

# Primary localized amyloidosis of bladder: Is there a need for cystoscopic surveillance?

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## Abstract

Amyloidosis is a heterogeneous group of disorders characterized by extracellular deposition of amorphous proteinaceous material in various tissues. Amyloidosis of bladder is of significant clinical interest to the urologist because of its presentation as urothelial cancer. Transurethral resection and histology examination is essential to exclude malignancy and to establish the benign nature of amyloidosis. Apart from managing the localized bladder amyloidosis, it is important to exclude systemic amyloidosis. Here in we describe two cases of localized, primary amyloidosis and discuss briefly their management and follow-up.

**Key Words:** Primary amyloidosis, urinary bladder, CT scan, cystoscopic surveillance

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Received: 14.12.2011, Accepted: 23.03.2012

## INTRODUCTION

Amyloidosis is a heterogeneous group of disorders characterized by extracellular deposition of amorphous proteinaceous material in various tissues. Primary amyloidosis (AL) is a systemic disease due to plasma cell dyscrasia involving multiple organs. Localized primary amyloidosis is an uncommon type of amyloidosis limited to one organ. Urinary tract is one the sites favored for primary amyloidosis and it is thought that chronic local inflammation leads to localized amyloid deposits. Clinical presentation is with macroscopic hematuria and lower urinary tract symptoms mimicking urinary tract malignancy. It has uncharacteristic cystoscopic appearances resembling invasive bladder neoplasm. Amyloidosis of bladder is of significant clinical interest to the urologist because of its presentation as urothelial cancer. Transurethral resection and histology examination is essential to exclude malignancy

and to establish the benign nature of amyloidosis. Apart from managing the localized bladder amyloidosis, it is important to exclude systemic amyloidosis. We describe two cases of primary bladder amyloidosis and their expectant management and follow-up for over 4 years.

## CASE REPORTS

### Case 1

A 71-year-old gentleman was referred to hematuria clinic for his single episode of visible painless haematuria. There was no history of lower urinary tract symptoms and no previous urological problems. He had dipstick hematuria and urine cytology was reported as benign. His ultrasound scan of kidneys and bladder revealed thickened posterior bladder wall and small simple renal cysts bilaterally. At flexible cystoscopy a solid lesion on the posterior bladder wall resembling invasive bladder was seen [Figure 1]. Transurethral resection was performed and the specimen was submitted for histopathological examination. Final histology reported a primary amyloidosis of AL type. A thorough systematic investigation including rectal biopsy, bone marrow biopsy and SAP (serum amyloid P component) scintigraphy showed no evidence of systemic amyloidosis. Three years from his initial diagnosis a small urethral lesion was noted which was biopsied and histology confirmed it as primary

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/0974-7796.120310

amyloid of AL type [Figure 2]. Since then he has remained asymptomatic without progression of vesical amyloidosis.

### Case 2

A 78-year-old gentleman attended hematuria clinic with two weeks history of intermittent, macroscopic hematuria which was associated with irritative lower urinary tract symptoms. Ultrasound scan of kidney and bladder revealed normal appearing kidneys bilaterally with slight thickening of the bladder, which was confirmed by CT scan [Figure 3]. A flexible cystoscopy showed a craggy appearing solid lesion with some hemorrhagic areas situated over the trigone of bladder and was not involving ureteric, resembling invasive bladder tumour. Transurethral resection was performed and submitted for histological examination. Histology was reported as primary (AL) amyloid and there was no evidence of either *in situ* or invasive urothelial malignancy. Systematic investigations were performed which were negative for systemic amyloidosis. There was no recurrence of vesical amyloidosis and he remains asymptomatic 4.5 years after initial diagnosis.

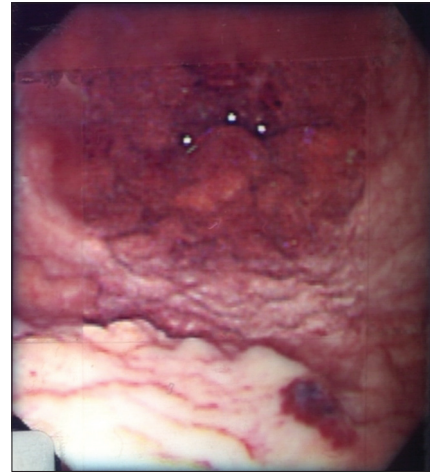
### DISCUSSION

Amyloidosis is a rare heterogeneous group of disorders characterized by the extracellular deposition of amorphous, fibrillar, proteinaceous material. All deposits have a uniform appearances and staining characteristics. Amyloid is not a chemically distinct entity and there are three major and several minor biochemical forms. Amyloidosis results from abnormal folding of protein which is deposited as fibrils in the extracellular space. Broadly amyloidosis is classified into primary (AL), secondary (AA) and hereditary (ATTR). Primary amyloidosis is due to plasma cell dyscrasias, including multiple myeloma and secondary amyloidosis is commonly associated with chronic inflammation.

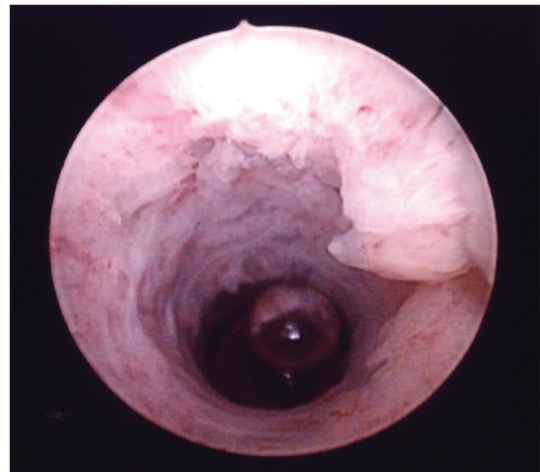
Primary urinary bladder amyloidosis is an uncommon clinical entity and is of particular interest to the urologist as it is often mistaken initially for bladder neoplasm. Bladder amyloidosis was first described in 1897 by Solomin during an autopsy<sup>[1]</sup> and since then over 200 cases have been reported in medical literature all over the world. Localized amyloidosis is known to occur in respiratory tract, skin and genitourinary tract involving renal pelvis, ureter, and bladder. Localized amyloidosis is usually found to be of AL (primary) type rarely deposits could be due to AA type.<sup>[1]</sup>

Majority of patients with localized bladder amyloidosis present with visible painless hematuria. In a large case series of 31 patients Tirzman *et al.* found 77% presented with visible hematuria and similarly Merriman *et al.* reported the incidence of hematuria as 62.5%. In the same study, Tirzman *et al.* noted

that 23% had lower urinary tract symptoms on presentation and 19% presented with both hematuria and lower urinary tract symptoms.



**Figure 1:** Amyloid deposit on the posterior wall of urinary bladder as seen on cystoscopy



**Figure 2:** Recurrent amyloidosis in anterior urethra



**Figure 3:** Thickening of the left lateral wall of the urinary bladder seen on the contrast-enhanced CT scan

Primary bladder amyloidosis has a male preponderance and usually occurs at a mean age of 55 years. The most preferred site of amyloid deposit is the posterior bladder wall (68%), followed by the trigone (26%).<sup>[1]</sup> In this case report, the amyloid deposits were typically found on the posterior wall (case 1) and trigone (case 2), coinciding with the previous studies. Multiple amyloid deposits are common (65%) noted in over 65% of cases as compared to single area of involvement in 26%, and diffuse involvement of bladder was noted in 10% of cases.<sup>[1,2]</sup> Cystoscopic appearances have been variously described as fleshy, nodular, protuberant lesion and polypoidal lesions which is initially interpreted as invasive neoplasm of bladder.

Aetiology of localized primary bladder amyloidosis is obscure and poorly understood. It has proposed that recurrent, chronic inflammation of the urinary bladder recruits lymphoplasmatic cells to the bladder submucosa. These monoclonal cells proliferate and secrete an abnormal type of light chain immunoglobulin, which are deposited in the bladder wall. This hypothesis is strengthened by the presence of secreting plasma cells in the close vicinity of amyloid fibrils on histopathological examination.<sup>[3]</sup> Amyloid typically displays a typical apple-green birefringence with Congo red stain under polarized light.

Transurethral resection of the lesion and histopathological examination is necessary to exclude malignancy and to establish the diagnosis of amyloidosis. Tirzman followed up 31 patients with localized bladder amyloidosis from 2 to 36 years; 25 % remained disease free, 21% had stable lesions and 54% recurred.<sup>[1]</sup> In most cases transurethral resection and fulguration is adequate to control the lesion. In this case report one of our patients developed a metachronous symptomatic amyloid deposit in anterior urethra which was detected 3 years after initial diagnosis on surveillance cystoscopy and no further surgical intervention was required. Tilp reported the first case of urethral amyloidosis in 1919 and about 16 cases have been reported since then. It presents as urethritis refractory to treatment and can appear as pink polypoidal lesion.<sup>[4]</sup>

There is no universal consensus for follow-up of such patients but, in view of high recurrence rate and rare, incidental detection of urothelial malignancy long-term follow-up and annual cystoscopy is advisable. Random biopsies of suspicious

looking areas may be considered. Merriman et al. reported two cases of primary amyloidosis in patients with known urothelial carcinoma during cystoscopic surveillance.<sup>[2]</sup> There are reports of concurrent urothelial carcinoma and carcinoma *in situ* detected along with localized urethral and bladder amyloidosis.<sup>[5]</sup>

Intravesical (Dimethyl Sulfoxide) and systemic (colchine) treatments have been described, but these are generally not required. In this case report, initial transurethral resection was adequate in symptom control and no further intravesical or systemic therapy was necessary.

## CONCLUSIONS

Localized primary bladder amyloidosis is a rare clinical entity. It mimics invasive bladder neoplasia of bladder in its clinical presentation, cystoscopic findings and on imaging. Transurethral resection and fulguration are adequate for the control hematuria. Histology is essential to exclude urothelial malignancy. Systemic investigations are recommended to exclude systemic amyloidosis. The long-term prognosis of localized bladder amyloidosis is excellent in the absence of systemic amyloidosis. There is no universal consensus on how best to follow-up such cases, due to the rarity of this condition and limited number of cases. In view of local recurrence and rare occurrence of bladder urothelial carcinoma, annual cystoscopic follow-up is advisable.

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**How to cite this article:** Bardapure M, Namasivayam SK, Rogawski K. Primary localized amyloidosis of bladder: Is there a need for cystoscopic surveillance?. *Urol Ann* 2013;5:309-11.

**Source of Support:** Nil, **Conflict of Interest:** None.