

BLADDER XANTHOMA: AN UNUSUAL BUT INCREASINGLY FREQUENT PRESENTATION OF A BENIGN BLADDER LESION

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Abstract

A 35-year-old male presented with multiple interrupted episodes of frank hematuria and persistent microscopic hematuria. CT urogram demonstrated a nonspecific lesion in the bladder. Cystoscopy showed a lesion in the bladder wall that was biopsied, and histopathology confirmed a xanthoma, a rare diagnosis in the bladder. This case report performs a review of current literature and examines necessary investigations, differential diagnoses, and management required for bladder xanthoma.

Keywords: *benign; bladder; foamy macrophages; histiocytes; xanthoma*

INTRODUCTION

Urinary bladder xanthoma (UBX) is a rare benign disorder of lipid-laden histiocytes, also known as foam cells,¹ which proliferate within the urothelial lining. Some studies have reported its possible association with cutaneous xanthoma and hyperlipidemia syndromes,² although there are no reported cases for both.³ Cutaneous xanthoma is typically found in the palmar and extensor surfaces, and its presence in other anatomical regions is poorly understood and often missed on clinical examination. Bladder xanthoma seems to be extremely rare. A PubMed literature search demonstrated 12 case reports and a single case series. This is likely to be an underreported finding in view of the benign nature of the disease and poor understanding among professional consensus.

CASE REPORT

A 35-year-old male presented with six episodes of frank hematuria and persistent microscopic hematuria. The patient also complained

of clots, dysuria, and suprapubic tenderness. Initial investigations included a blood profile, CT urogram, and a flexible cystoscopy.

CT urogram did not elicit a detailed analysis of the lesion, and noted only a small enhancing focus in the bladder. The flexible cystoscopy demonstrated a small, yellow, lipomatous-looking sandy patch in the posterior bladder wall (Figure 1). These macro-histological findings are typical of UBX.

Under rigid cystoscopy, two 2 × 3 × 3 mm biopsies of the lesion were taken. An analysis with H&E staining (Figure 2) demonstrated the typical microscopic appearance suggestive of an epithelial xanthoma. The initial histology report showed focal aggregates of foamy macrophages, congestion, and mild chronic inflammation in the lamina propria. There was no evidence of carcinoma in situ or malignancy. Immunohistochemistry for CD68 confirmed that these were indeed foamy macrophages.

The patient's blood samples did not demonstrate any specific metabolic disorders.

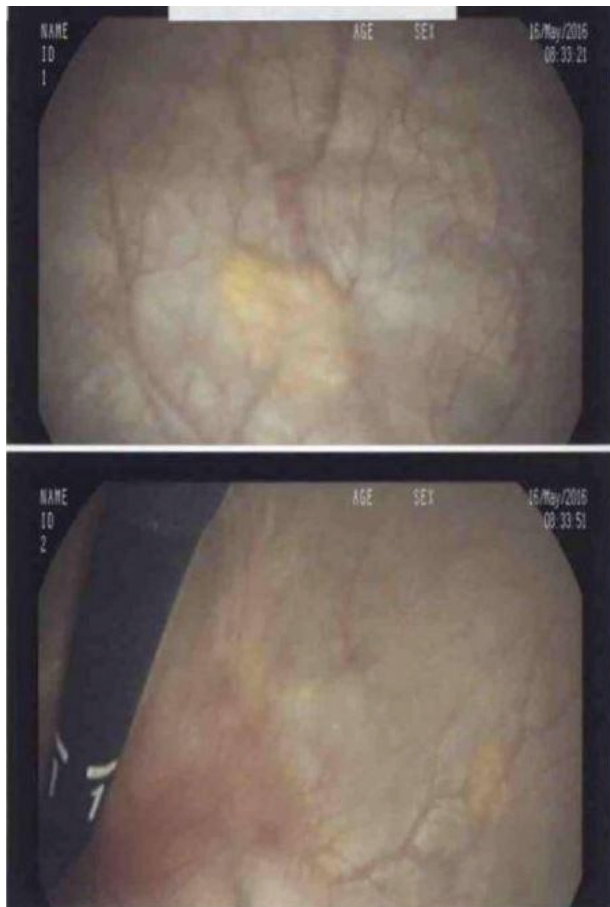


FIGURE 1 Flexible cystoscopy image demonstrating multifocal yellow lesions, a characteristic of xanthoma.

He was not diabetic and reported no significant medical history.

DISCUSSION

As mentioned above, UBX is a rare pathology, which is typically found incidentally during flexible cystoscopy. A literature search (Table 1) in PubMed provided 13 relevant reports with one case series of 17 patients and 12 case reports (two reports with 2 patients and 10 reports with single cases). The estimated incidence of bladder xanthomas associated with urothelial neoplasms was 0.34–0.38%,² based on a case series from two institutions. The incidence of isolated xanthomas is unknown due to

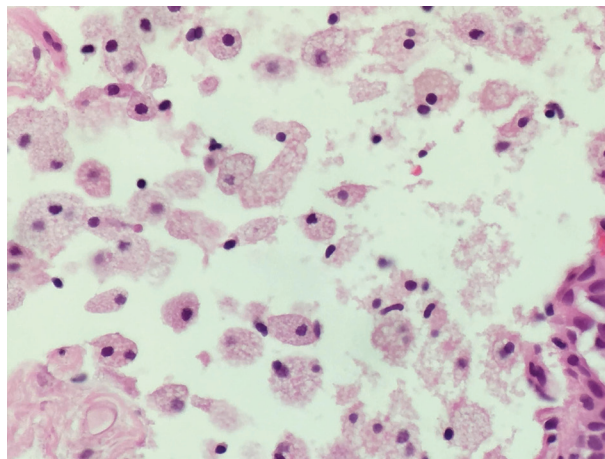


FIGURE 2 H&E staining of the lesion demonstrating foamy macrophages.

the benign nature of the condition but is considered to be rare, given lack of reporting.

Most patients are asymptomatic; however, some patients present with nonspecific lower abdominal pain and/or hematuria. Macroscopically, it is normally seen as a yellowish white plaque with a variable size of up to 20 mm with a velvety and irregular surface.⁷ The typical appearances are contributed by the numerous lipid-rich foamy cells.¹

Xanthomas are grossly classified as a reactive histolytic proliferation that can be seen in other parts of the body such as the skin and tendons. It can be suggestive of lipid metabolism disorders and is commonly seen in primary or secondary hyperlipidemia, usually due to diabetes mellitus. Hyperlipidemia is well established in cases of cutaneous xanthoma. In view of this, a global metabolic profile including lipids should be considered when working up patients with suspected UBX. Another hypothesis suggests that bladder xanthoma can also develop in response to a local inflammation or insult.¹³

Xanthoma is a benign condition with no known cases of malignant transformation. However, 15^{2,11–13} of the 31 cases reviewed during our literature search had coexisting neoplasms. Most of these neoplasms were incidental findings and were of low grade with minimal clinical significance. However, one

TABLE 1 Summary of the 13 articles found during literature review with a total of 31 patient cases. Sixteen cases from the top of the table describe xanthomas without associated neoplasms, and 15 cases on the bottom half of the table describe cases with associated neoplasms.

Authors	Location	Size	Histology	Carcinoma	Lipid disorder	Age	Gender	Presentation
Chitale et al. ⁴	Posterior wall	15 mm	Foam cells in the lamina propria with a normal overlying urothelium	NIL	NIL	63	Male	Macroscopic hematuria and passage of debris per urethra
Vimal et al. ⁵	Dome of bladder	5 × 5 mm	Foam cells in the lamina propria, Cytokeratin -ve, CD68 +ve	NIL	NA	46	Female	Microhematuria, urgency, incontinence
Lindboe ⁶	Dorsal to the right ureteral ostium	NA	Foam cells without multinuclear cell forms or an inflammatory response, CD68 +ve	NIL	NA	78	Female	F/U post-transurethral resections of noninvasive Grade 1 papillary urothelial carcinomas
Hassouna et al. ⁷	Near left ureteric orifice	NA	Foam cells, CD68 +ve	NIL	NIL	77	Male	Recurrent UTIs
Kobayashi et al. ⁸	Left lateral wall	NA	Aggregation of foam cells in the submucosa and a few lymphocytes	NIL	NIL	55	Male	Asymptomatic macroscopic hematuria
Al-Daraji et al. ⁹	Dome of bladder	NA	Foam cells, CD68 +ve	NIL	NIL	74	Female	Frequency and microscopic hematuria
	Dome of bladder	10 mm	Foam cells, CD68 +ve	NIL	NIL	53	Male	Microscopic hematuria
Raghavendran et al. ¹⁰	NA	NA	Large foamy histiocytes without any other inflammatory cells and scattered blood vessels	NIL	NA	34	Male	Left flank pain

(continues)

TABLE 1 (Continued)

Authors	Location	Size	Histology	Carcinoma	Lipid disorder	Age	Gender	Presentation
Miliauskas ³	Right of the trigone	5 × 5 mm	Foam cells	NIL	NIL	79	Male	Routine F/U; Bladder neck TCC 12 years ago treated with local excision and radiotherapy
Nishimura et al. ¹	Left posterior wall	10 × 10 mm	Foam cells	NIL	Hyperlipidemia	61	Male	Abdominal pain due to right ureteral stone
Yu et al. ²	No predilection	1–40 mm	Foam cells. CD68 +ve	NIL	Hyperlipidemia or hypercholesterolemia	Average 65.3	M:F = 1:1	Microscopic hematuria, irritative symptoms
	No predilection	4–19 mm	NA	Urothelial papilloma (n = 3); inverted papilloma (n = 1); PUN-LMP (n = 2) and low-grade noninvasive urothelial carcinoma (n = 5)	5 of the 11 cases had hypercholesterolemia	Average 62.5	All male	Microscopic hematuria, irritative symptoms, incidental
Piol et al. ¹¹	NA	NA	Plurifocal aggregates of foam cells. CD68 +ve	Carcinoma in situ (pTis), noninvasive high-grade papillary carcinoma (pTa-G3)	Primary dyslipidemia	75	Male	Macrohematuria
	NA	Microscopic	NA	Microinvasive urothelial papillary carcinoma	Primary dyslipidemia	68	Male	Macrohematuria and acute urinary retention
Shah et al. ¹²	Right anterosuperior bladder wall	61 × 23 × 43 mm	Foam cells in all layers of urinary bladder	6 × 5 cm urothelial papilloma	NIL	38	Female	Abdominal pain
Skopelitou et al. ¹³	Left of trigone	18 × 20 mm	Foam cells adjacent to TCC	Superficially invasive Grade 2 TCC	NIL	65	Male	Hematuria, dysuria, and lower abdominal pain.

PUN-LMP = papillary urothelial neoplasm of low malignant potential; TCC = transitional cell carcinoma; UTI = urinary tract infection

report¹³ did include a transitional cell carcinoma. Thus, we believe that it is best if the lesion is biopsied to aid diagnosis and rule out possible coexisting neoplasms.

Macroscopically, other differential diagnoses of a white patch in the bladder include malakoplakia, xanthogranulomatous cystitis, granular cell carcinoma, and signet ring carcinoma.² In order to differentiate between these conditions, histopathology is essential, which helps assess the microscopic architecture.

Malakoplakia is caused by impaired macrophage response to *Escherichia coli*. In histology, it shows von Hansemann cells which are large histiocytes, and small basophilic calculospherules called Michaelis–Gutmann bodies which can be stained with iron, Periodic acid–Schiff stain, or von Kossa stain.⁵

Xanthogranulomatous cystitis is a rare chronic inflammatory condition seen in the bladder dome. It is differentiated from xanthomas by the presence of multinucleated giant cells and chronic inflammatory cells.¹ Granular cell tumor is normally a benign neoplasm, which on histology shows polygonal cells with small eosinophilic granules. This is shown as a pink granular cytoplasm. Signet ring carcinoma stains diffusely with pancytokeratin and has the usual signet ring pathology.²

Microscopically on histological analysis, findings of UBX include foamy macrophages, which contain phagocytosed and oxidized low-density lipoprotein, without evidence of underlying inflammation in the submucosal lamina propria.⁴ Foamy macrophages in the bladder can be found in other conditions such as malakoplakia, xanthogranulomatous cystitis, atypical mycobacterial infection, and signet ring carcinoma.⁴ Immunohistochemistry staining for anti-CD68 has been demonstrated as a mainstay method for confirming foamy macrophages although the necessity of this to diagnose xanthoma has been questioned by Raghavendran et al.¹⁰

The management strategies are broad and include initial conservative management; however, in cases with uncontrollable bleeding or causing

lower urinary tract symptoms, cystodiathermy, cold cup biopsy, transurethral resection, and partial cystectomy have been utilized. In terms of follow-up, as xanthomas possess no malignant potential, a follow-up cystoscopy is considered unnecessary. However, referral to endocrine physicians may be recommended in view of dyslipidemia, which is associated with similar xanthomata.⁸

CONCLUSION

Bladder xanthomas are rare disorders of the bladder. Macroscopically, it appears as a white velvety patch for which there are other differential diagnoses. Therefore, biopsy is recommended to distinguish it from other lesions and make sure that there are no coexistent neoplasms. Other investigations such as testing for lipid disorders should also be performed. Resection of xanthoma is useful in cases where it is symptomatic.

DECLARATIONS

Conflicts of interest

No conflicts of interest to disclose.

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