We report on two cases of localized amyloidosis involving the ureter. The patients were a 64-year-old woman with right upper quadrant pain (case 1) and a 36-year-old woman suffering from left flank pain and intermittent gross hematuria (case 2). An intravenous pyelography of case 1 revealed multiple filling defects in the entire right ureter, whereas retrograde pyelography in case 2 showed diffuse narrowing in the mid and lower portions of the left ureter. Localized amyloidosis of the ureter was diagnosed in the two cases, and both had amyloid deposition in the renal pelvis and the urinary bladder. Right nephroureterectomy was performed in case 1, but a segmental resection of the ureter with preservation of the kidney was administered in case 2. These two cases demonstrate that ureteral amyloidosis can be associated with amyloid deposition in the renal pelvis and the urinary bladder. Although ureteral amyloidosis is a rare occurrence, it should be considered in the differential diagnosis of ureteral obstruction to avoid unnecessary radical surgery.

Key Words: Amyloidosis-Ureter-Renal Pelvis-Bladder

CASE REPORT

Case 1

A 64-year-old woman was admitted for one year history of right upper quadrant pain without hematuria or other urinary symptoms. Blood and urine examinations were within normal ranges, including urine cytology.

An intravenous pyelography revealed multiple filling defects along the entire length of the right ureter with severe hydronephrosis and a normal left urinary system. Multiple biopsies were taken through an ureteroscope in the sites of stricture, and the following pathologic diagnosis was of amyloidosis of the ureter. Cystoscopy showed multiple yellow elevated nodular lesions in the right lateral and posterior walls around the right ureteral orifice. Right nephroureterectomy and transurethral resection of the bladder were performed. Six months later a follow-up cystoscopy demonstrated recurrent amyloidosis of the bladder. A transurethral
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resection of the bladder was repeated. Grossly, the entire ureteral wall was diffusely thickened and rigid. The mucosa of the ureter and renal pelvis was ragged, multifocally hemorrhagic and ulcerated (Fig. 1). The kidney showed a normal appearance. Histologic findings revealed an extensive amorphous homogeneous eosinophilic extracellular deposit in the submucosa and in the muscle coats of the ureter and renal pelvis (Fig. 2A). The deposits were of a mahogany red color after Congo red staining and showed an apple green birefringence under a polarizing light microscope (Fig. 2B). A transurethral resection specimen of the bladder showed a nodular amyloid deposit in the submucosa and muscle layer. Bence-Jones proteinuria and monoclonal gammapathy were not found, thus excluding the possibility of an associated multiple myeloma. The patient is well six months after the second transurethral resection of the bladder.

Case 2

A 36-year old woman was admitted for the investigation of a 3-year history of intermittent gross hematuria and left flank pain. A retrograde pyelography showed diffuse narrowing in the mid and lower portions of the left ureter and left hydroureteronephrosis (Fig. 3). In view of the uncertain nature of the partial ureteral obstruction, exploration was undertaken. Tissues from the mid and distal ureters were sent for frozen section examination to exclude the clinical suspicion of ureteral transitional cell carcinoma. Amyloidosis of the distal ureter was diagnosed, and thus, the possibility of a malignant neoplasm was excluded. A distal segment of the ureter, measuring 12 cm in length, was excised and the left kidney was autotransplanted in the iliac fossa.

Two years after the operation the gross hematuria relapsed. A right retrograde pyelography revealed calyceal blunting of the right kidney with hydroureteronephrosis, and ureterocystoscopy showed

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Fig. 1. Gross photograph in case 1. The ureteral wall is diffusely thickened, and the mucosa of the ureter and renal pelvis is multifocally hemorrhagic and ulcerated.

Fig. 2. (A) There is extensive deposition of amorphous eosinophilic materials in the submucosa of the ureter beneath the urothelial epithelium (case 1). (B) The deposits exhibit apple green birefringence under a polarized light microscope (Congo-red stain) (case 1).
irregularly elevated to flat lesions in the upper calyx of the right renal pelvis, multiple yellow nodules on the bladder mucosa, and a small papillary mass at the inferomedial side of the left ureteral orifice. Biopsies were taken from the renal pelvis, bladder, and left ureteral orifice, and a double-J stent was inserted. A pathologic examination revealed amyloidosis of the renal pelvis, chronic cystitis, and a papillary nephrogenic adenoma in the left ureteral orifice. The amyloid deposition was diffusely present in the renal pelvis, particularly in the lamina propria, but the muscle layer was relatively spared. Amyloid deposition around the vascular wall was also seen. Two months later during a follow-up intravenous pyelogram, proximal and distal narrowings of the right ureter were observed, and the right hydronephrosis had aggravated. High-pressure balloon dilatation was performed to widen the narrowed portions of the right ureter. A retrograde pyelogram showed multiple nodular lesions in the upper calyx and renal pelvis. Pyelotomy was performed and resected lesions of the renal pelvis were confirmed to be affected by amyloidosis. The patient remains well after the pyelotomy.

**DISCUSSION**

Amyloidosis can be classified as “primary amyloidosis”, when no etiology is apparent with respect to amyloid deposition, or “secondary amyloidosis”, when it occurs as a complication of an underlying chronic inflammatory diseases or multiple myeloma. Moreover, amyloid deposition may be confined to one organ (localized) or involve multiple organ systems (systemic).

In the urinary tract, amyloid deposits are most frequently found in the renal parenchyma, but these are always seen in cases of systemic amyloidosis. Localized amyloid deposit in the urinary tract is rare, especially in the ureter or renal pelvis. The bladder is the most common site.

Less than 40 cases of primary ureteral amyloidosis have been reported since Lehmann described the first case in 1937. The age range of ureteral amyloidosis is wide (ranging from 12 years to 77 years), and approximately 75% of the reported cases occur in the 5th to 7th decades. The disease shows a female predominance (59%), similar to that of amyloidosis in the renal pelvis and in contrast to that found in the urinary bladder, where a slight male predominance has been reported. The main presenting symptoms of ureteral amyloidosis are abdominal pain and hematuria. Calcification in the ureteral wall on plain X-ray film is considered a diagnostic feature. Intravenous pyelography usually shows partial or complete obstruction of the ureter, with proximal hydroureter and hydronephrosis. In most cases an ureteral neoplasm is suspected and renal calculus, tuberculosis, stricture, and endometriosis are included in the preoperative diagnoses. Treatment includes a nephroureterectomy, ureter reimplantation, a resection with end-to-end anastomosis, a ureteral resection with renal autotransplantation, and ileal ureter replacement. In localized amyloidosis of the ureter, a biopsy is not commonly feasible and the diagnosis is usually established by the histologic examination of surgically removed tissue. However, as the condition is benign, conservative management is the more appropriate treatment. Therefore, it appears that a more precise preoperative diagnosis is essential in localized amyloidosis of the ureter to preserve the kidney. Moreover, a correct diagnosis of amyloidosis of the ureter during frozen section evaluation in doubtful cases may result in local resection and preservation of the kidney. Our second case was diagnosed intraoperatively on frozen section examination and nephrectomy was avoided. Although the first case was diagnosed as amyloidosis by ureteroscopic biopsy, nephroureterectomy was performed as the entire length of the ureter and renal pelvis were involved. However, isolated amyloidosis of the renal pelvis is much rarer and most cases have been combined with ureteral amyloidosis. The current two cases also showed amyloid deposition in the renal pelvis.

Amyloidosis of the bladder was first described at autopsy by Solomin in 1897. Since that time about 160 cases have been reported in the literature. The common symptoms in patients
with this condition are gross hematuria, irritative voiding symptoms, or both. In the majority of cases the cystoscopic appearance is that of an infiltrating neoplasm, thus making biopsy mandatory to establish the true nature of the lesion. Transurethral resection, fulguration and laser application have been the standard therapeutic modalities.\textsuperscript{14,15} Diffuse involvement of the bladder is difficult to manage and may require urinary diversion. In our case 1, transurethral resection of bladder lesions was performed, but amyloidosis of the bladder recurred six months later, and required a repeated transurethral resection. In case 2, there was a similar cystoscopic finding with amyloidosis of the bladder, but the biopsy demonstrated cystitis, confirming the diagnostic difficulty presented by amyloidosis without histologic confirmation. The recurrence rate of localized amyloidosis of the bladder is high, as evidenced by our two cases, with up to 54% of patients showing recurrence,\textsuperscript{15} and therefore, a long-term cystoscopic follow-up is recommended. Amyloidosis of the bladder can be present as an isolated form without the involvement of other urinary tracts, but it can also be associated with the involvement of other sites of urinary tract, as seen in case 1 (ureter and renal pelvis).

We report on two cases of ureteral amyloidosis. The first case demonstrated renal pelvic and bladder involvement and the other showed bilateral ureteral and renal pelvic involvement. In the second case the kidney was saved because a diagnosis of amyloidosis of the ureter was made during frozen section evaluation. Since amyloidosis of the urinary tract frequently recurs, long-term follow-up is recommended.

**REFERENCES**