Case - Renal amyloidosis: Adding to the differential of recurrent gross hematuria

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INTRODUCTION

Renal amyloidosis is a rare disease caused by abnormal accumulation of amyloid protein fibers in the kidney.[1] Amyloid light-chain (AL) amyloidosis is most common and involves amyloid deposits in the target organ produced by immunoglobulin light chain protein fragments.[2] AL amyloidosis typically presents as a systemic disease, which is a progressive and fatal disorder involving multiple organs.[2,3] Immunoglobin light chains are also responsible for localized diseases, with amyloid deposits at single anatomical sites.[4] The origin of the light chains becoming amyloid plaques locally are not well understood, though chronic inflammation and local immunoglobulin production may play a role in its development.[3,5]

Localized AL amyloidosis accounts for 7–12% of all amyloidosis cases.[3] Life expectancy is comparable to the general public, but the clinical course is marked by frequent local progressions that require additional treatment.[4] The rarity of localized renal amyloidosis has made treatment plans for physicians difficult. Herein, we report a case of biopsy-confirmed localized renal AL amyloidosis presenting as recurrent gross hematuria and review current management strategies of this rare diagnosis.

CASE REPORT

A 53-year-old female was referred to urology with a history of asymptomatic, self-resolving, recurrent gross hematuria. The patient was a lifelong non-smoker and denied history of urinary tract infections or nephrolithiasis. Family history included kidney cancer, ovarian cancer, and lymphoma. Two years prior, the patient had a gross hematuria workup; cystoscopy, urinary cytology, and computed tomography (CT) urogram at the time were all negative. A complete duplication of the right collecting system was identified.

Given the history of recurrent hematuria, CT urogram was repeated and again negative. Cystoscopy with bilateral retrograde pyelograms with isolated cytologies of the bladder and upper tracts were also negative. As the patient further complained of periodic asymptomatic gross hematuria, bilateral diagnostic ureteroscopies were performed. This demonstrated scant membranous tissue within the left distal ureter, which was successfully biopsied and dilated. Erythema was seen within the left renal pelvis, and within the upper tracts of both right collecting system moieties (Figure 1).

Endoscopic biopsies of all three sites revealed similar histologic features with masses and globules of eosinophilic material, which was birefringent with Congo red stain under polarized light consistent with amyloid (Figures 2, 3). Bilateral upper tract urinary cytologies acquired via ureteroscopic aspiration identified scant congophilic material consistent with amyloid. All samples were negative for high-grade urothelial cells. The diagnosis of bilateral amyloidosis was confirmed by a second out-of-province expert pathologist.

These findings prompted an urgent referral to hematology to investigate for systemic amyloidosis. Bone marrow biopsy did not demonstrate the presence of monoclonal plasma cells. There was no evidence of a monoclonal para protein or elevated serum free light chains. Biopsies of the skin, sigmoid, and rectum were also negative for amyloid on Congo red staining. Mass spectrometry of the left and right ureteric mucosa biopsies confirmed AL amyloidosis.

The patient was subsequently placed on close surveillance to monitor for the potential development of systemic disease. Through 24 months of followup to date, urinary cytologies remain consistent with amyloid congophilic material. CT urograms remain negative. Persistent stable erythema remains within the bilateral upper tracts on diagnostic ureteroscopy. Fortunately, there has been absence of systemic disease, and her hematuria has not recurred since the diagnosis has been made.

KEY MESSAGES

- Localized renal AL amyloidosis is a rare but benign condition that can mimic urothelial carcinoma, often presenting with recurrent gross hematuria.
- Diagnosis is challenging, requiring histologic confirmation with Congo red staining and mass spectrometry.
- Systemic involvement must be ruled out using bone marrow biopsy, serum-free light chains, and fat pad biopsy to ensure appropriate management.
- Treatment depends on symptom severity, with conservative management for stable cases and surgical resection for symptomatic lesions.

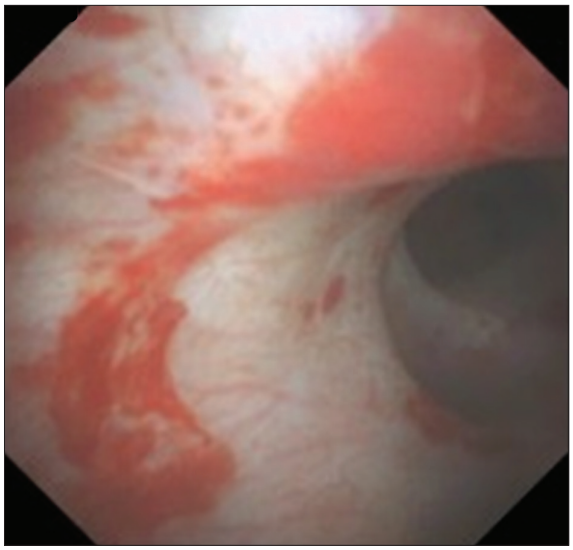

Figure 1. Erythema present within left renal pelvis.

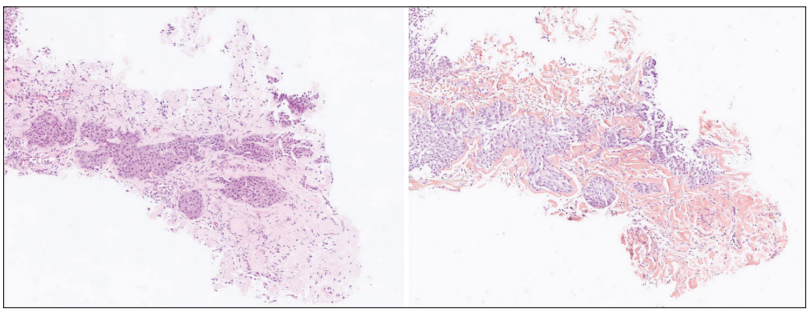

Figure 2. Endoscopic biopsy specimen of distal right ureter. Left: β-pleated amyloid sheet structure without staining. Right: β-pleated amyloid sheet structure with positive Congo red stain.

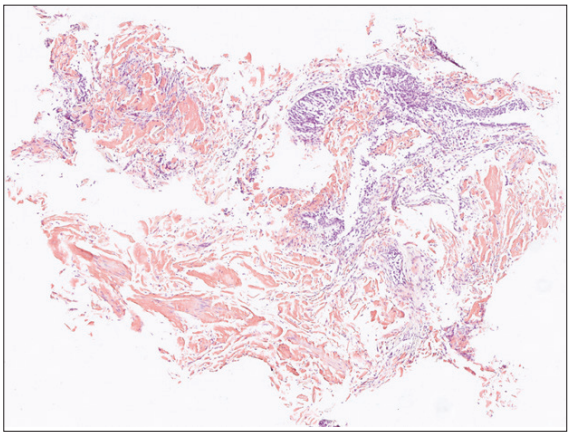

Figure 3. Endoscopic biopsy specimen of distal left ureter positive for Congo red stain.

DISCUSSION

Localized AL amyloidosis of the genitourinary tract is an exceedingly rare disease characterized by abnormal amyloid protein deposits in tissue.[1] The bladder is most commonly affected (50%), followed by the ureter (25%), urethra (20%), and renal pelvis (6%).[1,6] Bilaterality of the renal pelvis and ureter has only been documented in one previously published case.[1] Our case represents a most uncommon, bilateral localized renal AL amyloidosis involving the renal pelvis, ureters, and both moieties of a completely duplicated right-side collecting system.

Preoperative diagnosis of renal AL amyloidosis remains difficult to obtain due to the clinical and cystoscopic similarity of amyloidosis to urothelial cell carcinoma.[3] Patients commonly present with gross hematuria (60%).[1,6,7] Gross hematuria can be asymptomatic or associated with colicky pain, increased frequency, malaise, hydronephrosis, ureteral stricture, and/or dysuria.[1,5-7] On imagery, CT may show hyperattenuation due to calcification or hemorrhage, which can be difficult to discern.[6]

Magnetic resonance imaging (MRI) of amyloid deposits often show low T2 signal intensity, distinguishing them from transitional cell carcinoma, although lymphoma and desmoplastic metastases can also show low T2 intensity.[1,6] Overall, no imaging method is pathognomonic for renal AL, which would explain the consistent negative imagery findings within our case. Thus, diagnosis relies on histologic confirmation using Congo red staining, looking for the characteristic birefringence appearance under polarized light within biopsied tissue.[3]

Once the diagnosis of amyloid proteins is confirmed, it is crucial to rule out systemic disease, which would denote a poor prognosis. Patients can present with autoimmune disorders, such as Sjogren syndrome,

lymphoproliferative disease, marginal lymphoma, and monoclonal gammopathy of undetermined significance, as well as systemic AL amyloidosis.[4]

Staging evaluation includes incorporating fat pad and bone marrow biopsy, a 24-hour urine protein electrophoresis with immunofixation and serum-free light chains, and mass spectrometry for identifying immunoglobulin-derived amyloid fibrils.[3] Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is gold standard for amyloid typing.[3] A lack of monoclonal protein, abnormal serum free light chain ratio, or monoclonal marrow plasma cells by hematologic evaluation rules out systemic AL amyloidosis.[3]

Once localized amyloidosis is confirmed, there is very low risk of progression to systemic AL amyloidosis.[2-4] Thus, continued long-term monitoring for systemic disease may not be warranted.

A diagnosis of localized renal AL amyloidosis is considered benign, and treatment options depend on the severity of symptoms.[6] Treatment should begin conservatively, with regular surveillance imaging for hematuria and/or hydronephrosis.[2] First-line therapy for symptom relief is local surgery, with resection of any found pseudotumor. Surgery is the only curative treatment modality, as it removes both amyloid deposits and amyloidogenic b-cells.[1,3]

Endoscopic resection should be attempted, and in select cases, segmental resection may be required.[2] If this fails, nephrectomy or nephroureterectomy can be considered.[1]

Radiotherapy or corticosteroids can be used in patients not deemed surgical candidates. Radiotherapy has potential to be a future first-line therapy, but at present, it is underused and the effectiveness of radiotherapy requires further comparative assessment.[3] Corticosteroids can be useful to reduce ureteral stenosis, but do not treat already-established amyloid deposits.[3,8] In rare circumstances, where secondary lymphoma is present, chemotherapy can be used.[3] Following initial treatment, recurrence risk is <40%.[1] Moreover, projected 10-year overall survival is 92%.[3,4]

Given the absence of standardized surveillance or management guidelines for renal AL, we recommend shared followup with urology and hematology. Acknowledging the absence of systemic involvement or renal impairment in our case, rheumatology and nephrology followup is not required.

Our patient is receiving cystoscopic surveillance, including bilateral retrograde pyelograms, every six months. Repeat CT urography and/or bilateral diagnostic ureteroscopy are performed annually. The rational for continued ureteroscopy despite negative imagery is a reflection of our patient's initial diagnosis, where erythematous amyloid tissue was only detectable via ureteroscopy and biopsy. Surveillance ureteroscopy allows for assessment of progressive erythema or subtle findings, while CT allows for assessment of macroscopic disease. Should adverse findings be identified, surgical resection will be reconsidered. Otherwise, close surveillance is presently sufficient.

CONCLUSIONS

This case report outlines the current research available on treatment practices for localized renal AL amyloidosis. Given the rarity of this diagnosis, clinicians should engage a multidisciplinary approach to management.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

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