Primary Bladder Amyloidosis

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Abstract

Primary bladder amyloidosis is a rare disease, with only 200 cases reported worldwide. This condition is clinically important since it masquerades as a malignancy. We herein present a case of primary bladder amyloidosis presenting as painless hematuria and dysuria. Computed tomography and ultrasound showed thickening of the posterior bladder wall. Cystoscopy revealed abnormal bladder tissue suspicious of malignancy. However, transurethral resection of a bladder tumor showed no evidence of malignant cells. Amyloid was identified on Congo red staining. Therefore, the possibility of secondary amyloidosis was ruled out and a diagnosis of primary bladder amyloidosis was made. Nine months after undergoing primary resection, the patient’s amyloidosis recurred at the initial site.

Key words: primary bladder amyloidosis, localized bladder amyloidosis, transurethral resection, hematuria

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Introduction

Localized deposition of amyloid can occur in any organ in the absence of systemic involvement. Primary localized amyloidosis of the urinary bladder is a rare disorder; however, it is clinically important since it can masquerade as malignancy. The characteristic symptoms of primary bladder amyloidosis include painless gross or microscopic hematuria and dysuria. Imaging studies may suggest malignancy, and urine cytology is negative. Histopathology is necessary in order to exclude the possibility of malignancy, and transurethral resection is the primary treatment option for primary bladder amyloidosis. Recently, an increasing number of case reports describing this condition have been reported. Doctors in Internal Medicine should therefore be aware of this disease and consider it in the differential diagnosis in cases in which imaging suggests malignancy but cytology is negative.

Case Report

A 52-year-old woman, a former smoker with a history of nephrolithiasis, exhibited mild dysuria and hematuria. She presented to the emergency room (ER) where she initially underwent computed tomography (CT) to evaluate the nephrolithiasis, which showed several small punctate stones in the right kidney with posterior bladder wall thickening (Fig. 1). The results of a urinalysis were not consistent with infection, and a urine culture was negative. Ultrasound (US) (Fig. 2) and CT urograms confirmed these findings. Urine cytology revealed no malignant or atypical cells. Based on these findings, malignancy was suspected, and cystoscopy was performed. The cystoscopic examination revealed abnormal bladder mucosa highly suggestive of malignancy involving the trigone, posterior and bilateral bladder walls and bladder neck. Ureteral orifices were not identifiable. Transurethral resection of the bladder tumor was performed. The histologic sections demonstrated reactive tissue with abundant acute and chronic inflammation, including pustules within the urothelium, and prominent lymphoplasmacytic infiltrates in the lamina propria. There were also large deposits of amorphous, acellular, eosinophilic substances throughout the lamina propria and many of the vessel walls. This material was consistent with amyloid deposition on routine Hematoxylin and Eosin staining (Fig. 3). Staining with Congo red confirmed the presence of amyloid (Fig. 4). The muscularis propria was identified, appearing to remain uninvolved by this process. Typing studies performed by PhenoPath Laboratories in Seattle, Washington revealed the amyloid to be...
be positive for lambda light chains and amyloid P proteins but negative or weak for transthyretin, amyloid A and kappa light chains. This is the immunoprofile for the AL (Lamda) subtype, typical of most cases of localized bladder amyloidosis. These findings, along with the patient’s clinical presentation and cystoscopy findings, were highly suggestive of primary amyloidosis of the urinary bladder. A further evaluation excluded the possibility of systemic amyloidosis. In addition, chest X-ray and electrocardiogram findings were normal, and a urinalysis did not show proteinuria. Furthermore, no proliferation of lymphocytes or protein gaps were noted on a complete metabolic panel. Moreover, the findings of serum protein electrophoresis and urine protein electrophoresis were normal, and the levels of kappa and lambda free light chains were within the normal limits. The patient had no clinical symptoms of systemic amyloidosis, such as diarrhea or peripheral neuropathy; therefore, she was diagnosed with primary bladder amyloidosis. Follow-up cystoscopy performed three months later was negative, as were the findings of several US examinations. The patient continued to be well until nine months after the first resection when she felt bladder pressure and noted hematuria. CT revealed thickening of the left side of bladder, and she underwent repeat cystoscopy, which revealed findings consistent with recurrence. She subsequently underwent a second transurethral resection of a bladder tumor (TURBT) procedure (Fig. 5), the results of which were again consistent with a diagnosis of primary bladder amyloidosis. She has remained under close follow-up for six months since the second resection and is currently doing very well without any symptoms suggestive of recurrence.

**Discussion**

Primary bladder amyloidosis is a very rare disease. According to Michael et al., only 200 cases have been reported in the literature to date (1). The patient usually presents with...
gross painless hematuria and irritating urinary symptoms. The disease is almost evenly distributed over the fifth, sixth and seventh decades of life in men, whereas it is diagnosed in the sixth decade of life in most women (2). This condition has an equal sex preponderance. Localized amyloidosis is the term used for local amyloid deposition in tissues, such as the tracheobronchial tree, urinary tract or skin. These deposits are derived from monoclonal light chains, although they are not the result of an underlying systemic clonal plasma cell disorder. Chronic cystitis and inflammation can lead to the synthesis and accumulation of misfolded amyloid precursor proteins, particularly light chain immunoglobulin proteins (3). Patients with localized amyloidosis do not develop systemic disease or require chemotherapy. However, the potential for recurrence warrants a full workup, as a case of coexistent malignancy has been reported (4). Localized amyloidosis is most commonly found in the upper respiratory tract (nasopharynx), urinary bladder, colon, skin, nails and orbit (5). Complications include nasal bleeding, colonic bleeding, tracheobronchial obstruction and hematuria. The differential diagnosis comprises neoplasia, lymphoma and hemorrhagic cystitis. Awareness of this disease is important because it mimics malignancy of the bladder. In addition, the condition is difficult to diagnose with cystoscopy, as it can appear very similar to carcinoma. There are no pathognomonic radiological features, and obtaining a histological diagnosis is essential; the disease is easily diagnosed based on the presence of amyloid deposits in the resection specimen. Excluding causes of secondary amyloidosis, such as rheumatoid arthritis, inflammatory bowel disease and psoriasis, is also imperative. The clinical course is usually benign, and surgical excision may be the only treatment required. Although other treatments, such as dimethyl sulfoxide installation (6) or colchicine therapy (7), have been reported, there remains limited evidence to support their clinical utility. Follow-up with cystoscopy is recommended, as the recurrence rate post-resection is estimated to be as high as 50% (8). Infrequently, cystectomy may be required in cases of significant uncontrolled hematuria.

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References