytokines that favor cell proliferation, migration, angiogenesis and inhibition of apoptosis, resulting in these changes. Conditions that are associated with this chronic inflammation include: chronic or recurrent urinary tract infection, chronic bladder catheter use, neurogenic bladder, bladder lithiasis, presence of foreign bodies, bladder exstrophy, and prolonged exposure to cyclophosphamide (1, 4, 5). In the present case, as evidenced in the tomographic study, the patient had bladder lithiasis, and a history of repeated urinary tract infections that generated this chronic inflammation.

In most patients, squamous cell carcinoma of the bladder manifests with hematuria; however, there may be less common and non-specific symptoms, urinary irritative symptoms, urinary obstruction and weight loss (4).

Figure 1. Ultrasound, 2D, axial transverse plane. Urinary bladder with irregularity of its walls, associated with mobile intravesical lithiasis. Unequal mass with lobulated margins and heterogeneous echogenicity depending on the bladder wall.

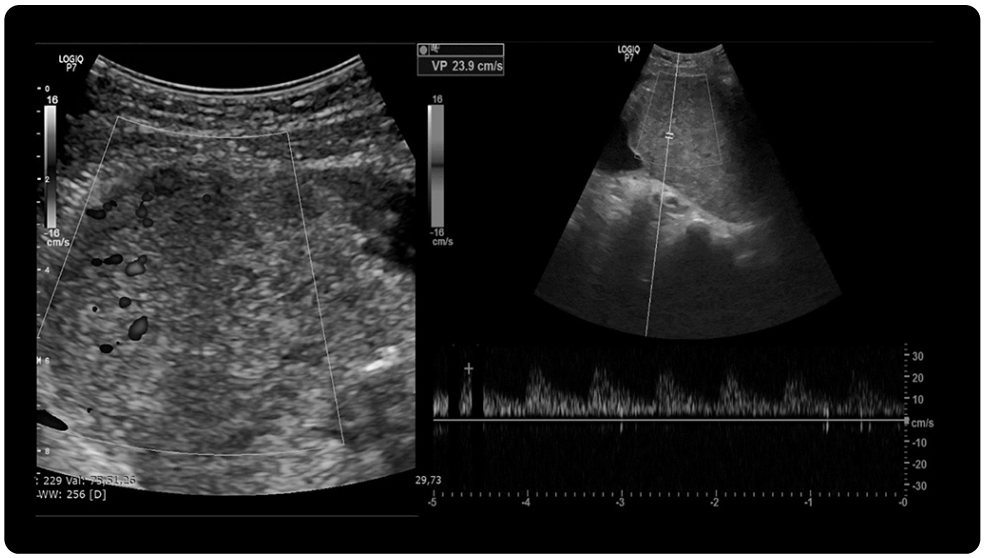

Figure 2. 2D ultrasound, duplex/triplex mode in axial and longitudinal plane. Solid mass, irregular, heterogeneous echogenicity, dependent on the right inferolateral wall of the bladder with loss of cleavage planes. It shows internal flow on color Doppler analysis with low resistance monophasic wave morphology and low peak systolic velocity (PV) of 23.9 cm/s.

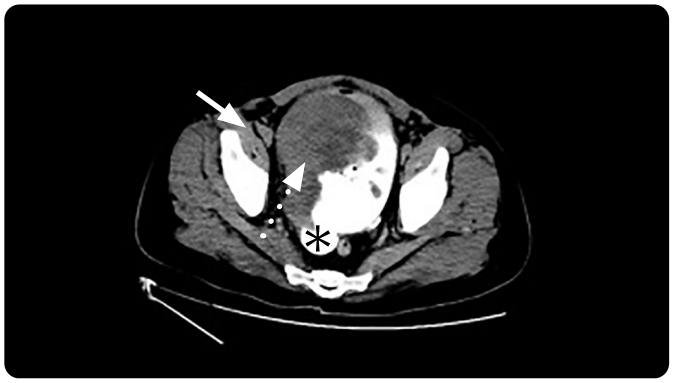

Figure 3. Multidetector computed urotomography, with contrast medium, transverse section in excretory phase. Irregular mass, with wide base, with partially defined margins, depending on the right inferolateral wall of the bladder, with extension towards the base and neck of the bladder, obstructing both ureterovesical junctions; it presents heterogeneous enhancement with the administration of contrast medium (solid arrow), with areas of central necrosis (dotted arrow). It is associated with striation of perivesical fat and prevesical space, suggesting extramural involvement. Adenomegaly in internal iliac chains, dominant left 1.3 cm in the short axis. Diverticulum in the vesical base of 2.8 cm (asterisk).

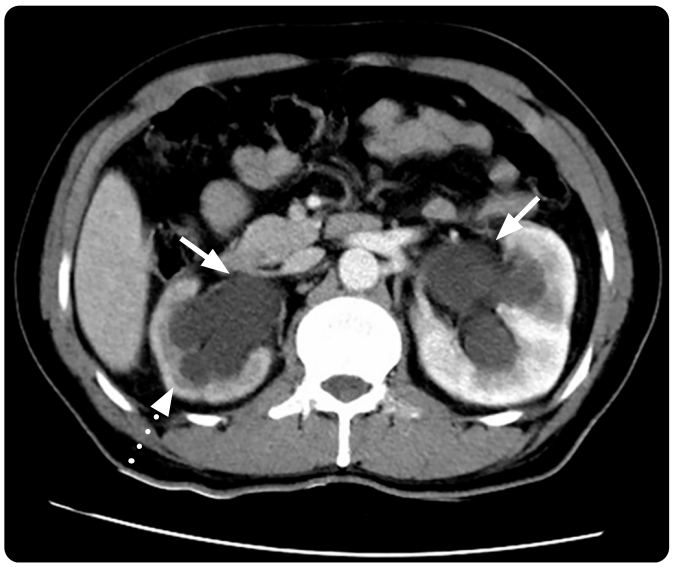

Figure 4. CT urography, transverse section. Bilateral renal lithiasis (not shown in the image). Bilateral hydronephrosis of the urinary tract (solid arrows). Asymmetry in renal size with smaller right kidney with thinning of its parenchyma (dotted arrow).

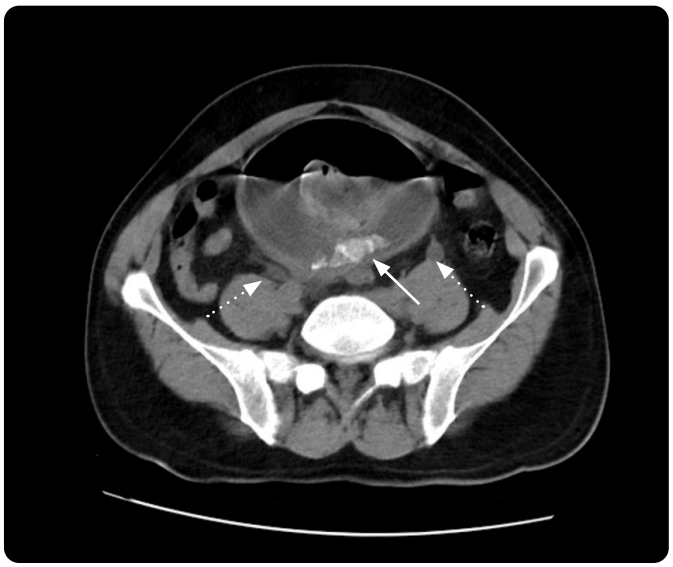

Figure 5. Multidetector computed urotomography, single phase axial view. High density image, irregular, 4.4 cm and 200 HU of density in the declivity zone, compatible with bladder lithiasis (solid arrow). Hydroaerial level in the bladder secondary to manipulation of the urinary tract. Bilateral ureteral dilatation (dotted arrows).

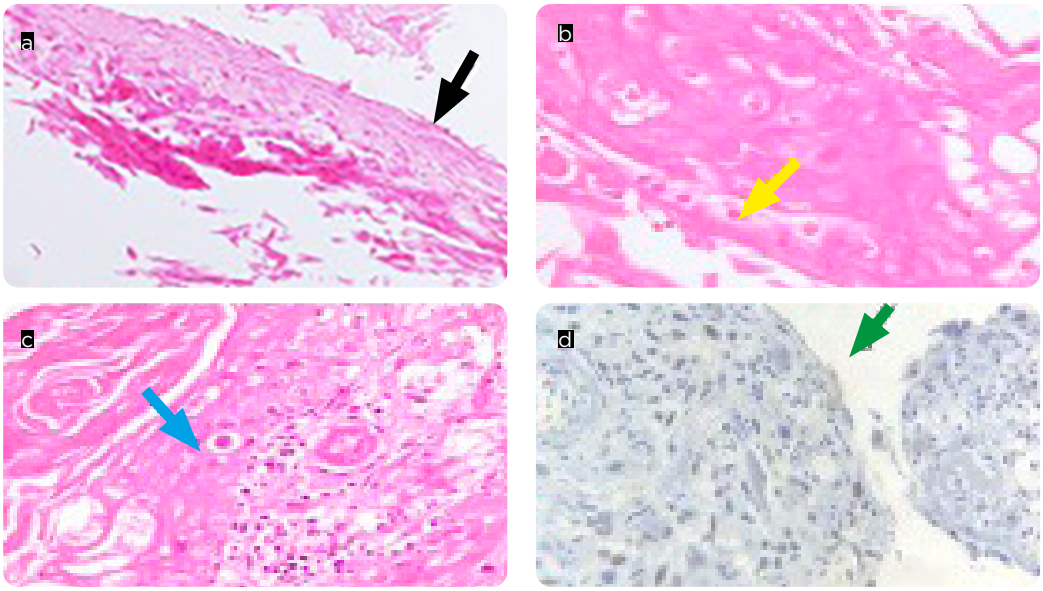

Figure 6. Histopathology. a) Hematoxylin-eosin stain: shows lamellar keratin (black arrow). b) Phantom cells, keratinocytes without nucleus (yellow arrow). c) Horny pearls (blue arrow). d) Nuclear p63 labeling, of viable sample, positive, indicating squamous differentiation (green arrow).

Two variants of squamous cell carcinoma have been described: NAS and AS. The former is more prevalent in endemic regions, such as South America, Southeast Asia, and the Middle East, with a higher prevalence in men than in women - 5:1 ratio. The latter has been documented more frequently in patients with spinal cord injury, prolonged bladder catheter use, chronic bladder irritation from multiple causes, and urinary stasis, conditions that favor chronic inflammation as mentioned; similarly, a higher prevalence has been described in men than in women with a 3:2 ratio (1).

Macroscopically, it is usually a large, bulky and, in some cases, predominantly flat exophytic tumor with an ulcer-like appearance; it typically has a whitish coloration and is often necrotic with keratin material on the surface (6).

Microscopically the degree of differentiation is variable, irregularly infiltrating malignant squamous cell nests or sheets with stromal invasion, keratin bead-like squamous differentiation, keratinization of individual cells or intercellular bridges are seen; findings may be focal in poorly differentiated tumors. Does not show components of conventional urothelial carcinoma or urothelial carcinoma in situ; if present, the tumor is designated as urothelial carcinoma with squamous differentiation and not as a squamous cell carcinoma.They usually show positive CK5/6, p63, CK14 and desmogelin-3 markers (6).

Regarding the approach, it is considered that any patient with suspected bladder cancer should be evaluated by cystoscopy, which allows direct visualization of the bladder and biopsy. It is typically seen as a solitary, large, extensive mass associated with leukoplakia (1, 7).

In terms of imaging evaluation, computed tomography (CT) and magnetic resonance imaging (MRI) play a very important role in staging. Ultrasonography (US) is less accurate in the diagnosis of these pathologies; however, in many patients it is the first study performed and it is usually an incidental finding, a hypoechoic image in polypoid or plaque form that is projected in the bladder lumen, in addition, echogenic areas related to calcifications or fibrosis. In the evaluation with color Doppler, increased flow in the lesion is observed (7).

CT is the main imaging modality in the evaluation of bladder tumors. The accuracy of local staging varies between 55 % and 92 %. There are multiple acquisition protocols, the most frequent consisting of a single administration of a bolus of contrast medium with acquisitions in arterial, venous and excretory phases (7, 8).

In the study without contrast medium, a low density lesion can be identified, which projects towards the bladder lumen, or as a focal thickening of the wall; the presence of calcifications has been described. After the administration of intravenous contrast medium, in the arterial phase, enhancement of the lesion is observed, which usually has a polypoid or plaque shape. In the late phases, a filling defect of the lesion occupied by urine, with high attenuation, can be identified as the bladder fills. Focal or, unusually, diffuse bladder wall thickening may be identified. Assessment of the depth of wall invasion is limited by this imaging modality. In lymph node staging, the accuracy of CT is 50-97 % (7). It must be determined if there is regional lymphatic involvement, which includes perivesical, obturator, internal and external iliac, sacral and common iliac nodes; in addition, it is always recommended to evaluate and describe if there is extranodal involvement (9).

MRI is superior to CT in terms of its multiplanar capability and higher soft tissue contrast, but has been shown to have similar staging accuracy (72 %-96 %). Staging accuracy is improved with gadolinium administration. In these patients, multiparametric evaluation with conventional and functional sequences is used (7,10), which allows differentiation of the layers of the bladder wall and provides the ability to distinguish between cancer with involvement of the muscular layer and those that do not; patients with invasion are at greater risk of metastatic disease. Survival after radical cystectomy is 68 % for patients with pathology confined to the bladder, compared to those with extravesical extension, with survival of 25-30 % (11). Patients who do not show invasion have a variable prognosis depending on the individual risk profile, with recurrence between 30-80 %, progression 25 %-50 % and cancer-related death 16 %-23 % in 5 years after treatment, with bladder preservation (11). In order to assess whether invasion is present or not,

the VI-RADS (Vesical Imaging-Reporting and Data System) bladder imaging data and reporting system has been developed. Recent validation of this system has found it to have adequate diagnostic accuracy (11). T2-weighted MR images in axial, coronal and sagittal planes, diffusion sequences (DWI) with high b values (b = 800-1000 s/mm2), and sequences with dynamic contrast medium (DCE) administration should be included in the protocol; in addition, T1-weighted images should be included. Images of the entire bladder, proximal urethra, pelvic nodes and prostate should be included, if the patient is male; in the case of female patients, the uterus, ovaries, fallopian tubes and vagina should be included (11, 12).

T1-weighted images are useful to evaluate perivesical fat, determine extravesical involvement, evaluate pelvic nodes and identify bone metastases. The intravesical lesion has an intermediate signal intensity in relation to the fat (7, 10, 13).

In T1-weighted images with contrast medium, the lesion shows enhancement. In dynamic sequences, the lesion, mucosa and bladder submucosa show early enhancement compared to the muscle wall, which shows delayed enhancement approximately 60 seconds after gadolinium administration. In addition, this sequence allows assessment of adjacent organ involvement (7, 10).

T2-weighted images are used to evaluate the detrusor muscle, tumor depth and invasion of surrounding organs. In this sequence, the lesion has an intermediate signal, slightly higher than that of the bladder wall. The detrusor muscle normally has a low signal in this sequence; when alteration of this signal is observed, invasion of the muscular layer must be suspected (10, 13).

Conclusion

Squamous cell carcinoma of the bladder is a rare malignant lesion, with very low incidence and widely related to factors predisposing to chronic inflammation of the bladder. Diagnostic imaging, mainly CT and MRI, play an important role in the detection and staging of these lesions; although MRI has greater functionality, as it allows the evaluation of the layers of the bladder wall, in order to better guide the management of these patients.

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Correspondence

Julio Jesús Goenaga Pareja
Transversal 43C # 102-153
Barranquilla, Atlántico
jjgoenaga@uninorte.edu.co

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