doi: 10.3978/j.issn.2095-6959.2021.10.001
View this article at: https://dx.doi.org/10.3978/j.issn.2095-6959.2021.10.001

· International Clinical and Pathological Column ·

An unexpected urinary bladder xanthoma: Case report

Martina Mandarano[1], Guido Bellezza[1], Giovanni Cochetti[2], Giulio Metro[3], Ettore Mearini[2], Rachele Del Sordo[1]

(1. Department of Medicine and Surgery, Section of Anatomic Pathology and Histology, University of Perugia, Perugia, Italy;
2. Department of Medicine and Surgery, Division of Urology Clinic, University of Perugia, Perugia, Italy;
3. Medical Oncology, Santa Maria della Misericordia Hospital, Perugia, Italy)

Abstract In spite of the fact that xanthomas of the skin, tendons and mucosae are relatively common conditions, urinary bladder xanthoma is a rare benign lesion, only occasionally reported in literature. It usually appears as an exophytic mass into the bladder cavity, which often worries the clinicians, because it is considered as a neoplasm that need both an excision and follow-up. We herein describe the 32nd case, accidentally identified in a 63-year-old man with a right urinary bladder mass on follow-up abdominal ultrasound scan for a previous open pyeloplasty. He also referred mild obstructive lower urinary tract symptoms. Consequently, a cystoscopy with biopsies was performed and the subsequent histopathological examination was consistent with the diagnosis of urinary bladder xanthoma. Therefore, no additional therapeutics interventions were needed, and the patient currently presents nor symptoms, recurrences, or other pathologies. Although its rarity, it is important to correctly identify urinary bladder xanthoma, differentiating it from other pathological entities which present similar histopathological characteristics, but which sometimes could be associated with a patients' dismal prognosis. Moreover, an accurate diagnosis of urinary bladder xanthoma can avoid both additional treatments and follow up, but also allows to recognize some potential detrimental pathologies which could be associated with it, such as either an altered lipid metabolism or urothelial neoplasms. Proper and prompt recognition and treatment of these last can notably improve patient's outcome.

Keywords Urinary bladder xanthoma (UBX); rare urinary bladder lesion; incidental urological finding; case report

Xanthoma is usually a benign lesion, which occurs more commonly in the skin and tendons, often along with abnormality of lipid metabolism[1-2]. Despite of this, urinary bladder xanthoma (UBX) is a very rare entity, accounting for only 31 cases reported in the worldwide literature[3-6]. Endoscopically, it appears as an exophytic yellowish mass. On microscopy, lipid-laden foamy macrophages within the lamina propria, without any others inflammatory or giant cells, characterize the UBX[3]. UBX usually presents either as isolated mass or together with urothelial neoplasms[3,6-7]. Noteworthy, UBX is important to be recognized, because both follow-up and surgical excision are not needed, unlike other disorders which enter in differential diagnosis with it[3-4]. We herein describe the 32nd case of UBX, unexpectedly examined at our institution.

We present the following article in accordance with the CARE reporting checklist (available at https://dx.doi.org/10.3978/j.issn.2095-6959.2021.10.001).

1 Case presentation

A 63-year-old Caucasian male patient, former heavy smoker, suffering from glaucoma, bronchial asthma and hearing loss, underwent abdominal ultrasound scan (US) on 3rd April 2018 during follow-up for left

Submitted May 07, 2021. Accepted for publication May 11, 2021.

Corresponding author: Martina Mandarano. Email: martina.mandarano@unipg.it

pyeloureteral junction syndrome successfully treated by open pyeloplasty 40 years before, as reported in Table 1.

Moreover, the patient referred mild obstructive lower urinary tract symptoms related to a benign prostatic hyperplasia. There was neither hematuria nor abnormal lipid profile.

The US performed (Table 1) showed a 5 mm hyperechoic, not fixed, right bladder mass. Therefore, both a cystoscopy (Table 1) and an abdomen-pelvis CT scan (Table 1) were performed, which highlighted a vegetative neoplasm of the right lateral bladder wall, with narrow base and adherent calcifications.

The diagnostic hypothesis of a urothelial neoplasm was made without particular effort, and a cystoscopy with biopsies was performed (Table 1), which revealed multiple urinary bladder yellowish fragments, made up of papillary structures without epithelial atypia—excluding a urothelial carcinoma, but not other neoplastic lesions—along with several histiocytes within the lamina propria (Figure 1A)—opening issues regarding the differential diagnosis of urinary bladder conditions in which histiocytic cells are participating, with both benign and malignant behavior, such as physiological urothelium, malakoplakia, xanthogranulomatous cystitis, urinary bladder xanthoma, superficial layers of urothelial neoplasms, granular cells tumor and signet ring carcinoma. Therefore, the histiocytes were analyzed with immunohistochemistry (Figure 1B-1D), whose results are listed in Table 2. Moreover, the cells were not proliferating (0 mitosis/10 high power field and Ki-67/Mib-1=0). There were neither other inflammatory cells, giant cells nor Michaelis-Gutmann inclusion bodies [negativity for Periodic Acid Schiff stains (PAS) and PAS-D]. These findings were consistent with the diagnosis of urinary bladder xanthoma.

According to the good prognosis of these lesion, the patient did not undergo further therapies and follow-up. However, the patient's follow-up for his treated left pyeloureteral junction syndrome allowed to know that he is currently alive and without urinary bladder recurrences/pathologies.

Table 1 Case report timelines

Episode of care/diagnostic test	Date	Finding(s)
Left open pyeloplasty	1978	Pyeloureteral junction syndrome
Abdominal US—follow-up procedure	3rd April 2018	5 mm urinary bladder right mass
Cystoscopy	16th April 2018	Vegetative neoplasm of the right lateral bladder wall
Abdomen-pelvis CT	21st May 2018	Vegetative neoplasm of the right lateral bladder wall
Cystoscopy with Biopsies	21st June 2018	Multiple urinary bladder yellowish fragments

US, ultrasound scan; CT, computerized tomography.

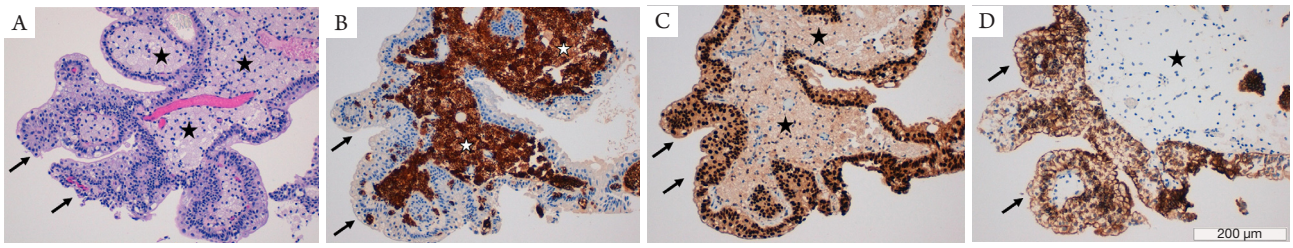

Figure 1 Histopathological findings

(A) Hematoxylin and eosin stain, showing the papillary architecture of the lesion; the black stars indicate the foamy gray macrophagic cells within the lamina propria of papillary stalk; the black arrows show the urothelial lining layer. (B) CD68 positive immunohistochemical stain highlighting the histiocytic (white stars) nature of the lamina propria cells; the black arrows indicate the negative transitional cells. (C) Nuclear GATA3 positivity confirming the urothelial nature of the epithelial lining cells (black arrows); on the other hand, the negative stain (black stars) corroborates the histiocytic nature of the foamy cells within the lamina propria. (D) Also, the cytoplasmic negativity for Cytokeratin 20 allows to define the foamy cells of lamina propria as histiocytes (black star). The black arrows show the urothelial positive cells. Original magnification: ×200; the scale bar indicates 200 μm.

Table 2 Immunohistochemical analysis of histiocytic cells

Antibody	Clone	Dilution	Brand	Result
CD68	KPI	RU	Cell Marque	+
S-100	Polyclonal	RU	Leica	–
p53	DO-7	RU	Leica	–
p63	7JUL	RU	Leica	–
GATA 3	L50-823	RU	Cell Marque	–
Panck	5D3 and LP34	1:100	Leica	–
CK 20	KS20.8	RU	Leica	–

RU, ready to use; GATA 3, GATA binding protein 3; Panck, pancytokeratin; CK 20, cytokeratin 20.

2 Discussion

A further case of urinary bladder xanthoma (UBX), a rare pathological lesion described on only thirty-one occasions in literature[3-6], was observed. Although exceedingly rare at urinary bladder level, xanthoma is common in other sites, such as the skin, tendons or mucosae, e.g., the gastric one[2-3,8]. However, UBX should be recognized because it is a benign lesion with good prognosis, which does not need neither follow-up nor more careful management, otherwise required for other bladder masses[1-2,5].

UBX shows a variable male to female ratio[1,3,5-7]. It arises almost always in old patients (mean age 62.5 years)[3]; this lesion is usually asymptomatic, even if the patient could present hematuria, lower abdominal pain or urinary retention[1,3,7]. The UBX has the appearance of flat either yellow or yellow-white plaques or patches of the mucosa, which measure from few millimeters to few centimeters. No preferred site of localization onto bladder walls has been described[3]. The pathogenesis is still unknown, although an association with lipid disorders has been reported, such as either lipid profile alterations or secondary hyperlipidemia due to diabetes mellitus or primary biliary cirrhosis[1,3,7-8]. Moreover, UBX could be associated with local trauma, such as local surgery and inflammation[7-8]. It was supposed that the lipid metabolism alteration within the urinary bladder mucosa could explain its development. Moreover, it has been suggested that endothelial, stromal and epithelial cells may be transformed into xanthoma cells[7-8]. However, the described case was no associated with an impaired lipid metabolism, arising further debate about UBX pathogenesis.

Urothelial neoplasms could be sometimes associated to the UBX, supposing a combined effect of exposure to local predisposing factors, such as either an increased lymphovascular permeability or an altered serum lipoprotein level[3,7]. However, xanthomas are usually associated with low malignant potential urothelial neoplasms[3,5-6]; especially, only two cases were described in association with a high-grade invasive urothelial cell carcinoma[6-7].

Furthermore, it has to be considered that foamy macrophages in the lamina propria could be physiologically present in the urothelium or in the superficial layers of urothelial neoplasms[3].

Many pathologic lesions should be differentiated from UBX.

Firstly, the xanthogranulomatous cystitis, which localizes preferentially in either the bladder dome or bladder anterior wall; it is characterized by the presence not only of histiocytes, but also of multinucleated giant cells, inflammatory cells and cholesterol clefts, which are not usually found in xanthomas, such as in the current case[1,3-4,8].

It is also to take into account malakoplakia, in which Escherichia Coli elicits an abnormal macrophage response; however, the lack of the distinctive Michaelis-Gutmann bodies[3-4,8-9] in the current case, confirmed by the negativity of PAS and PAS-D stains, allowed us to exclude this pathology.

In addition, granular cells tumor, a usually benign neoplasm, characterized by a granular eosinophilic cytoplasm, could mimic UBX. However, this latter presents a slightly basophilic foamy cytoplasm and the typical positivity for both CD68 and S-100 of granular cells tumor allows the correct diagnosis[3-4].

Finally, a signet ring carcinoma—both as rare primitive histotype of urinary bladder carcinoma and as a metastatic localization—could simulate an UBX, but the neoplastic cells usually exhibit a characteristic signet ring morphology and also a diffuse immunostain for pancytokeratin[3-4,8].

Urinary bladder xanthoma is a localized benign lesion, with both no malignant potential and a good prognosis. Although rare, it should be considered among the clinical-pathological differential diagnosis of no malignant urinary bladder masses in old patients. The biopsy during cystoscopy could be an efficient tool for the correct histological diagnosis, avoiding both unrequired and harmful overtreatment, such as unnecessary resections. Moreover, no follow-up is needed. However, both the patients' lipid profile and the simultaneous presence of a urothelial neoplasm should be investigated, due to the possible relationship between UBX and these underlying potential detrimental conditions. For these reasons, properly and promptly recognition of UBX can improve substantially the patient's outcome.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Journal of Clinical and Pathological Research* for the series "International Clinical and Pathological Column". The article has undergone external peer review.

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://dx.doi.org/10.3978/j.issn.2095-6959.2021.10.001

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.3978/j.issn.2095-6959.2021.10.001). The series "International Clinical and Pathological Column" was commissioned by the editorial office without any funding or sponsorship. GB serves as an unpaid editorial board member of *Journal of Clinical and Pathological Research* from Apr 2021 to Mar 2023. GM serves as an unpaid editorial board member of *Journal of Clinical and Pathological Research* from Apr 2021 to Mar 2023. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and the Harmonized Tripartite Guideline for Good Clinical Practice from the International Conference on Harmonization. All patient's information, data and images were properly anonymized, to respect confidentiality and protection of patients' data, in compliance with the processing of data covered and protected by the Italian Privacy Law and by the GDPR (General Data Protection Regulation, EU regulation n.2016/679) and it is impossible for the patient to be identified.

References

1. Shah SJ, Ajitsaria V, Singh V. Urinary bladder xanthomatous cystitis[J]. Indian J Urol, 2017, 33(1): 79-81.
2. Hassouna H, Broome JD, Swalem K, et al. Xanthoma of the urinary bladder: a rare benign condition which may be mistaken for malignancy[J]. BMJ Case Rep, 2014, 2014: bcr2014203836.
3. Yu DC, Patel P, Bonert M, et al. Urinary bladder xanthoma: a multi-institutional series of 17 cases[J]. Histopathology, 2015, 67(2): 255-261.
4. Raghavendran M, Venugopal A, Kaushik VN. Urinary bladder xanthoma—is immunohistochemistry necessary?[J]. Urol Case Rep, 2016, 8: 36-37.
5. Martí Mestre J, Delagneau Rivas J, Bosch Princep R, et al. Xantoma vesical. Hallazgo cistoscopico[J]. Actas Urol Esp, 2004, 28(8): 617-619.
6. Piol N, Mantica G, Banchero R, et al. Urinary bladder xanthoma: Two case reports and a review of the literature[J]. Arch Esp Urol, 2018, 71(10): 862-866.
7. Skopelitou A, Mitselou A, Gloustianou G. Xanthoma of the bladder associated with transitional cell carcinoma[J]. J Urol, 2000, 164(4): 1303-1304.
8. Miliauskas JR. Bladder xanthoma[J]. Histopathology, 1992, 21(2): 177-178.
9. Vimal M, Masih D, Manipadam MT, et al. Xanthoma of the urinary bladder—a rare entity[J]. Indian J Urol, 2012, 28(4): 461-462.

Cite this article as: Mandarano M, Bellezza G, Cochetti G, Metro G, Mearini E, Del Sordo R. An unexpected urinary bladder xanthoma: Case report[J]. Journal of Clinical and Pathological Research, 2021, 41(10): 2227-2230. doi: 10.3978/j.issn.2095-6959.2021.10.001