
CASE REPORT

Localised Ureteric Amyloidosis Mimicking Urothelial Tumour

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ABSTRACT

Amyloidosis is a pathological process characterised by extracellular deposition of fibrillar protein. Systemic amyloidosis with multiple organ involvement is more common than localised amyloidosis. Localised amyloid deposition in the urinary tract is uncommon and isolated involvement of the ureter and renal pelvis is a rare presentation of this uncommon disease. Primary localised amyloidosis of the renal pelvis and ureter can closely resemble malignancy in its presentation, ureteroscopic appearance, and imaging features. This report is of two patients with primary localised amyloidosis involving the renal pelvis and ureter. Both patients first presented with haematuria with loin pain and urothelial tumour was suspected. Diagnosis was only made by histological analysis. In this article, important aspects of the clinical and imaging findings are discussed and the literature is reviewed.

Key Words: Amyloidosis; Ureter; Ureteral neoplasms; Urologic neoplasms

中文摘要

類似泌尿道上皮腫瘤的輸尿管局限性澱粉樣變性

馮啟邦、黃文鳳、簡偉權、劉詠詩、戴志健

澱粉樣變性是一種病理過程，特徵為纖維蛋白在細胞外沉積。多器官受累的系統性澱粉樣變性較局限性澱粉樣變性常見。泌尿道的局限性澱粉樣蛋白沉積很少見，輸尿管和腎盂孤立受累更是這種病的罕見病徵。腎盂和輸尿管的原發局限性澱粉樣變性的症狀、輸尿管鏡表現和影像學特徵非常類似惡性腫瘤。本文報告兩個累及腎盂和輸尿管的原發局限性澱粉樣變性的病例。兩名患者病發時出現血尿與腰痛，起初懷疑是泌尿道上皮腫瘤。診斷只能靠組織學分析。本文探討澱粉樣變性關鍵性的臨床和影像學表現並作文獻回顧。

INTRODUCTION

Amyloidosis comprises a constellation of disease entities characterised by extracellular deposition of eosinophilic fibrillar protein in various tissues and organs. Amyloidosis can be classified as systemic or

localised on the basis of the distribution of amyloid deposition.¹⁻⁴ Infrequently, the urinary tract and supporting retroperitoneum are involved and, rarely, the ureter, renal pelvis, and urethra are affected.³ Clinically, the presenting signs and symptoms include haematuria,

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ureteric stricture, and hydroureteronephrosis. The most common findings of amyloid deposition on computed tomography (CT) are focal or diffuse wall thickening in the urinary tract with intramural calcification.^{5,6} Since the presenting symptoms closely resemble those of malignancy involving the ureters, it is extremely difficult to diagnose this condition by clinical and imaging features alone. Histological correlation is necessary to establish an accurate diagnosis, and imaging findings may help direct the location of biopsy. This report is of two patients who presented with haematuria and hydronephrosis. They were suspected to have ureteric malignancy. The diagnosis of amyloidosis of the ureter was only made by biopsy and histology confirmation.

CASE REPORTS

Case 1

A 32-year-old woman was admitted to the Pamela Youde Nethersole Eastern Hospital for gross haematuria and left-sided loin pain in January 2012. She had had dysuria, non-specific left-sided loin discomfort, gross haematuria, and turbid urine since October 2011. She was treated for urinary tract infection by her general practitioner and was prescribed multiple courses of antibiotics. However, her symptoms persisted with increasing left-sided loin pain and whole-stream haematuria. At admission, ultrasonography showed mild left hydronephrosis and hydroureter. Contrast CT of the abdomen and pelvis was arranged for evaluation of haematuria and loin pain.

Mild left hydronephrosis and moderately dilated left renal pelvis were seen on the pre-contrast scan. A few tiny punctate calcifications were seen at the wall of the left renal pelvis and left proximal ureter. A mildly dilated left proximal ureter with stenosis at the mid-portion of the left ureter was found. Post-contrast CT scan confirmed the presence of mild diffuse ureteric wall thickening with enhancement and peri-ureteric fat stranding in the mid and distal portions of the left ureter (Figure 1). A small focal bulge was noted at the left vesico-ureteric junction. Delay-phase CT scan showed no significant contrast hold up, with free flow of contrast into the bladder when compared with the right ureter. No enlarged abdominal lymph node was detected.

In view of the CT findings of suspected ureteric neoplasm, cystoscopy, ureteroscopy, and insertion of a double J catheter were arranged. Cystoscopy showed an elevated and friable lesion with contact



Figure 1. Computed tomography scan performed in (a) April 2012 showing mild diffuse wall thickening and mild peri-ureteric fat stranding at the mid-portion of the left ureter (arrows); and (b) May 2013 showing increase in wall thickening and peri-ureteric fat stranding at the mid-portion of the left ureter (arrows).

bleeding surrounded the left ureteric opening. No other suspicious lesion was seen in the urinary bladder. Left retrograde pyelogram showed irregular filling defects in the left ureter (Figure 2) with abnormal contrast hold up. Left ureteroscopy showed erythematous and friable mucosa along the left ureter. Biopsies of the lesions at the left ureteric opening and left ureter were performed and sent for histology study. A double J catheter was inserted into the left ureter.

Histology sections of the biopsies at the left ureteric opening and left ureter showed scanty surface urothelium with no significant atypia. The underlying stroma demonstrated abundant patches of acellular

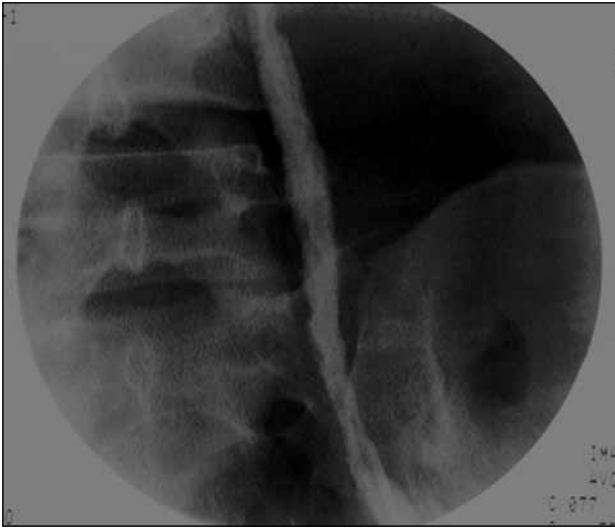


Figure 2. Retrograde pyelogram image showing irregular filling defects in the mid and distal portions of the left ureter.

lightly eosinophilic material, which showed apple-green birefringence under polarised light (Figure 3). No significant inflammatory or plasma cell infiltrate was seen. These findings were consistent with amyloidosis.

Dynamic mercapto-acetyl-triglycine (MAG3) scintigraphy, which is a radioisotope study for evaluation of renal function, was performed after the double J catheter was removed. The left kidney showed satisfactory tracer extraction and excretion with time to peak count (Tmax) of 3.2 minutes. Although the left renal pelvis and upper ureter were prominent in size, there was free drainage of excreted tracer into the urinary bladder. The right kidney also showed satisfactory tracer extraction and excretion with free drainage of excreted tracer into the urinary bladder. The differential renal function was 53% for the left kidney and 47% for the right kidney.

Other than intermittent episodes of gross haematuria, the patient had been largely asymptomatic. Follow-up contrast CT scan in May 2013 again showed a few tiny punctate calcifications on the wall of the left renal pelvis and left proximal ureter. The degree of left hydronephrosis and left proximal hydroureter was similar. However, there was progression of diffuse left ureteric wall thickening and perifocal fat stranding in the mid and distal left ureter. The focal bulging at the left vesico-ureteric junction extending to the left ureteric opening showed interval increase in size (Figure 4). Again, delay-phase CT scan showed no significant

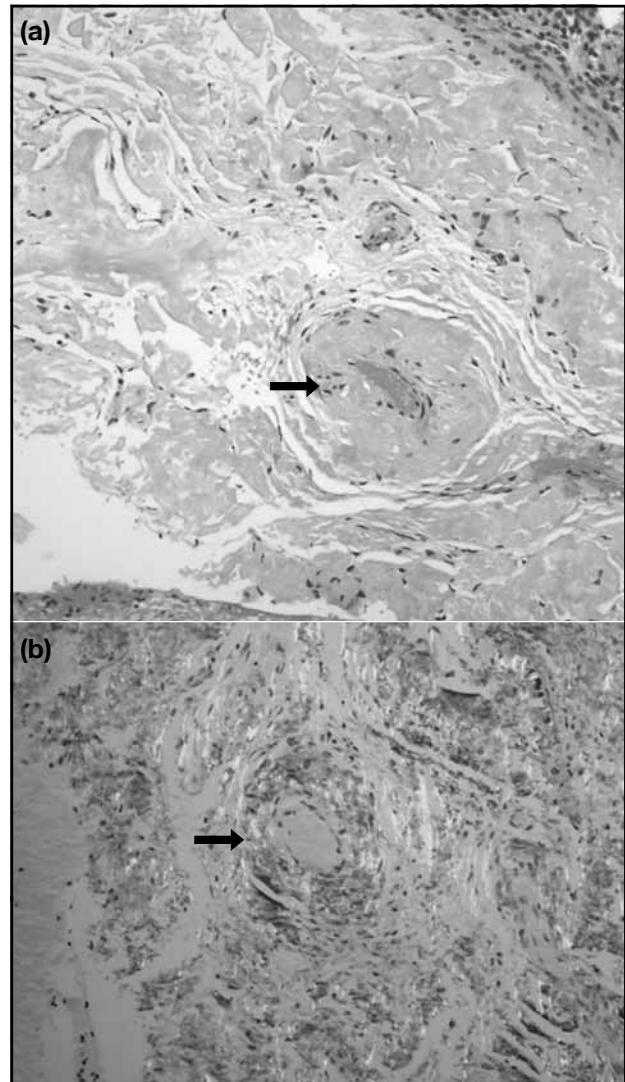


Figure 3. Histology of the left ureteric biopsy: (a) Haematoxylin and eosin stain showing amorphous eosinophilic deposit in the blood vessel wall (arrow) with no significant plasma cell infiltrate; (b) Congo red stain under polarised microscopy showing apple-green birefringence in the blood vessel wall (arrow) compatible with amyloid deposit (original magnification, x 20).

contrast hold up with free flow of contrast into the bladder. Similar to the previous CT scan, no enlarged abdominal lymph node was found. Since the disease was localised and the patient was largely symptom-free with normal renal function in both kidneys, she opted for conservative management and was closely followed up by the urologist.

Case 2

A 69-year-old man presented with haematuria and non-specific left-sided loin pain since November 2011. CT urogram showed a moderately dilated right renal

pelvis and right proximal ureter. Diffuse thickening of urothelium affecting the entire right renal pelvis and right ureter down to the right vesico-ureteric junction was noted. Amorphous tiny calcifications were seen in the thickened urothelium at the interpolar region of the right kidney and right renal pelvis (Figure 5). Subsequent cystoscopy showed an irregular mass

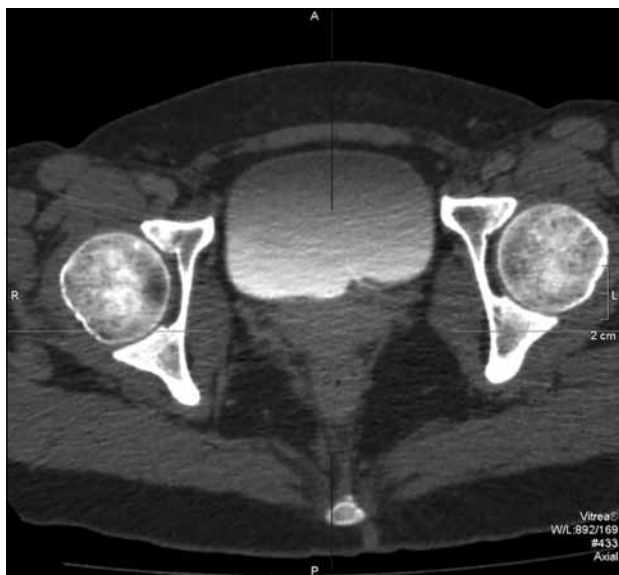


Figure 4. Computed tomography scan showing focal bulging at the left vesico-ureteric junction extending to the left ureteric opening.



Figure 5. Computed tomography scan showing amorphous calcifications in the thickened urothelium at the interpolar region of the right kidney and right renal pelvis.

with friable mucosa at the right vesico-ureteric junction. Biopsy was taken for suspected malignancy, but histology showed no evidence of dysplasia or malignancy.

In the progression CT scan done in mid-2012, interval progression of urothelial thickening and obstruction in the right renal pelvis and ureter were noted. In view of worsening of symptoms and associated radiological features, right partial ureterectomy and reimplantation of the right ureter into the bladder (psoas hitch) were performed at the end of 2012 for suspected urothelial tumour. Intra-operative frozen sections of the biopsies taken at the right renal pelvis, proximal ureter, ureteric margin, and vesico-ureteric junction showed no evidence of malignancy. However, the histology sections of the biopsies showed amorphous pinkish depositions in the subserosa with foreign body giant cell reaction. Similar to the first patient, Congo red and crystal violet stains confirmed the presence of amyloid deposits. Overall, the features were compatible with amyloidosis.

Blood for immunoglobulin pattern, serum protein electrophoresis, and bone marrow biopsy showed no evidence of systemic amyloidosis. There was improvement in symptoms with no further loin pain and haematuria.

DISCUSSION

Amyloidosis can be classified as ‘primary’, when no aetiology is apparent with respect to amyloid deposition, or ‘secondary’, when it occurs as a complication of an underlying chronic inflammatory disease such as Crohn’s disease, rheumatoid arthritis, Reiter syndrome, or ankylosing spondylitis.^{7,8} Amyloidosis can also be categorised as ‘localised’ when amyloid deposition is confined to one organ or the more common ‘systemic’ form when multiple organs are involved. Localised disease is only present in approximately 10% to 20% of patients.³ Systemic amyloidosis is progressive and usually fatal, while localised amyloidosis generally only requires supportive or localised treatment. Therefore, the distinction between localised and systemic disease is clinically important. The diagnosis can be made by demonstrating the presence of amyloid deposits in subcutaneous fat, rectal mucosa, bone marrow, urine, or serum. Patients who present with localised amyloidosis have no demonstrable monoclonal protein in the serum, urine, or bone marrow plasmacytosis.⁸ The incidence of amyloidosis is 8 in 1 million people each year.³ Overall,

the incidence has been gradually increasing, particularly secondary amyloidosis, presumably due to the longer life expectancy of patients with chronic diseases.^{3,9}

The incidence of localised amyloidosis involving the urogenital tract is unknown, but it is rare. In the urogenital tract, amyloid depositions are most frequently found in the renal parenchyma, but these are always seen in systemic amyloidosis. When amyloid is detected in the urinary tract, but not the kidney, it is generally a localised form.¹⁰⁻¹² Localised amyloidosis of the urinary bladder is more common than that of the renal pelvis, ureter, and urethra. Clinically, most patients present with haematuria and non-specific loin pain.¹² Most cases are in women aged 40 to 60 years.¹¹ Therefore, due to its rarity and bizarre clinical presentation, localised ureteral amyloidosis is unlikely to be diagnosed preoperatively and is commonly misdiagnosed as a neoplasm.

Similarly, the imaging findings of localised amyloidosis are usually non-specific. Amyloid deposition in the ureter is usually unilateral and often involves the lower ureter.^{3,11} Common imaging findings include focal or diffuse areas of wall thickening, intra-ureteral filling defects, irregular ureteral narrowing, and stricture with concomitant hydronephrosis.^{3,11} All of these findings were found on the CT scans for these patients. The progression of diffuse left ureteric wall thickening and peri-ureteric fat stranding in the mid and distal left ureter in the follow-up CT scans of both patients was suggestive of disease progression. Among the imaging features, it has been mentioned that submucosal or intramural calcification of the renal pelvis and ureter is characteristic of amyloidosis.^{3,5,13} CT scan of both patients demonstrated the presence of tiny punctate calcifications in the renal pelvis. Weiwei et al⁵ suggested that diffuse ureteric wall thickening versus an 'indurated appearance' and absence of space occupying effect are two possible features that distinguish ureteric amyloidosis from malignancy. However, since these imaging findings are still non-specific and indistinguishable from those of urothelial carcinoma, biopsy and histological analysis are essential to establish the diagnosis.

Dynamic MAG3 scintigraphy performed for the first patient showed satisfactory tracer extraction and excretion in both kidneys. This result signified that the excretory function of the kidney was not affected, even though there was presence of hydronephrosis. Hence, relief of obstruction by operation or diversion was not

necessary.

Since the presentation of localised primary amyloidosis of the ureter generally mimics cancer of the respective anatomical site, resection of the lesion remains the primary treatment. However, following confirmation of histological diagnosis, further treatment remains likely, especially for symptomatic patients.¹ Treatment with ureteric stenting and an occlusive dressing technique using dimethyl sulfoxide for 6 months, leading to complete resolution of the lesion, has been described in the literature.¹⁴

CONCLUSION

Although the clinical and imaging findings of amyloidosis involving the renal pelvis and ureter are often non-specific and mimic those of urothelial tumour, awareness of the relevant imaging findings helps to alert physicians to this condition. Localised ureteric amyloidosis should be considered a differential diagnosis, especially in women with ureteric wall thickening, ureteric stricture, and hydronephrosis. The presence of submucosal or intramural calcification of the renal pelvis and ureter on CT scan is characteristic of amyloidosis. Biopsy and histological analysis are essential to establish the diagnosis of ureteric amyloidosis and are therefore recommended for differentiation from urothelial tumour and to avoid unnecessary operation.

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