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Primary localised bladder amyloidosis – A case report with review of the literature

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A B S T R A C T

Primary bladder amyloidosis, a mimicker of bladder malignancy, is a rare but important differential diagnosis for patients presenting with haematuria. We report the case of a 58-year-old man who initially presented with macroscopic haematuria and irritative urinary tract symptoms. There was no radiological evidence of a bladder mass lesion, but cystoscopy revealed an erythematous papillary lesion in the posterior bladder wall concerning for bladder malignancy. Histology demonstrated primary bladder amyloidosis, which was completely excised intraoperatively. He is undergoing regular cystoscopic surveillance and there has been no disease recurrence for 4 years since the initial diagnosis.

1. Introduction

Primary localised bladder amyloidosis is a rare disease that remains poorly understood with a lack of standardised consensus management guidelines. It can present as painless haematuria, lower urinary tract or cystitis-like symptoms, and is a mimicker of bladder cancer. Unlike bladder cancer however, localised bladder amyloidosis appears to have a benign course and is often cured by endoscopic complete resection of the lesion. Here, we report on a case of primary localised bladder amyloidosis.

2. Case presentation

A 58-year-old male non-smoker presented with a first episode of macrohaematuria. Bleeding was fresh red in colour. Associated symptoms included longstanding urinary urge incontinence and terminal dysuria. He denied fevers or flank pain. He was not on anticoagulation medication and had no other significant medical co-morbidities. Examination of his penis demonstrated evidence of mild phimosis with erections. A digital rectal examination revealed a benign, smooth prostate of approximately 40 cc. CT urogram demonstrated normal bladder thickness and no radiological evidence of bladder mass or renal lesion, nor any hydroureteronephrosis.

Cystoscopy revealed an isolated, erythematous posterior bladder wall lesion approximately 5mm in diameter, concerning for bladder malignancy (Fig. 1). The patient went on to have a transurethral resection of bladder tumour (TURBT). Histopathology revealed amyloidosis in bladder mucosa with moderate plasma cell infiltrate and chronic inflammation. There was no evidence of malignant cells (Fig. 2). The bladder stroma showed extensive deposits of fibrinoid and pale eosinophilic material on Congo-red stains with an apple-green birefringence in polarised light.

A diagnosis of bladder amyloidosis was made. In Situ Hybridization immunostaining for kappa and lambda light chains demonstrated increased lambda stranding at amyloid deposition sites, raising the possibility of light-chain restriction and a monoclonal population of plasma cells. The patient underwent evaluation for systemic amyloidosis, all of which returned negative. Bone marrow aspiration revealed mildly increased plasma cell component of 5%–10% on immunochemistry, however, no abnormal population of plasma cells. Therefore, systemic amyloidosis was ruled out and a diagnosis of localised primary bladder amyloid light-chain (AL) amyloidosis was made.

The patient was commenced on oral colchicine. A repeat cystoscopy approximately 6 months following TURBT revealed complete macroscopic resolution of the amyloid lesion with scarred tissue and no residual erythema. Thereafter, yearly cystoscopic surveillance is being conducted to monitor disease progression. At the time of publication, the patient has been disease-free for 4 years since initial TURBT.

3. Discussion

Amyloidosis is a rare disorder characterised by misfolding of proteins

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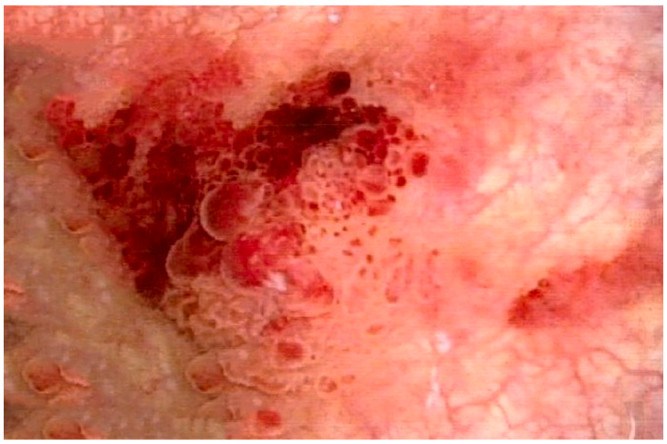

Fig. 1. Erythematous, papillary patch on posterior bladder wall mucosa visualised on cystoscopy as part of workup for macroscopic haematuria.

and extracellular deposition as insoluble fibrils. If it deposits into only one organ, it is referred to as localised amyloidosis; if it deposits into multiple organs, it is referred to as systemic amyloidosis. Primary localised amyloidosis is a diagnosis of exclusion, and the patient needs to be comprehensively assessed for systemic amyloidosis in the first instance. Primary localised bladder amyloidosis is a rare urological disease globally which is still not well understood, and there currently is no general consensus on best management.[1] If left untreated, bladder amyloidosis can progressively enlarge and cause obstructive uropathy and oliguria or anuria.

Patients with bladder amyloidosis generally present with macroscopic haematuria, irritative urinary tract symptoms or cystitis-like symptoms. Amongst previously published case reports studies, there is high variability in radiological manifestations of bladder amyloidosis, with some reporting no significant findings on CT intravenous pyelogram. This highlights the great importance of cystoscopic assessment for any haematuria workup.

The treatment goals of patients with localised primary bladder amyloidosis focus on excision of the amyloid lesion, management of complications that may arise from amyloid deposits in the bladder and close follow-up.[2] In most cases of primary bladder amyloidosis, transurethral resection of the bladder lesion has been reported as the treatment of choice.[1] However, in cases of multifocal amyloidosis unable to be completely resected or disease recurrence refractory to resection, various medical treatment options have been utilised such as colchicine to reduce local inflammation, or intravesical dimethyl sulfoxide in an attempt to dissolve the insoluble amyloid fibrils. For patients with symptomatic bladder amyloidosis refractory to all treatments, partial or total cystectomy can be considered. However, the rarity of bladder amyloidosis has meant a paucity of high-quality prospective studies such as randomised control trials to define the optimal therapy and true efficacy of these interventions.

A review of the literature yielded four published case series and retrospective studies with highly variable results (Table 1). Across the four studies, a significant proportion of patients diagnosed with bladder amyloidosis received transurethral resection or laser as part of their treatment.[2–5] A high degree of variability was noted in both follow-up duration following initial treatment and rate of disease recurrence. Zhou et al. (2014) reported a median follow-up period of 64 months (IQR 33.5–90.5 months) with recurrence rates as low as 0%, whilst Tirzaman et al. (2000) reported a median follow-up period of 120 months (IQR 24–864 months) and the rate of recurrence was as high as 42%.[2,5] Our review of the literature thus far has shown that recurrences are relatively common in localised bladder amyloidosis, whilst progression to systemic amyloidosis has not been reported.

A recently published systematic review by Pyrgidis et al. (2021) examined 76 publications consisting of case reports, case series and retrospective studies with 184 patients and found that 35.3% of patients had disease recurrence with a time frame of 20 months from initial treatment to first recurrence.[1] Due to the high frequency and early time frame for recurrence of bladder amyloidosis, the study proposed follow-up cystoscopy at 3, 12 and 24 months following initial resection, similar to the time frame of cystoscopic surveillance undertaken by our patient.

4. Conclusion

Although rare, bladder amyloidosis warrants clinical awareness as it is a mimicker of bladder cancer. Despite its benign properties, if left untreated, bladder amyloidosis has the potential to progress in size and cause obstructive uropathy. In most cases, it solely requires an endoscopic resection and appropriate surveillance for disease recurrence. Given the current paucity of data, research efforts should be directed towards prospective studies such as randomised control trials to better

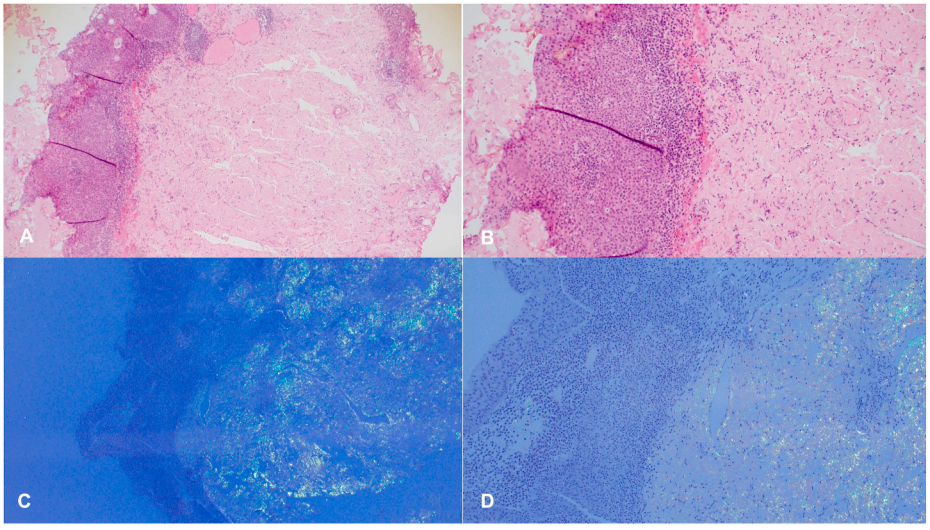

Fig. 2. (A) H&E stain on cytology slides obtained from amyloid bladder biopsy, demonstrating surface urothelium underlying subepithelial plasma cells and underlying lamina propria containing amyloid (x20). (B) H&E stain (x100). (C) Congo red slide demonstrate evidence of apple green birefringence indicative of amyloid (x20). (D) Congo red slide (x100). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Previously published case series and retrospective studies of localised bladder amyloidosis.

Author (year)	Sample size, n	Gender, n (%)	Median Age, (Q1-Q3), years	Localised vs systemic amyloid, n (%)	Amyloid subtype, n (%)	Median F/U period, (Q1-Q3), months	Treatment, n (%)	Disease Recurrence, n (%)
Sirohi et al. (2019)	29	M = 24 (83) F = 5 (17)	77 (48–102)	Localised = 18 (62) Systemic = 11 (38)	ATTR = 10 (34) AL = 3 (10) Amyloid P = 1[3] Indeterminate = 2 (7) NR = 13 (45)	17 (3–108)	TU biopsy = 18 (62) TUR = 9 (31) Cystoprostatectomy = 2 (7)	3 (10)
Zhou et al. (2014)	7	M = 4 (57) F = 3 (43)	68 (62–78)	Localised = 6 (86) Systemic = 1 (14)	AL = 4 (57) NR = 3 (43)	64 (33.5–90.5)	TUR = 7 (100)	0 (0)
Merrimen et al. (2006)	9	M = 5 (56) F = 4 (44)	72 (63–80)	Localised = 9 (100) Systemic = 0 (0)	AL = 9 (100)	24 (12–31.5)	TUR = 8 (89) Total cystectomy = 1 (11)	2 (22)
Tirzaman et al. (2000)	31	M = 22 (71) F = 9 (29)	55 (28–80)	Localised = 31 (100) Systemic = 0 (0)	AL = 24 (77) ATTR = 3 (10) NR = 4 (13)	120 (24–864)	TU biopsy with laser = 17 (55) TUR = 8 (26) Partial cystectomy = 3 (10) Total cystectomy = 1[3] NR = 2 (6)	13 (42)

M = male, F = female, AL = amyloid light chain, ATTR = amyloid transthyretin, TU = transurethral, TUR = transurethral resection, NR = not reported.

define optimal therapy for localised bladder amyloidosis.

Financial disclosure

There are no financial conflicts of interest to disclose.

Contributors

BAY was involved in writing the original draft, reviewing and editing manuscript and data curation. NAS assisted with drafting. BHD was involved in conceptualisation, review and editing.

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