Primary amyloidosis of the bladder; a mimicker of bladder cancer

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FITZPATRICK R, PATERSON NR, BELANGER EC, MCCURDY A, WATTERSON J. Primary amyloidosis of the bladder; a mimicker of bladder cancer. *Can J Urol* 2017;24(3):8868-8870.

Amyloidosis is a protein folding disorder characterized by the deposition of fibrillar proteins into solid organs or tissues. Primary localized amyloidosis of the bladder is very rare and can mimic bladder cancer in its presentation with hematuria, lower urinary tract symptoms or a mass on imaging. A case of localized amyloidosis of the bladder in a 48-year-old man with painless gross hematuria and evidence of bladder mass on ultrasound is presented. Amyloidosis is a rare but important non-malignant process of the bladder. We present a review of the literature and suggestions for management of this rare bladder disease.

Key Words: amyloidosis, urinary bladder

Introduction

Amyloidosis is a heterogeneous group of disorders caused by the accumulation of amorphous proteinaceous material deposits within the extracellular space in various body tissues.[1] It is classified as primary (AL), secondary (AA) or hereditary (ATTR) and can be found focally or systemically.[2] It typically presents in men and women in their 5th to 7th decade of life.[3] Commonly involved organ systems include the lungs, larynx, skin, tongue and periorbital area.[4] Genitourinary tract involvement is uncommon and isolated amyloidosis of the bladder is exceptionally rare, with less than 200 cases reported in the literature.[5] Amyloidosis of the bladder is clinically important for urologists as it can mimic bladder cancer. Patients with isolated bladder amyloidosis typically present with gross hematuria (60%), irritative voiding symptoms (20%) or both (20%).[6] Furthermore, the cystoscopic appearance can be misleading, as bladder amyloidosis can appear as multiple yellow plaques with ulcerations, a hemorrhagic papillary lesion, or diffuse irregular bladder wall thickening.[7] There are no clinical or radiographic features that are pathognomonic of the disease, thus histopathology with Congo red staining is the only reliable diagnostic tool.[8]

Accepted for publication May 2017

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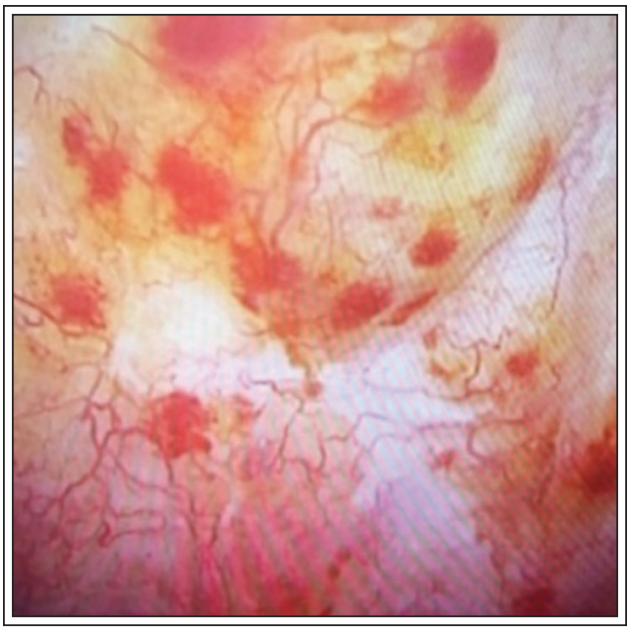

Figure 1. Cystoscopic findings of amyloid in the bladder.

Case report

A 48-year-old man was referred for evaluation of painless gross hematuria. Past medical history was significant for psoriasis, hypertension, dyslipidemia, nephrolithiasis and hemorrhoids. Cystoscopy demonstrated a diffuse yellowish lesion in the posterior bladder that was erythematous, friable and non-papillary in appearance, Figure 1. There were also vague mucosal changes with dystrophic calcifications noted within the trigone which were suspicious for early papillary change. Urinary cytology was negative. A CT urogram revealed diffuse irregular thickening of the posterior bladder wall, Figure 2. He was subsequently brought to the operating room for a transurethral resection of the bladder where representative biopsies were taken from the posterior lesion and papillary changes within the trigone.

Microscopic examination revealed eosinophilic, amorphous material in the subepithelial connective tissue. There were associated multi-nucleated foreign body giant cells. The Congo red stain confirmed the classic apple-green birefringence under polarized light consistent with amyloid, Figure 3. The surrounding area demonstrated edema and chronic inflammation without evidence of urothelial dysplasia or vessel involvement. Muscularis was not sampled. Mass spectrometry showed AL amyloid deposition, consistent with primary bladder amyloidosis.

Hematology consultation was requested to evaluate for systemic amyloidosis. Functional inquiry failed to reveal any constitutional, cardiorespiratory, gastrointestinal, or neurological symptoms. Serum chemistry profile was unremarkable. Serum and urine protein electrophoreses and serum free light chain assay were negative for a monoclonal protein. Based on the negative systemic work up, primary AL amyloidosis localized to the bladder was diagnosed. Recommendations for long term urological follow up with repeat surveillance cystoscopy were given to the patient.

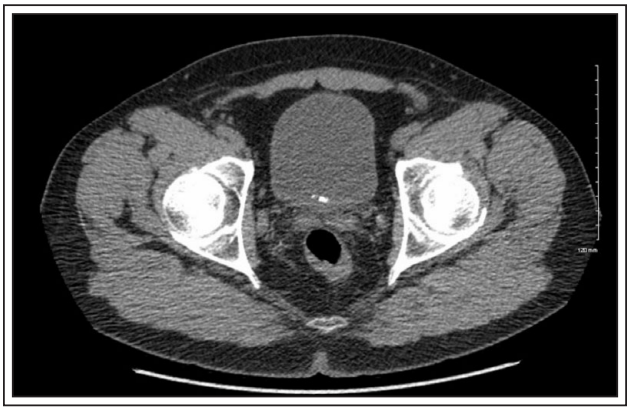

Figure 2. Axial slice of a computed tomography scan demonstrating increased thickness and calcification in the posterior bladder wall.

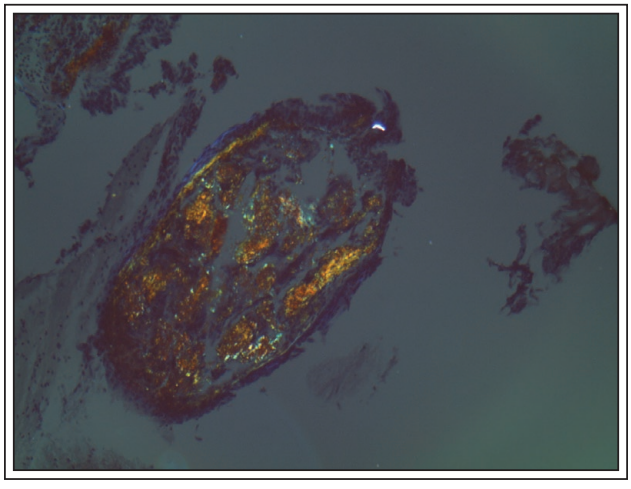

Figure 3. Transurethral resection of bladder tumor specimen showing areas of green birefringence under polarized light (Congo red stain, 100X).

Discussion

Amyloidosis of the bladder can be focal or systemic. The AL type is the most common form of localized bladder amyloidosis whereas the AA type is associated with conditions of chronic inflammation such as rheumatoid arthritis or chronic cystitis.[7,8] AL amyloidosis localized to the bladder is rare with approximately 200 cases reported in the literature.[5] It can present similarly to urothelial carcinoma of the bladder, as was seen in our case. On cross sectional imaging, amyloid can appear as a thickening or a polypoid mass extending from the bladder wall.[2] On cystoscopic examination the appearance can vary from an ulcerated, erythematous and friable area to a solid, well circumscribed sessile or papillary mass.[3] Histologically, it affects the stroma and lamina propria. It can be characterized by a chemotaxis of giant cells towards the amyloid deposits and possible vessel wall involvement.[7]

Definitive diagnosis is made by Congo red staining showing apple-green birefringence on polarization microscopy.[9] Mass spectrometry has been used more recently to allow typing of the amyloid deposits.[9] Once a diagnosis has been made, a work up for systemic amyloidosis should be undertaken. This can include but is not limited to: serum and 24 hour urine protein electrophoresis and immunofixation, serum free light chain assay, complete blood count with differential, antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, and rheumatoid factor. Echocardiography and nerve conduction studies should be considered if there is clinical suspicion of cardiac and nerve involvement.

Various treatments for primary amyloidosis of the bladder have been reported. The most common is transurethral resection for diagnosis and symptom control.[3] Other proposed treatments that aim to help manage patient symptoms or control active bleeding have included dimethyl sulfoxide (DMSO) instillation, steroids, anti-inflammatories and partial or complete cystectomy.[3] Given that the rate of recurrence is as high as 50%, monitoring with surveillance cystoscopy should be considered.[3] In the absence of a validated surveillance protocol,[5] cystoscopy should be performed every 6 to 12 months or in the presence of symptom recurrence.

The association between systemic amyloidosis and neoplastic processes including multiple myeloma, lymphoma, renal cell carcinoma and medullary thyroid carcinoma is well documented.[5,9] However, the relationship between bladder amyloidosis and urothelial carcinoma (UC) is less clear. The majority of reported cases fail to demonstrate an association, however one series found synchronous urothelial carcinoma lesions in half of their 18 amyloidosis cases.[9] Therefore, obtaining tissue is paramount to making a disease diagnosis as well as ruling out concomitant UC.

Conclusions

Primary localized bladder amyloidosis is a very rare condition which clinically and radiologically presents similarly to urothelial carcinoma. Treatment with resection is recommended for diagnosis and to rule out coexisting malignant neoplasms. There are no clinical or radiographic features that are pathognomonic of the disease, thus histopathology with Congo red staining is the only reliable diagnostic tool. Hematologic consultation is required to rule out systemic amyloidosis. Given the high bladder recurrence rate and the inability to rule out concomitant urothelial carcinoma without tissue diagnosis, long-term cystoscopic surveillance is recommended. □

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