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Case Report

Primary amyloidosis of urinary bladder: Mimicking transitional cell carcinoma bladder?

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Introduction

Amyloidosis consists of extracellular deposition of amyloid (starch like), a protein with a fibrillary structure, in one or more body sites. It was first described by Virchow in 1853.¹ In the urinary tract, amyloid deposition usually starts from kidney to renal pelvis, ureters, urinary bladder, urethra and even penis. The kidney is nearly always involved in secondary amyloidosis and in approximately 50% of the cases of primary amyloidosis. Amyloidosis of the urinary bladder is uncommon, but amongst the various sites in the lower urinary tract, it is the most commonly involved organ.^{2,3} Both sexes are equally affected between the fifth

and seventh decade. Painless gross haematuria is the main presenting symptoms in most (>75%) cases.² Both primary and secondary amyloidosis may involve the bladder, isolated primary vesical amyloidosis being more common than secondary involvement⁴ and the lesions can be easily confused with malignancy because of its appearance on imaging as well as on cystoscopy.^{3,4} Hence, a high index of suspicion is always warranted whenever one encounters such pathology.

Case report

A 45 year old male patient presented with history of intermittent episodes of gross total painless haematuria of 2 months duration at a peripheral center. Basic evaluation with urine cytology for malignant cells was negative so was ultrasound kidney, ureter and bladder (US KUB). He underwent cystoscopy and multiple biopsies of urinary bladder. Findings were unhealthy bladder mucosa over both lateral walls, trigone and around bladder neck. Histopathology report was features of carcinoma in situ (CIS) with squamous metaplasia. Patient was referred to our center for further management. Repeat evaluation done at our center: Urine cytology X 3 – negative for malignant cells. US KUB was reported as normal. CECT abdomen showed bilateral prominent ureters (Left > Right) with subtle thickness of urinary bladder wall (05 mm) on right side (Fig. 1). Cystoscopy and resection of lesion around left ureteric orifice was done. Findings revealed a velvety carpet like mucosa over anterior

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Fig. 1 – CECT revealing a thickened urinary bladder wall more on right side (Block Arrow) with irregular bladder wall thickening more on left side (Filled Arrow). The perivesical fat planes are maintained.

wall, right anterolateral wall and trigone of bladder (Fig. 2). The histology of this biopsy along with review of slides of previous biopsy on microscopy showed bladder tissue with dense homogenous eosinophilic material which stained orange red on congo red stain (Fig. 3) and showed apple green birefringence on polarization (Fig. 4). There was no evidence of urothelial carcinoma or CIS. Few areas of squamous metaplasia were noted. Thus histopathology was suggestive of amyloidosis of urinary bladder. Patient underwent a serum electrophoresis analysis and bone marrow biopsy which were essentially normal, however his urine analysis was positive for amyloid deposits but did not show any Bence Jones proteins. These findings ruled out a systemic amyloidosis and hence we diagnosed it as a case of primary amyloidosis of urinary bladder. Patient has been kept under regular follow up with three monthly check cystoscopy. Though he complains of occasional episodes of gross haematuria we have not offered any active treatment for his amyloidosis of urinary bladder. The literature also recommends regular follow up with symptomatic treatment of bladder pain or any associated lower urinary tract symptoms (LUTS) after transurethral resection of lesion. Patient has been on regular follow up for last one and half year and has not shown any evidence of recurrence.

Fig. 2 – CPE showed unhealthy mucosa with thickening at left anterolateral wall (Bold Arrow) which was biopsied.

Fig. 3 – (H & E; 10X) Microphotograph shows Transitional lining with amorphous eosinophilic substance beneath.

Discussion

Primary amyloidosis of the urinary bladder is a rare entity with less than 90 cases reported. It mimics transitional cell carcinoma both clinically and cystoscopically. Both these entities have similar symptoms of irritative voiding, pelvic pain and haematuria hence a conclusive histological examination is a must for definite diagnosis and management. Amyloidosis encompasses a heterogeneous group of disorders which are characterized by extracellular deposition of eosinophilic fibrillar protein in various tissues and organs.

The etiology of amyloidosis remains unknown and mechanism proposed are usually immunological.⁵ In case of bladder amyloidosis it is considered that repeated mucosal and submucosal inflammation causes an influx of lymphoplasmacellular elements one of which becomes monoclonal. This monoclonal in turn proliferates and secretes an aberrant type of light polypeptide chain, which is amyloidogenic and there is formation of fibril deposition in the bladder tissue.⁶

Primary systemic amyloidosis with vesical involvement is usually not accompanied by LUTS, whereas primary localized

Fig. 4 – Congo red stain; 40X Showing apple green birefringence's under polarizing microscopy.

bladder amyloidosis is almost always accompanied by such clinical features.⁷ The incidence of gross haematuria has been reported to be 58%–77% and irritative voiding symptoms have been reported in 23% of cases in different studies.⁸ There being no pathognomonic clinical or radiological features with problem being surmounted by resemblance to malignancy on cystoscopy (raised erythematous, papillary or haemorrhagic lesions) as was seen in our case, histopathology becomes the sole criteria for diagnosis.⁵ Even then the diagnosis may be missed on routine histological examination unless staining with congo red is done. Once the biopsy confirms amyloidosis a thorough search for possible underlying disease and associated secondary amyloidosis should be made.

Primary bladder amyloidosis is generally treated conservatively with transurethral resection and fulguration. Medical treatment with substances such as colchicines⁹ nitrofurazone and dimethyl sulfoxide¹⁰ as primary or adjuvant therapy has been tried for symptomatic relief. Cystectomy may be required in diffuse bladder involvement.⁹ Procedures such as ligation of internal iliac arteries or cystectomy are occasionally necessary for control of massive hemorrhage in secondary bladder amyloidosis. It is rare to have massive hemorrhage in primary bladder amyloidosis because it is predominantly submucosal and muscular involvement vis a vis in secondary bladder amyloidosis where the blood vessel are primarily involved. Symptomatic local recurrence is common and usually amenable to repeat transurethral resection.⁵ Literature recommends a long term follow up.

Conclusion

Amyloidosis of the bladder is a rare condition which presents a diagnostic challenge both to urologist and pathologist. The condition is of interest because it resembles malignancy both in symptoms and gross appearance. High index of suspicion is required because it can be missed on routine histological examinations until special stains like Congo red and immunohistochemistry are considered. The treatment is usually

conservative with observation or transurethral resection and long term regular follow up.

Conflicts of interest

All authors have none to declare.

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