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Case Report

A case of bladder amyloidosis with bilateral circumferential lower ureteric calcification.

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Abstract

A 74-years old man with haematuria was found to have a bladder mass and left lower ureteric obstruction. The CT urogram showed lower ureteric calcification bilaterally. The endoscopic resection of the bladder mass showed amyloidosis. Resection of the stenosed left ureter with Boari flap reconstruction produced good results. Histopathology confirmed the presence of ureteric wall calcium deposits. Bilateral ureteric amyloidosis and calcification is rare. However, it is usually localized and has a good outcome. A high degree of suspicion will prompt early diagnosis which will prevent more extensive resection surgery.

Key words: Amyloidosis, Ureteric calcification, Upper urinary tract obstruction, Hematuria

Introduction

Amyloids are insoluble fibrillar proteins that are deposited extracellularly in a range of organs leading to a heterogeneous group of conditions known as amyloidosis. It can be systemic or local (1, 2).In contrast to systemic amyloidosis, local amyloidosis is non progressive and fatality is rare. Most common site of urinary tract amyloidosis is the bladder and ureteric involvement is rare (2). Bilateral ureteric involvement with calcification of ureteric wall is rarer (3, 6.)Ureteric amyloidosis is rarely diagnosed preoperatively (1).More importantly ureteric amyloidosis may mimic malignancy and may be over-treated with nephroureterectomy (2, 4) .We describe a case of bilateral lower ureteric calcification due to amyloidosis, which was managed with Ureteroneocystostomy and a Boari flap.

Case report

A 74-year-old man presented with intermittent painless visible haematuria and left loin pain of one-month duration. He did not have dysuria, frequency or fever. He was a rubber tapper by profession and a non-smoker. He had no other comorbidities. His physical examination was unremarkable.

The ultrasound scan KUB revealed an irregular bladder lesion and left sided mild hydronephrosis. He had a normal serum creatinine level (0.92 mg/dl) and serum prostate specific antigen (PSA) level was 3.5 ng/dl. Trans urethral resection of the suspected bladder tumour (TURBT) was performed (Figure 1). The histopathology showed masses of eosinophilic extracellular deposits in the bladder wall

without associated inflammation or evidence of malignancy (Figure 2A and 2B). Due to the suspicion of amyloidosis, Congo red stain was done which revealed the eosinophilic deposits to be stained salmon pink (Figure 2C). The classical apple green birefringence under polarized light confirmed the presence of amyloid (Figure 2D).A CT urogram (CTU) showed calcification of left lateral wall of the bladder and walls of distal ureters with left hydronephrosis (Figure 3). The calcification was more pronounced in the left ureter. Bladder wall calcifications were mottled. Urine for acid-fast bacilli and culture for Mycobacterium tuberculosis were negative. He had not travelled abroad.

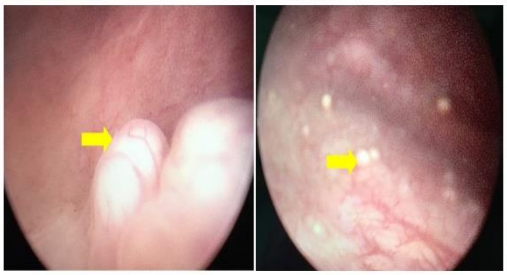

Fig 1. *Cystoscopic appearance of bladder lesions*

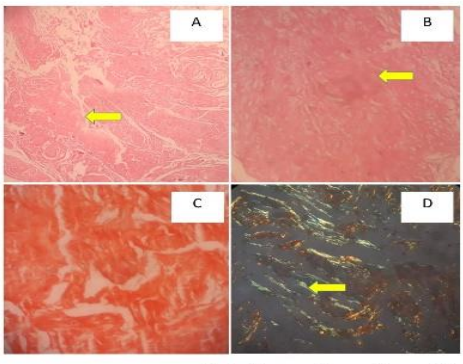

Fig 2.*Microscopic appearance of bladder (A) Masses of eosinophilic extracellular deposit in bladder wall (yellow arrow) (H&Ex40 (C) Salmon pink yellow colour. Congo redx40 (D) Apple green birefringence (yellow arrow) (Congo red with polarizer x10)*

The left ureteric reimplantation was planned. During surgery the left lower ureter was thickened, hard and brittle suggestive of calcification for about 5 cm and proximal segment was grossly dilated. The lumen was stenosed and a further 3 cm of proximal ureter was resected owing to unhealthy fragile mucosa with tiny multiple lumps. Left ureteric reimplantation was performed using a Boari flap.

The histopathological examination of resected ureter after Congo red staining and examination under polarized light confirmed the presence of amyloid. The Vonkossa stain showed granular calcium deposits within amyloid deposits of the ureteric wall (Figure 4). Two years later the patient is asymptomatic and ultrasonography showed normal upper tracts.

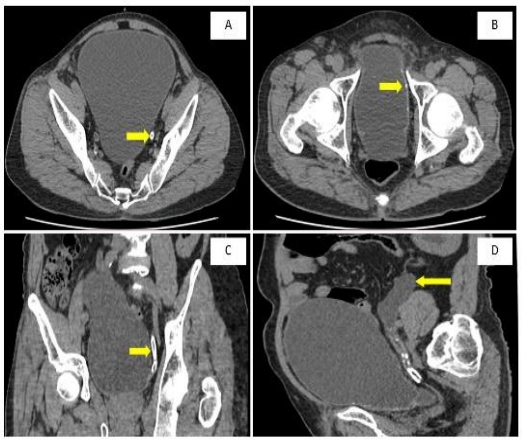

Fig 3. *Non-contrast pictures of the CT urogram showing (circumferential calcification of ureteric walls (B) calcifications of the bladder wall (C) calcification of the ureteric wall (D) dilated left ureter proximal to the calcified lower segment*

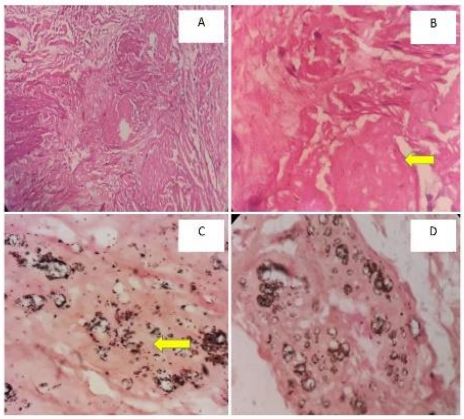

Fig 4. *Microscopic appearance of ureter (A) Masses of eosinophilic extracellular deposits in (yellow arrow) H&Ex20 (B) H&Ex40 (C and D) Granular calcium deposits within the amyloid Vonkassa stain x100*

Discussion

A group of diseases caused by extracellular deposition of amorphous, insoluble proteins is called amyloidosis. It is divided into four types - primary, secondary, hereditary and d β2-microglobulin-associated. Only the first two types are common (2). The primary type also known as AL type is often idiopathic and contains monoclonal λ-chain deposits predominantly (2, 6). The secondary amyloidosis (AA type) is linked to chronic inflammatory conditions such as tuberculosis (3, 6).This may resolve with the treatment of the underlying cause. (3) Based on the distribution, amyloidosis can be classified as local or systemic. In contrast to local, systemic amyloidosis can be progressive and fatal involving multiple organs. Most organ-confined amyloidosis is of AL type (6).Skin, respiratory tract and urinary tract are the commonest sites of local amyloidosis (2). Although any part of the urinary tract can be involved with local amyloidosis, bladder is the most commonly affected (5).Urinary tract amyloidosis is mostly of primary type and the exact aetiology is not clear (2, 3).

Painless visible haematuria is the commonest presentation of primary urinary tract amyloidosis (2, 3, 5, 6) .Focal inflammation, necrosis and ulceration of the urothelium due to amyloid depositions may cause bleeding (3).Diagnosis of amyloidosis preoperatively is a challenge (3). This case was no exception. With his occupational history in rubber industry, ultrasonically detected bladder lesion was assumed as a cancer and TURBT was performed. Apart from TURBT, cystodiathermy, laser fulguration and partial cystectomy have been carried out in the reported cases (2).

According to the 34 reported cases of ureteric amyloidosis, mean age is 54 years and male to female ratio is 1:1.8 (4). In two thirds of the cases, preoperative diagnosis could not be made necessitating nephroureterectomy (4).

A ureterorenoscopy guided cup biopsy can diagnose ureteric amyloidosis, such overtreatment is becoming less common (2).Intraoperative frozen sections have allowed local resection in some cases (4, 6).In the index case, a presumptive diagnosis of upper tract amyloidosis was made on the CT findings of ureteric wall calcification along with the previously diagnosed bladder amyloidosis. However, it is worth noting that simultaneous amyloidosis and upper tract urothelial cell carcinoma is a possibility (3).

Calcification of ureters due to amyloid deposition is rare, particularly the bilateral involvement. Other causes of ureteric calcification and stenosis include tuberculosis and schistosomiasis (5, 6). Rounded, spotty, irregular calcifications are considered pathognomonic of ureteritis caused by bilharziasis. Tuberculosis,

produces irregular or homogeneous calcifications particularly in the distal third of the ureter. In both these conditions calcification is not confined to submucosa as in amyloidosis (5).As tuberculosis is prevalent in Sri Lanka it was crucial to exclude the possibility of genito-urinary tuberculosis by appropriate investigations. Apart from histology, urine for acid fast bacilli and urine culture for Mycobacterium tuberculosis were essential for this purpose. In our patient, there was circumferential calcification of the ureter for a length of about 5 cm on the operated side. In some of the reported cases the calcification was not solid as this but mottled in appearance (6).

Although bladder amyloidosis is commonly primary and rarely life threatening, it can lead to progressive bilateral ureteric involvement (3).Therefore, long term follow-up with upper tract surveillance of these patients is necessary. However, Tudor et al. has followed up a patient after similar surgery for 8 years without any progression or recurrence. They have not used any medication to treat primary amyloidosis and interestingly the hydronephrosis has been fully resolved when imaging done six years after surgery (2).In this patient there were no macroscopic amyloid lesions observed within the bladder during surgery which allowed the successful formation of a Boari flap. However, there were some glomerulations like appearance of the mucosa. The same mucosal appearance has been described in the literature (2, 3). The left distal ureter was stony hard and the lumen was obliterated. Similar ureteric appearance has been described by others too (4, 5). Despite the presence of features suggestive of severe inflammation in the dilated proximal ureter, the anastomosis healed exceptionally well. All these findings are suggestive of the localized nature of the primary amyloidosis of the urinary tract.

The upper tract amyloidosis has the potential to cause renal loss (6). However, conservative management of upper tract amyloidosis has been described as the progress of the disease is slow (2). Accordingly, conservative management without any surgical or medical intervention has been successful up to six years with no clinical or pathological progress (2).Because our patient had no symptoms on the right side and there was no significant obstruction, we offered surveillance with regular upper tract imaging and renal function tests. Pharmacological agents such as dimethyl sulfoxide and colchicine have been attempted as treatment for urinary tract amyloidosis with little success (2).

Conclusion

Ureteric amyloidosis with calcification is a rare cause of haematuria and ureteric obstruction. Awareness of this possibility may aid early diagnosis and would prevent an unnecessary nephroureterectomy. It is usually of the primary type and has a good prognosis after appropriate excisional surgery followed by reconstruction of the urinary tract.

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