

Vesical Amyloidosis Masquerading as Bladder Cancer with Hematuria

Iqbal Singh^{1*}, Mohit Joshi², Usha Rani Singh³, Nirupama Khan³

Division of Urology¹, Departments of Surgery² & Pathology³, University College of Medical Sciences (University of Delhi) & GTBH, Delhi-95, India.

Abstract

To describe and report a case of an episodic painless hematuria, in a middle aged gentleman whose initial radiological work up and cystoscopic findings suggested localized carcinoma of the urinary bladder. Nuclear matrix protein and urine cytology were negative for urothelial tumor. Transurethral resection of bladder wall mass and pathology confirmed amyloidoma (vesical amyloidosis). Absence of clinical stigmata of secondary disease and appropriate histopathology confirmed the diagnosis of primary vesical amyloidosis. Diagnosis of vesical amyloidosis was based on the awareness of the existence of this entity and the use of appropriate histopathology and surgical resection was performed. We conclude that early diagnosis and prompt resection is necessary for localized vesical amyloidosis presenting primarily with hematuria.

Keywords: Amyloidosis, Vesical Amyloidosis, Urinary Bladder, Hematuria

Introduction

Vesical amyloidosis (VA) is a rare cause of hematuria with very few previously reported cases (1-4). The term amyloidosis covers a varied group of disorders in which proteinaceous (amyloid) material is deposited in various body tissues. The current case presented with gross hematuria and acute urinary retention and the CT scan suggested a bladder tumor like mass in the posterior wall. Cystoscopy showed velvety growth in the posterior wall of bladder which was biopsied and diagnosed on histopathology as VA. The case history, histological findings and the treatment of VA are being discussed. Vesical amyloidosis may mimic bladder carcinoma and may cause hematuria.

symptomatic localized amyloidosis of the urinary bladder have been reported in the literature. We report one such rare case, and discuss various treatment modalities.

Case Report

A 50-year-old man presented with acute urinary retention following painless gross total intermittent hematuria for the preceding two months. There was no history of dysuria, urosepsis, trauma, abdominal pain, blood dyscrasias, cardiovascular disease or systemic tuberculosis. General physical examination, local and systemic examination(s) were unremarkable. Digital rectal examination suggested grade I prostatomegaly.

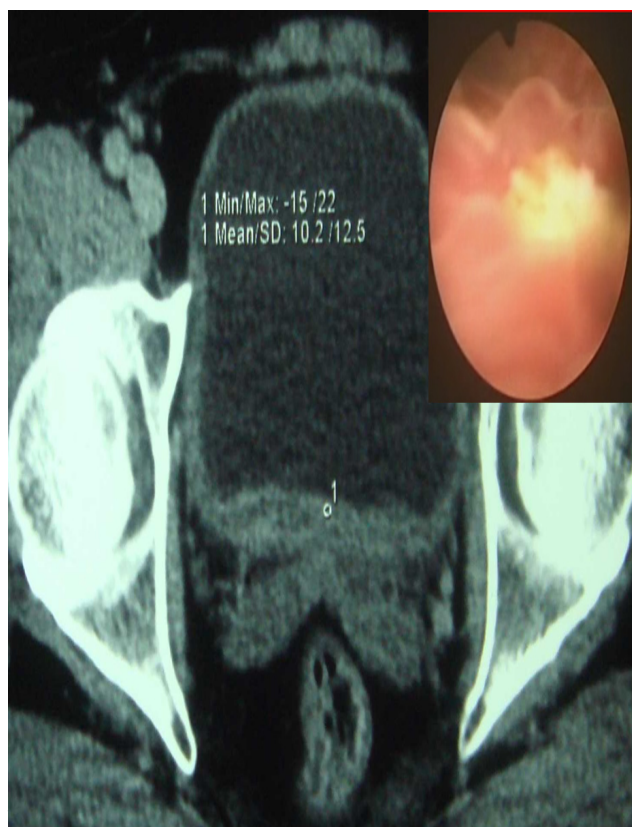
Hematological and coagulation parameters were within normal limits. Urine analysis showed several RBCs and mild albuminuria. Urine cytology for malignant cells and urinary NMP and urine-AFB were negative. Abdominal ultrasound showed normal

*Correspondence:

Iqbal Singh*, M.Ch (Urology)
Division of Urology, Department of Surgery
University College of Medical Sciences (University of Delhi) & GTBH,
F-14 South Extension Part-2, New Delhi-110049, India.
Fax: 91-11-22590495,
Email: iqbalsinghp@yahoo.co.uk
Received: 29 May 2010
Revised: 1 sep 2010
Accepted: 8 sep 2010

upper tracts with blood clots in urinary bladder and a heterogeneous five cm mass arising from the posterior wall of the urinary bladder. Contrast enhanced computerized tomographic (CECT) scan of abdomen showed homogenous mass arising from the posterior wall of urinary bladder. Cystoscopy revealed blood clots and a velvety carpet like exophytic growth arising from the posterior wall of the urinary bladder (Fig-1) with an inset demonstrating the cystoscopic view of the same. A clinical diagnosis of carcinoma in situ versus chronic cystitis was suspected.

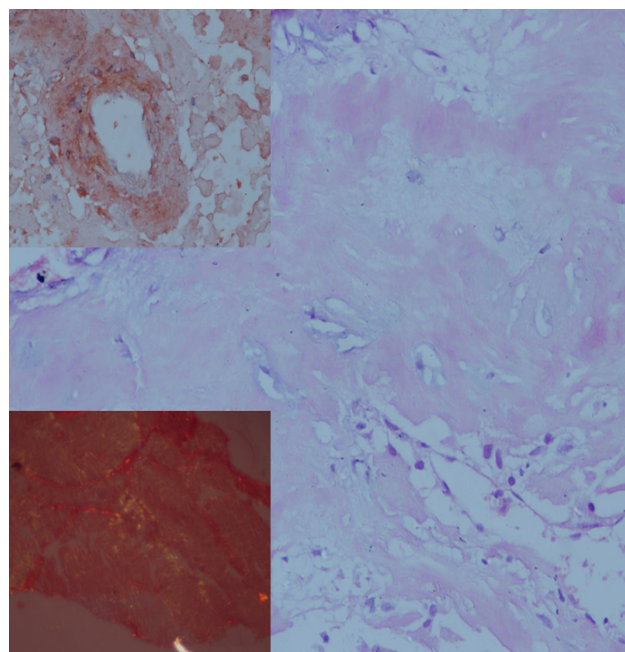
Fig-1. Computed tomographic scan showing the lesion with thickening arising from the posterior wall of the bladder (an inset showing the cystoscopic view of the same).



of the posterior bladder wall lesion was performed. Histopathology with H&E (Fig-2) and Congo-Red stains revealed sub epithelial hemorrhage with an extracellular amorphous pink amyloid deposit in the

sub-mucosal layers of the bladder wall and vessel walls (inset top left) that persisted after treatment with potassium permanganate and an apple green birefringence under polarized light (inset bottom left). Metachromasia was seen on staining with crystal violet that was negative for Masson Trichrome (thereby excluding fibrosis). Further work up (normal serum electrophoresis, negative urinary Bence Jones proteins, normal rectal, abdominal fat aspirate and bone marrow biopsy) ruled out any evidence of systemic amyloidosis. Based on these findings with special staining, the diagnosis of primary localized VA was confirmed. The patient was followed and is currently asymptomatic one year after surgery. Follow up cystoscopy was unremarkable with mild cystitis.

Fig-2. (H & E x100) stained slide of vesical tissue showing evidence of an eosinophilic hyaline like acellular deposit (amyloid) in the submucosal bladder wall. An inset on (top left) shows the same deposit in the arteriolar wall, and another inset on (bottom left) shows Apple green birefringence of congo-red staining on polarisation (Congo red stain x 100).



Amyloidosis is characterized by the deposition of a hyaline, eosinophilic protein like material in the extracellular space of certain tissues and organs. It is classified into primary (idiopathic), secondary (systemic) and hereditary forms. The amyloid deposits may be localized to one particular organ or it may be systemic. Amyloidosis is a systemic disease that commonly involves the gastrointestinal tract, muscular or adipose tissue. Localized amyloidosis of the urinary tract presenting with hematuria due to an amyloidoma is an uncommon occurrence (1), even though bladder is the most frequent organ involved (2). The diagnosis may be suspected on CECT, confirmed by pathological examination of cystoscopy samples as the condition is known to mimic malignancy both clinically and radiologically (3, 4).

Primary amyloidosis refers to the clinical features resulting from amyloid deposition without any other associated disease. It was first described by Solomin et al, in 1897 (5), since then many cases have been reported. Urinary bladder is the most common site (2), although involvement of prostate/ureter has been reported (4). The lung, larynx, skin, urinary bladder tongue and eye may also be involved in localized amyloidosis (6). Primary localized amyloidosis of lower urinary tract is rare, the clinical, cystoscopic and radiological features of which are indistinguishable from neoplastic or inflammatory lesions. Primary VA is characterized by a generally benign course with mucosal and sub-mucosal amyloid deposits relatively sparing the deeper blood vessels. Secondary VA is characterized by amyloid deposits in the walls of the blood vessels that impair the contractile ability of the arterioles, generally presenting with massive bleeding and complications like bladder rupture or hemodynamic instability (7).

About 15 biochemically distinct forms of amyloid proteins exist, with AL (amyloid light chain) and AA (amyloid associated) being most common. AL is derived from plasma cells, contains immunoglobulin (Ig) light chains, is associated with monoclonal

B cell proliferation and is found most commonly in the primary amyloidosis while AA is a non-Ig protein usually found in secondary amyloidosis that is synthesized by liver in response to cytokines from chronically inflamed tissues due to other systemic diseases. Cases of localized AA type amyloid deposition in the urinary bladder, although rare, have been reported (3, 6). The precise pathophysiology of amyloidosis is unknown but it is believed that monoclonal lymphoid proliferations due to chronic inflammation of the urinary tract may be the source of the amyloid AL proteins (3).

VA can mimic bladder malignancy (6, 7) and it may present with intermittent gross painless hematuria. Alternatively, it may present with frequency, urgency, voiding difficulties, dysuria, nocturia, suprapubic pain, anterior pelvic mass and renal function impairment. Systemic and local examination is usually unremarkable. Radiological and cystoscopic findings reveal an irregular exophytic lesion(s). Definitive diagnosis is by histopathology and complementary investigations are needed to eliminate systemic involvement. Analysis of the type of amyloid can help target these investigations.

Various therapeutic options have been suggested for the treatment of symptomatic VA (6). The treatment needs to be individualized for each patient depending upon the type of amyloidosis- primary or secondary and localized or systemic, site and size of the lesion. Surgical treatment for amyloidosis causing hematuria includes; fulguration and laser ablation for small lesions with transurethral resection (TUR) as in the present case, with partial cystectomy reserved for larger lesions, while ureteric obstruction may necessitate JJ stenting. Total cystectomy may be indicated early for extensive VA with intractable hemorrhage, especially in AA type of VA. Medical management of VA may include intravesical Dimethylsulfoxide (DMSO) or targeted therapy with colchicine, epharantine and eprodisate for vesical AA. TUR followed by adjuvant intravesical DMSO

(to reduce recurrence) may be preferred for localized VA. Since our patient had controllable hematuria with localized VA amenable to resection, with a normal follow up cystoscopy, no further therapy was instituted. He is currently doing fine on a further follow up of one year.

Conclusion

VA should be considered early in the differential diagnosis of patients presenting with recurrent hematuria whose symptoms suggest bladder cancer with negative urine cytology. Early diagnosis and prompt ablation with fulguration/resection with regular cystoscopic follow up is necessary for primary or localized VA presenting with hemorrhagic cystitis.

Conflict of interest:

None declared.

References

1. DeSouza MA, Rekhi B, Thyavihally YB, Tongaonkar HB, Desai SB. Localized amyloidosis of the urinary bladder, clinically masquerading as bladder cancer. *Indian J Pathol Microbiol.* 2008;51:415-7.
2. Haouas N, Colas JM. Primary localized bladder amyloidosis. *Rev Med Suisse.* 2007;3:1334-6.
3. Merrimen JL, Alkhudair WK, Gupta R. Localized amyloidosis of the urinary tract: case series of nine patients. *Urology.* 2006;67:904-9.
4. Singh SK, Wadhwa P, Nada R, Mohan VC, Singh P, Jha V. Localized primary amyloidosis of the prostate, bladder and ureters. *Int Urol Nephrol.* 2005;37:495-7.
5. Malek RS, Wahner-Roedler DL, Gertz MA, Kyle RA. Primary localized amyloidosis of the urinary bladder: experience with dimethylsulfoxide therapy. *J Urol.* 2002;168:1018-20.
6. Akram CK, Al-Marhoon MS, Josephkunju M, Grant CS, Rao TV. Primary localized AA type amyloidosis of urinary bladder: case report of rare cause of episodic painless hematuria. *Urology.* 2006; 68:15-7.
7. Tirzaman O, Wahner-Roedler DL, Malek RS, Sebo TJ, Li CY, Kyle RA. Primary localized amyloidosis of the urinary bladder: a case series of 31 patients. *Mayo Clin Proc.* 2000;75:1264-8.