



Amyloidosis of the urothelium (Bladder, ureter, renal pelvis and urethra): A Review of the Literature

Anthony Kodzo-Grey Venyo^{1*}, Khalid Ahmed²

1. North Manchester General Hospital, Department of Urology, Manchester United Kingdom
2. Royal Oldham Hospital, Department of Histopathology, Oldham, United Kingdom

ABSTRACT

Primary amyloidosis involving urinary tract is a rare. In this we reviewed the literature on primary amyloidosis of the urinary bladder, ureter, renal pelvis and urethra. Various internet search engines were used to identify reported cases and case series regarding primary amyloidosis of lining of the urinary tract. Amyloidosis of the urinary tract may either be primary or part of a systemic disease. Localized amyloidosis is of unknown aetiology but mostly of AL-type amyloid immunoglobulin light chains. Systemic amyloidosis can be either primary (AL-type amyloid), secondary (AA-type amyloid) or familial (ATTR-type amyloid). Systemic secondary urinary bladder amyloidosis tends to be associated with autoimmune disease and chronic infection. Familial cases of systemic amyloidosis tend to be associated with mutations in the transthyretin gene. Primary amyloidosis of the urinary tract may present with haematuria; lower urinary tract symptoms; loin pain. Useful investigations in the diagnosis of urothelial amyloidosis include: urinalysis; urine cytology; ultrasound scan of renal tract; intravenous urography; computed tomography scan; urethrocytostcopy; retrograde ureteropyelogram and ureterorenoscopy; tumour specimen obtained by biopsy or resected lesion. In view of the benign biological behaviour of amyloidosis conservative treatment is the best modality of treatment however, radical surgical excisions have been undertaken when a definitive diagnosis had not been established and these surgical treatments have been carried out based upon a presumptive diagnosis of a malignant tumour. Surgical resection of the amyloid tumour is considered the first-line therapeutic method (TUR resection of bladder lesion; biopsy/resection or local segmental resection of a ureteric amyloid tumour; resection of urethral amyloid lesion). Pharmacotherapy can be used when the lesion is difficult to completely resect, or when a patient is unable tolerate surgery. Colchicine or dimethyl sulfoxide may be beneficial for the control of the progression or recurrence of amyloidosis. Because of reported recurrences, careful surveillance protocol is necessary. Diagnosis of amyloidosis is established by the characteristic eosinophilic amorphous material seen during microscopic examination of the biopsy specimen and positive Congo red staining and apple green birefringence. It can recur but this must be treated ideally by conservative surgery.

Key Words: Amyloidosis; Urinary bladder, Congo red; birefringence; apple green; amorphous; eosinophilic;

*Corresponding Author: Dr Anthony Kodzo-Grey Venyo, North Manchester General Hospital, Department of Urology, Manchester, United Kingdom. Email: akodzogrey@yahoo.co.uk
Received: May 5, 2013, Accepted: August 17, 2013.
This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Amyloidosis of the urinary bladder refers to deposition of amyloid in the urinary bladder. Amyloidosis is almost invariably a primary urinary bladder tumour; it is only very rarely part of a systemic disease. Amyloidosis of the ureter, renal pelvis or urethra refers to deposition of amyloid in the respective organs.

Epidemiology and Sites involved: Amyloidosis of the urinary bladder tends to occur in older patients who are older than 50 years of age. Amyloidosis of the urinary bladder is rare and less than 200 cases have so far been reported. Amyloidosis of the urinary bladder tends to affect the posterior wall of the urinary bladder. [1] Most cases of primary amyloidosis occur in the urinary bladder but few cases have been found in the ureter, renal pelvis and urethra.

Aetiology: The aetiology of amyloidosis of the urinary bladder /ureter/ renal pelvis / urethra depends upon whether the amyloidosis is primary amyloidosis or part of a systemic disease.

Localized Amyloid: Localized amyloidosis is of unknown aetiology but mostly AL-type amyloid immunoglobulin light chains). Merrimen and associates [2] reported 9 cases of primary localized amyloidosis of the urinary tract and correlated the pathologic findings with clinical and

cystoscopic information. They reviewed the medical records of patients who were diagnosed with amyloidosis of the ureters, urinary bladder, or urethra from 1976 to 2003. They also performed histochemical and immunoperoxidase stains on the tissues. They reported that they identified eight cases of amyloidosis of the urinary bladder, and one case involving the renal pelvis / ureter. None of the nine cases showed evidence of systemic amyloidosis. Of the eight patients with amyloidosis of the urinary bladder, the presentation in 5 of these was visible haematuria, and 1 had irritative bladder symptoms, and in 2 patients the amyloidosis was detected during cystoscopic follow-up for urothelial carcinoma. The patient who had amyloidosis of the renal pelvis/ureter presented with flank pain and visible haematuria. The clinical impression was malignancy in 75% of the urinary bladder cases. Most of the patients with urinary bladder involvement were treated by means of localized bladder resection; nevertheless, 1 patient underwent total cystectomy for symptom control. Of 5 patients with follow-up information, 2 developed recurrence. Merrimen and associates [2] reported that the pathologic assessment diagnosed amyloid deposits consistent with primary or AL-type amyloid in all cases. They also reported that Immunoperoxidase stains revealed lymphoid cells in the vicinity of the amyloid deposits to be lamda-restricted in 78% of cases. Merrimen and associates [2] concluded that:

- Primary amyloidosis of the urinary bladder is a rare is a rare condition which mimics malignancy in its clinical presentation and cystoscopic appearance and on diagnostic imaging.
- In their study all cases of urinary amyloid deposits represented localized amyloidosis rather than manifestation of systemic amyloidosis.
- Monoclonal lymphoid populations evolving from chronic inflammation in the urinary tract may be the source of the amyloid AL proteins.

Systemic amyloid: Systemic amyloidosis can be either primary (AL-type amyloid), secondary (AA-type amyloid) or familial (ATTR-type amyloid). Systemic secondary urinary bladder amyloidosis tends to be associated with autoimmune disease and chronic infection. Familial cases of systemic amyloidosis tend to be associated with mutations in the transthyretin gene.

Clinical features: Patients with amyloidosis of the urinary bladder tend to present with visible haematuria. Patients with amyloidosis of the ureter and or renal pelvis may present with haematuria and or loin pain. Those patients who have amyloidosis of the urethra may present with haematuria and lower urinary tract symptoms. Most of the cases of primary amyloidosis of the urinary tract system involved the urinary bladder and occasionally cases of amyloidosis of the ureter, renal pelvis or the urethra have been reported hence the review would focus more on amyloidosis of the urinary bladder.

Tirzaman and associates [3] evaluated the presentation and prognosis of primary localized amyloidosis of the urinary bladder. They reviewed the medical records of 31 patients with primary localized amyloidosis of the urinary bladder. They performed immunohistochemical amyloid typing on bladder biopsies of 27 patients. They reported that:

- The median age of the 22 men and 9 women was 55 years.
- Twenty-four patients (77%) presented with visible haematuria (associated with irritative urinary tract symptoms in 6 patients), and 7 (23%) had only lower urinary tract symptoms.
- Multiple bladder areas were involved in 20 patients (65%), a single area was involved in 8 (26%), and diffuse involvement in 3 (10%)
- Twenty four patients had immunoglobulin light chain, and 3 had transthyretin-related amyloid.
- Localized recurrences were common.
- None of the patients developed systemic amyloid.

Tirzaman and associates [3] concluded that:

- Primary localized amyloidosis of the urinary bladder can be easily confused with a neoplasm,
- Immunohistochemical amyloid typing is important.
- Transthyretin-related amyloid of the urinary bladder requires no further work-up.
- Repeated work-ups for systemic amyloidosis are not necessary for patients with light chain-related amyloidosis of the urinary bladder.
- Early eradication with fulguration or laser therapy is indicated.
- Cystoscopic follow-up is necessary.

Amyloidosis of the urinary bladder may clinically mimic carcinoma of the urinary bladder. DeSouza and associates [4] described 2 cases of localized amyloidosis of the urinary bladder which clinically, radiologically and on cystoscopy masqueraded as carcinoma of bladder. They stated that amyloidosis in both these cases was ascertained on biopsy, supplemented with special stains.

Urinary dysfunction is found in 50% of patients with familial amyloidotic polyneuropathy. Andrade [5] studied lower urinary dysfunction in familial amyloidotic polyneuropathy (FAP). Andrade [5] studied fifty-four with familial amyloidotic polyneuropathy and performed clinical examination, urodynamics and ultrasound scan of the urinary tract of the patients. Andrade [5] reported that urinary symptoms appeared during the first three years of the disease in 50% of the patients. The initial urinary symptom was dysuria in 39% and incontinence in 24% of the patients, sensitivity and contractility disturbances of the detrusor were found at the initial stages. Andrade [5] found non-relaxing urethral sphincter in 51.7% and

Venyo A K G, Ahmed K. (September 2013) Amyloidosis of the urothelium (bladder, ureter, renal pelvis and urethra): A review of the literature. *Jour of Med Sc & Tech*; 2(3); Page No: dyssynergia in 37.5% of the cases. Andrade furthermore reported that:

- Ultrasound scan of the renal tract revealed thickening of the vesical wall in 42.5% of the patients, more common in males (M: 16; F: 7).
- Opening of the vesical neck was found in 56% of cases (M: 19; F: 11) with paradoxical closure during the attempt to void. Fluctuations in the opening of the vesical neck were found in 8 patients, also more frequently in males (M: 6; F: 2).

Andrade [5] concluded that in addition to reduced sensation, underactive detrusor, opening of the vesical neck and external sphincter deficit, they found data that suggested failure of relaxation of the internal and external sphincter. The overdistension associated with an open vesical neck and external sphincter deficit justified incontinence in those patients. The retention was due to inadequate contraction of the detrusor, probably associated with non-relaxing of a role. Andrade [5] iterated that early therapeutic intervention in these patients is vital to avoid secondary injuries.

Primary amyloidosis has a high rate of local recurrence but the prognosis of secondary amyloidosis depends upon the primary cause.

Diagnosis of Amyloidosis (Macroscopic and microscopic descriptions); Macroscopic examination of amyloidosis of the urinary bladder tends to reveal mucosa erythema in diffuse amyloidosis, sometimes with petechiae and focal necrosis. In the case of localized cases of amyloidosis nodular mucosal lesions resembling carcinoma are found in the urinary bladder.

Microscopic examination of amyloidosis of the urinary bladder may reveal the following features [1]:

- Large masses of eosinophilic proteinaceous material with haemorrhage in lamina propria.
- Variable foreign body giant cell reaction to amyloid
- There may be associated atypical epithelium due to attenuation of urothelium.
- Rarely perivascular amyloid deposits, especially in systemic amyloidosis.
- Rare / no inflammatory cells (see figures 1 to 9 which show various microscopic features of a case of amyloidosis involving the urinary bladder).

Positive stains

The ensuing stains tend to be positive in amyloidosis of the urinary bladder:

- Congo red shows apple green birefringence when exposed to polarized light.

- Amyloid panel (kappa and lambda light chains, prealbumin, beta-2-microglobulin, SAA1).
- Immunofluorescence with Thioflavin T [1]

Electron microscopy

Non-branching, randomly distributed, rigid fibrils measuring 8 nm to 10 nm are usually seen as well as associated ground substance.

Differential Diagnosis

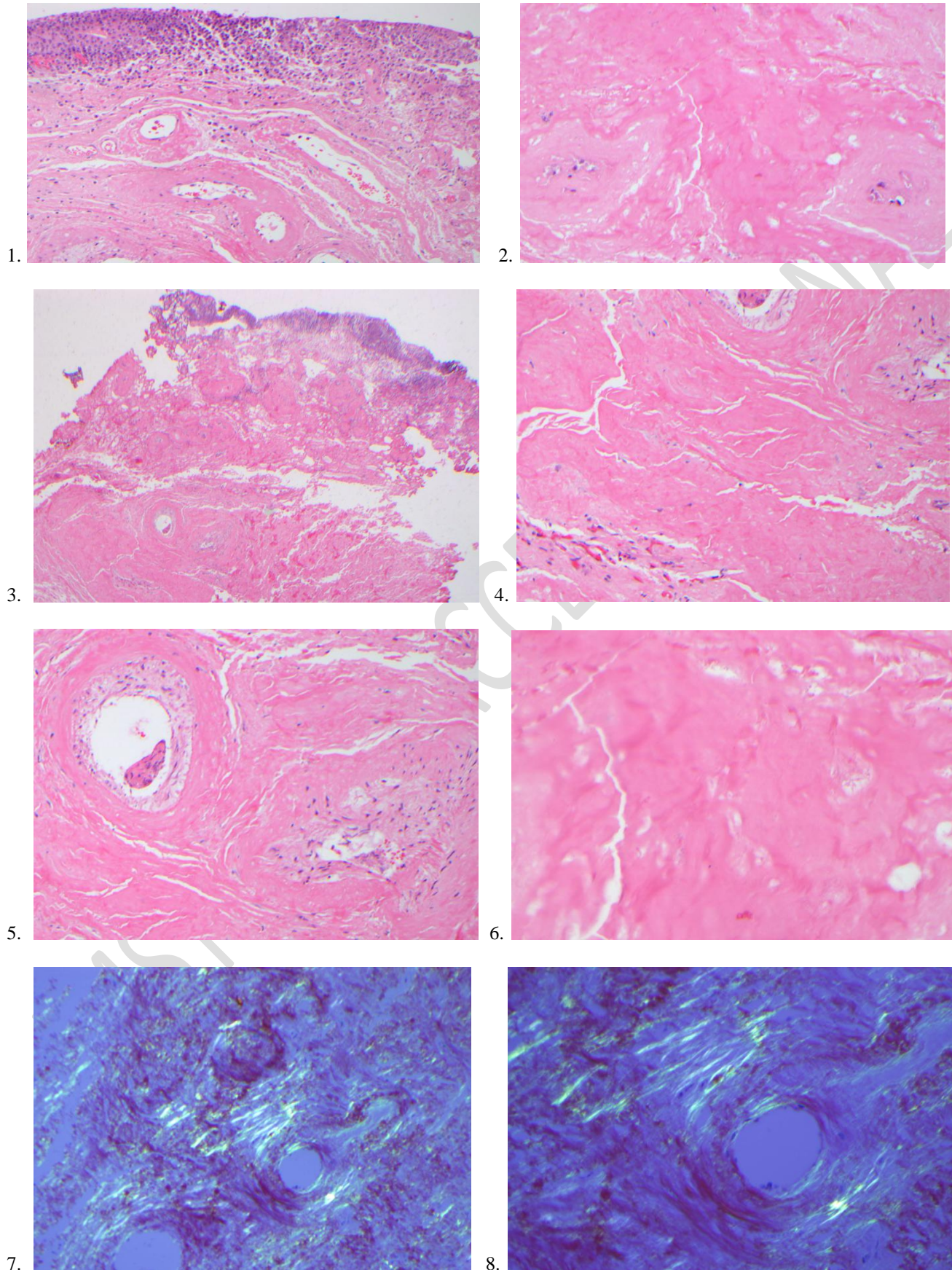
Fibrosis is a differential diagnosis of amyloidosis of the urinary bladder. The characteristic features of fibrosis include: positivity for trichrome stain; negativity for Congo Red; and no Thioflavin T immunofluorescence [1].

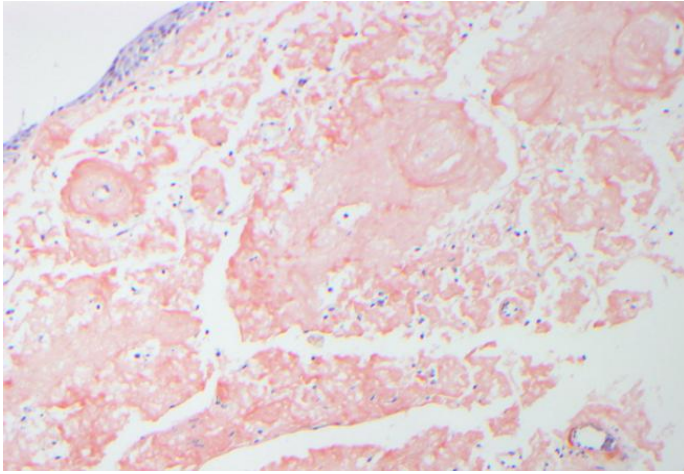
Treatment

Trans-urethral resection and fulguration of the amyloid tumour is the usual curative modality of treatment, since it is not associated with myeloma, [6] it also controls bleeding.[6] Partial cystectomy may be performed for large mass-forming lesions. [1] Lipper and Kahn [6] studied four examples of amyloid tumours in order to determine whether there was an association with myelomatosis. Three patients had follow-up examination of 12 years, 9 years, and 2 ½ years, respectively. They reported that a local recurrence developed in one patient and a second lesion developed in this patient and in one other who also had transient monoclonal 7S globulin peak. In spite of these findings, none of their patients developed myelomatosis. They stated that their study of the scanty literature on amyloid tumours revealed that only patients with lesions of the lung and urinary bladder have had long-term follow-up. They had invariably remained free of disease. A number of reports of bone lesions had inferred that amyloid tumours occurring here (there) signify solitary myeloma despite a lack of follow-up confirmation. Their longest surviving patient developed two bone lesions over a 12 year period without developing myelomatosis. Lipper and Kahn stipulated that their findings led them to conclude that there is little evidence to regard the presence of an amyloid tumour at any site as a manifestation of solitary myeloma or myelomatosis. [6]

Discussion

According to Garcia-Escudero López and associates [7] Solomin in 1897 published the first description of amyloidosis of the urinary bladder in the world literature and in 1947 Luis Cifuentes-Delatte described the disease in his monograph *Cistitis y Cistopatías*, and documented 6 cases found in the literature [8]





1. Haematoxylin and Eosin stain low power x 4 magnification showing surface urothelium and underlying amorphous eosinophilic amyloid in the lamina propria and around the vessels 2. Haematoxylin and Eosin staining high power x 20 magnification showing amyloid in lamina propria and blood vessels 3. Haematoxylin and Eosin staining low power x 10 magnification showing amyloid in lamina propria and blood vessels 4. High power x 40 magnification showing amyloid 5. High power magnification x 40 magnification showing amyloid in lamina propria and vessels Figure 6 High power x 40 magnification showing amyloid in lamina propria and vessels Figure 7 showing apple green birefringence of amyloid Figure 8 showing apple green birefringence of amyloid Figure 9 Positive Congo red staining for amyloid

Kidney involvement by amyloidosis is almost invariably seen in the context of secondary amyloidosis. [9] On the other hand, the urinary bladder is fundamentally affected by amyloidosis in the context of localized amyloidosis. [3] [10] [11] [12]

Malek and associates [12] reviewed the published literature on localized amyloidosis of the urinary bladder by which time about 160 cases had been reported in the literature including one in the Spanish literature [13] but now about 200 cases have been reported in the literature. Amyloidosis is more common in males (71%). The initial presentations of amyloidosis consist of asymptomatic haematuria (58%), irritating lower urinary tract symptoms (20%), and a combination of both (22%). [7]

The first case of secondary amyloidosis of the urinary bladder was published by Bender and Nelly in 1969. [14]. Garcia-Escudero Lopez and associates [7] stated that by 2010 no more than 30 cases of secondary amyloidosis of the urinary bladder had been published in the world literature and the largest series up to 2010 (5 cases) was published by Nurmi and associates [15] in 1987 and in this series massive haematuria was cited and the reported mortality rate was 30%.

Garcia-Escudero Lopez and associates [7] stated that they had found references relating to a total of 7 cases of amyloidosis of the urinary bladder. [13], [16] [17] [18] [19] [20] [21] nevertheless, as was established from necropsy studies of systemic amyloidosis, it was clear that bladder involvement by amyloidosis is more common than actual clinical manifestations of the disease. [15] [17]

Jain and associates [22] reported six cases of localized urinary bladder amyloidosis that were clinically and cystoscopically suspected as urinary bladder tumour or cystitis which had occurred over a period of 10 years. Histological examination in all the cases revealed a diagnosis of primary amyloidosis. None of the cases had any stigmata of secondary disease. The cases were treated

by means of simple trans-urethral resection of the bladder lesion. Two out of the six cases recurred after 3 to 5 years following the initial presentation and were asymptomatic thereafter. Jain and associates [22] concluded that amyloidosis of the bladder is a rare condition which often mimics bladder neoplasm clinically and cystoscopically and histological examination is a must for definite diagnosis and proper management.

Wilkinson and associates [23] reported a 69-year-old lady who was referred with a history of intermittent visible painless haematuria. Her investigations including serum renal, liver and bone profiles were normal. Her urine cytology was unremarkable. Her serum and urine electrophoresis were normal. Her renal ultrasound-scan and skeletal survey were normal. She had a computed tomography scan of abdomen and pelvis which revealed an unusual appearance of the urinary bladder with markedly enlarged pelvic veins. There was no associated perivesical lymphadenopathy. She underwent cystoscopy which revealed a haemorrhagic oedematous patch on the left lateral sidewall of the urinary bladder. She underwent trans-urethral resection of the lesion. Histological examination of the resected specimen showed no evidence of carcinoma. Staining with alkaline Congo red revealed a salmon pink appearance. Apple green birefringence was detected under polarised light. No staining was identified at immunohistochemistry using mono-specific antibodies reactive with serum amyloid A -protein, transthyretin, apolipoprotein A1 or, with kappa and lambda light chains. The amyloid did not stain with any of these antibodies. She was diagnosed with primary amyloidosis of the urinary bladder. Her haematuria resolved and she was put under a yearly surveillance cystoscopy protocol. Wilkinson and associates iterated that:

- Amyloidosis is characterized by the extracellular deposition of proteins.
- Amyloidosis may be primary or secondary depending upon whether it is due to underlying immune dyscrasia or secondary to chronic inflammatory disorder.

- While systemic amyloid can occur anywhere in the urinary tract, including the kidney, ureter, urethra or corpora.
- Primary localized urinary bladder amyloidosis is a rare urological disease with approximately 200 cases reported in the literature as stated by a number of authors. [11] [23] [24]
- The composition of amyloid can be demonstrated immunohistochemically. AL and AA amyloid deposits can be distinguished to some extent histochemically by treating with potassium permanganate (KMNO₄)
- Amyloidosis is characterized by the extracellular deposition of proteins. Amyloidosis is a heterogeneous group of disorders which may affect single or multiple organ systems. It may represent a generalized or localized disease process.
- Isolated bladder amyloidosis classically presents with painless frank haematuria and irritative voiding symptoms.
- Recurrence rates post-resection is estimated to be around 50%.
- Trans-urethral resection is the treatment of choice with primary bladder amyloidosis. Medical treatments such as intravesical dimethyl sulfoxide instillations and oral colchicine have also been tried with limited success.
- While no official guidelines exist for surveillance, most centres would advocate follow-up cystoscopy at 1 to 3 year intervals.

Khan and associates [26] stated that chronic cystitis and inflammation lead to the synthesis and accumulation of miss-folded amyloid precursor protein, particularly light chain immunoglobulin protein.

Tirzaman and associates [3] stated that:

- Characteristically, primary amyloidosis deposits superficially beneath the surface mucosa sometimes extending into the superficial smooth muscle of the urinary bladder.
- In secondary amyloidosis, the amyloid tends to accumulate in the bladder vasculature thus explaining why secondary amyloid with diffuse bladder involvement has a high mortality of 30% with its potential for massive haemorrhage.

Agarwal and associates [27] reported the clinico-pathological analysis of six patients (five men and one woman) with primary amyloidosis of urinary bladder. The age of the patients at presentation was 53 years to 77 years (mean 67 years). The diagnosis of all the six cases was made histologically from tissue obtained by biopsy of the bladder lesion. The tissues were randomly formalin fixed, paraffin embedded and stained with haematoxylin and eosin. Special stains, for example, Congo red were used

once the diagnosis of amyloid was suspected and was confirmed using polarized light. They reported that four patients presented with haematuria and two had abdominal pain associated with haematuria. Intravenous urography in all cases was normal. Cystoscopy in two cases revealed elevated areas and in one case the lesion appeared as a large papilliferous growth. The suspected diagnosis in all cases was neoplasm. Five cases underwent biopsy of the lesion. Trans-urethral resection of the papilliferous growth was undertaken in one case. Light microscopy of the tissue submitted revealed typical features localized amyloidosis. These revealed extracellular aggregates of homogeneous eosinophilic material, predominantly in the lamina propria and inner half of the muscle. The deposits gave a red reaction with congo red and showed apple-green birefringence with cross polarized light. Minor deposits were present in vessel walls and there was a focal foreign body giant cell reaction to scanty granular deposit of amyloid. Agarwal and associates [27] reported that one patient died of carcinoma of stomach 9 years after the diagnosis of amyloidosis. Another patient was well at 3 years post diagnosis, one which was diagnosed 3 months prior to the publication of the paper was well and asymptomatic. However, 3 of the cases were lost to follow-up. Agarwal and associates [27] made the ensuing iterations:

- In the cases of bladder amyloidosis a pathogenetic mechanism can be postulated as postulated by Fujihara and Glenner. [28]
- Chronic and recurrent mucosal and sub-mucosal inflammation leading to chronic cystitis causes an influx of lymphoplasmacellular elements, one of which becomes monoclonal. The monoclonal proliferates and secretes aberrant type of light polypeptide chain which is amyloidogenic as postulated by Glenner. [29]
- By means of lysosomal proteolysis of phagocytic cells or other physiological means, these light chains are formed into amyloid fibrils and deposited as aggregates in the bladder tissue.
- Some authors have used intravesical instillation of dimethylsulphoxide to prevent recurrent haematuria successfully [30]
- Oral colchicine had avoided the need for cystectomy in another patient with uncontrolled haematuria as reported by Livingstone and associates. [31]
- Some patients even required partial or total cystectomy with ileal loop diversion as reported by Malek and associates [32]
- If the inconvenience to the patient is insignificant, conservative therapy is preferable and majority of the patients can be managed in this way. However, long-term follow-up is recommended.

Gupta and associates [33] reported a 64-year-old man who for over a period of 26 years preceding his presentation with haematuria, was treated in the same institution for chronic primary amyloidosis of urinary bladder with

repeated trans-urethral resection and he had undergone 6 resections of the lesion over a seven year period. He had ultrasound scan of the renal tract which showed multiple solid lesions on the right lateral and posterior wall of the bladder with mild right hydronephrosis. He underwent cystoscopy which revealed multiple yellowish fat-like deposits in the membranous urethra and right lateral wall as well as multiple solid nodular lesions in the urinary bladder. He underwent resection of the lesions with deep muscle biopsy and histological examination of the specimen revealed high-grade solid muscle-invasive transitional cell carcinoma (Muscle-invasive G3 tumour), and focal osseous metaplasia with amyloidosis. He had a computed tomography scan which showed multiple nodules with thick bladder and multiple focal calcifications as well as right-sided-mild hydronephrosis. He underwent radical cystectomy with ileal conduit construction. Macroscopic examination of the cystectomy specimen showed multiple nodular areas of tumour ulceration with whole thickened bladder. Microscopic examination of the specimen confirmed sarcomatoid differentiation transitional cell carcinoma with amyloidosis by the presence of apple green birefringence in the section stained with alkaline Congo red under a polarized light. The ureteric margins bilaterally were positive for amyloid but negative for malignancy. The final pathological staging was pT3b N1M0. At his latest follow-up he was alive and well and he was referred for adjuvant chemotherapy. Gupta and associates [33] stated that:

- Historically the terminology of amyloidosis was coined in 1854 by Virchow and Solonis was the first to describe bladder amyloidosis in 1897 at autopsy.
- As stated by Biyani and associates [34] the association of amyloidosis with high-grade transitional cell carcinoma is very rare and review of the literature revealed only two previous reports preceding the publication of their case
- Amyloidosis of the bladder primarily affects the posterior and postero-lateral walls with unknown aetiology.
- Urinary dysfunction is found in 50% of cases due to amyloidotic neuropathy. .

Srinath and associates [35] reported a 30-year-old woman who presented with occasional painless visible haematuria of 6 years duration. She had undergone trans-urethral resection of bladder tumour elsewhere four years prior to her presentation. Histological examination of her resected lesion was reported as bladder amyloidosis. She was empirically given antituberculous treatment. Check cystoscopy and trans-urethral resection of residual lesions in the right lateral and posterior bladder walls was done 8 weeks later. She had intravenous urography which was normal. She underwent cystoscopy and trans-urethral resection of her urinary bladder lesions. The cystoscopy revealed multiple yellowish, sessile tumours over the posterior and both lateral bladder walls. Histological examination of the specimen showed extracellular and

perivesical deposits of amorphous eosinophilic material in the sub-mucosa and muscle. There was a mild lymphocytic response. The transitional epithelium was unremarkable. The deposits after staining with Congo red showed apple green birefringence under polarizing light thus confirming the diagnosis of amyloidosis. Diagnostic work-up for infertility revealed pelvic endometriosis and tubal adhesions. She had been followed-up for a year with no evidence of recurrence or haematuria. Srinath and associates [35] stated that their case was unique in that to their knowledge primary bladder amyloidosis had not been previously described in a patient as young as 25 years at first presentation and that the association with endometriosis appeared to be incidental.

Patel and associates [36] reported a 38-year-old man who presented with dysuria, occasional urinary urgency and haematuria. Urinalysis revealed haematuria but urine cytology was normal. Intravenous urogram revealed irregularity at the base of the urinary bladder and the upper renal tracts were normal. He underwent cystoscopy which revealed a diffuse left lateral wall lesion with a normal surrounding mucosa. The lesion was around 3 cm x 3 cm mass well away from the left ureteric orifice. He underwent trans-urethral resection of the lesion and histological examination of the lesion revealed urinary bladder amyloidosis with negative surgical margins. The patient was advised to undergo evaluation to rule out systemic amyloidosis. Nevertheless, he was lost to follow-up. After 3 months, he presented with recurrent haematuria. His radiological investigations this time were normal. He underwent another cystoscopy which revealed yellowish submucosal 2 cm x 2 cm nodules at the lateral and anterior walls with normal surrounding mucosa. Trans-urethral resection of the lesion was undertaken. The presence of amorphous eosinophilic deposits that stained positive with Congo red on the histological examination of the specimen diagnosed recurrent urinary amyloidosis. He had systemic evaluation for amyloidosis including rectal biopsy, abdominal and heart sonography, retinal examination, serum electrophoresis, and Bence Jones protein. There was no evidence of systemic amyloidosis. Patel and associates [36] prescribed the patient oral colchicine 2 mg orally twice daily and intravesical dimethyl sulfoxide (DMSO). He was put on annual follow-up cystoscopy and computed tomography scan every 2 years. He had a cystoscopy at the end of his 1-year follow-up which did not reveal any evidence of recurrence.

Goswami and associates [37] reported a 35-year-old man who presented with intermittent profuse painless haematuria. He had excretory urography which showed normal upper urinary tracts and a small filling defect projecting into the lumen from the left side of the bladder. He underwent cystoscopy which revealed a 1 cm x 2 cm solid, nodular, circumscribed mass with a haemorrhagic surface arising from the base of the bladder just medial to and above the left ureteric orifice. He underwent trans-

urethral resection of the lesion. Histological examination of the specimen revealed massive deposits of structure-less eosinophilic material in the sub-epithelial region. Congo red staining of the specimen revealed the classical apple-green birefringence under polarized light. He was subsequently investigated for evidence of systemic amyloidosis and the investigations included: urine for Bence-Jones protein, serum protein, serum electrophoresis, serum liver function tests, VDRL, creatinine clearance, radiological survey of spine, skull and ribs, sternal marrow biopsy and rectal biopsy. All the tests were negative for amyloidosis. After 2 years of follow-up he has remained well with no evidence of systemic disease.

Kamoi and associates [38] reported a 76-year-old man who presented with visible haematuria. He had cystoscopy which showed sub-mucosal haematoma in the anterior wall and a broad based mass occupying the trigone without normal mucosa covered by calcification. Trans-urethral biopsy and resection was performed. Histopathological examination of the specimen revealed AL-type amyloidosis occupying the sub-mucosal extracellular space. The patient was given occlusive dressing with dimethyl sulfoxide. At 12 months, he had cystoscopy and magnetic resonance imaging which revealed improvement of the mass-like lesion in the bladder wall.

Adil Altwainrgi [39] reported a case of primary amyloidosis of the urinary bladder in which the patient presented with painless haematuria and irritative urinary symptoms. Radiological investigations showed multiple small masses within the urinary bladder with suspicion of transitional cell carcinoma. Cystoscopy revealed multiple masses within the urinary bladder, some showing haemorrhagic papules and papillary projections over the masses. Histology of the biopsy specimen was negative for malignancy. Immunohistochemical staining with Congo red stain showed the presence of amyloid fibrils within the biopsy material. Further investigations of systemic illness excluded secondary amyloidosis. Trans-urethral resection of the lesion was undertaken. There was no evidence of recurrence at the patient's follow-up.

Williams and associates [40] reported a 27 year old man who presented with dysuria, pain in the base of the penis and haematuria, which occurred at the beginning of micturition for the preceding four days. His symptoms had not responded to co-trimoxazole 960 mg twice per day for two days prescribed by his general practitioner. On examination there was evidence of a profuse mucopurulent urethral discharge and meatal erythema. No other abnormality was noted. On gram stain of the urethral discharge, greater than 10 polymorphonuclear leucocytes per high power field were seen in several fields. Haematuria was found on dipstick urinalysis. His endo-urethral swabs for *Neisseria gonorrhoea* and chlamydia ELISA were negative. His syphilis serology was negative.

A diagnosis of non-gonococcal urethritis was made and the patient was commenced on Deteclo (triple tetracycline) one tablet twice per day for 14 days. His midstream specimen of urine was subsequently reported to show an excess of white and red blood cells ($50 \text{ cells} \times 10^6 / 1$) but no growth. He was reviewed 2 weeks later and at that time he continued to have symptoms of intermittent visible haematuria associated with exercise, urinary frequency, nocturia, poor urinary stream, with some degree of hesitancy. Microscopic haematuria again was present on urinalysis. Phase contrast microscopy of the urine showed 75% dysmorphic red blood cells suggestive of a renal cause for the bleeding. In view of the presence of dysmorphic red blood cells a renal biopsy was considered, however, the patient refused to have renal biopsy. His urological investigations were indicative of obstructive pattern of micturition. He underwent urethroscopy which revealed extensive ulceration of the posterior urethra, with polypoid lesions projecting from these areas. Histological examination of specimens of the urethral lesion which was biopsied showed islands of amorphous eosinophilic material associated with foreign body giant cell reaction within the stroma suggestive of amyloid. Birefringence with Congo red was present but there was no typical apple green birefringence of amyloid. After the urethroscopy the patient continued to have poor urinary flow and he had micturating cystogram which showed an irregular area in the lining of the junction of bulbar and spongy urethra. The patient underwent a repeat urethroscopy and resection of the lesion as well as full thickness biopsy was taken. The site bled profusely, but the bleeding was controlled by digital pressure and a catheter was inserted for two days post operatively. After his catheter was removed he had no problems voiding. Histology of the resected specimen on this occasion confirmed amyloid. Up to the time of publication of this case report, the patient's follow-up had been uneventful. The patient declined to have a rectal biopsy to exclude systemic amyloidosis. Williams and associates [40] stated that:

- Isolated urethral amyloidosis is a rare condition.
- The symptoms of urethral amyloidosis mimic urethritis per se and gonococcal urethritis has been implicated as a possible aetiological factor by some authors. [41] [42] [43]
- The first case of amyloidosis of the urethra was reported at autopsy in 1909 by Tilp [44] and subsequently up to the time of publication of their case report 15 reports of amyloidosis of the urethra had been published in males aged between 27 years and 82 years (mean age 53 years). A past history of gonorrhoea was obtained in five patients. But, this predated the diagnosis of amyloid by 30 to 48 years and therefore may be a coincidental finding rather than aetiology.
- The most common presenting complaints of amyloidosis of the urethra are macroscopic haematuria (eight cases), or a bloody urethral discharge (two cases). This is probably as a result of ulceration of the

amyloid tumour and distortion of the blood vessels by the amyloid.

- Urethral symptoms which are suggestive of an obstructive lesion were reported in nine cases of amyloidosis of the urethra and a palpable mass was also reported in the penile shaft in two cases of amyloidosis of the urethra. These clinical features are shared with neoplastic lesions, most commonly carcinoma. Hence in order to differentiate between the two diseases cystourethroscopy and biopsy are mandatory.
- The aetiology of amyloid is believed to be an immunocytic response probably produced by adjacent monoclonal plasmacytic infiltrates which result from local infection. If gonorrhoea is implicated then the incidence of isolated urethral amyloid should be much higher.
- The management of urethral amyloid is variable, and this depends largely on the clinical features of the lesion and the presumptive initial diagnosis. Most of the reported patients had no treatment, but urethroscopy, cystotomy, and in some case trans-urethral resection to remove the tumour or to relieve urethral obstruction have been necessary. Urethrectomy was performed on one patient where an erroneous clinical diagnosis of carcinoma was made as was reported by Karisary [45]

Williams and associates [40] concluded that their case illustrates the need for careful assessment of patients with non-specific urethritis and concomitant haematuria.

Ichioka and associates [46] reported a case of primary amyloidosis of urethra in which the lesion exhibited low signal intensity on T1-weighted images and was well-enhanced on gadolinium-enhanced T1-weighted images. The gross appearance at cystoscopy suggested urethral malignancy but the low-signal intensity was atypical for malignant tissue. Ichioka and associates [46] stated that because magnetic resonance imaging clearly demonstrated the local extent and depth of the lesion, it was useful in making their decision to perform conservative resection.

Provet and associates [47] in their report of the 18th case of primary amyloidosis of the urethra stated that up to 1989 August only 17 cases of primary amyloidosis of the urethra had been reported and that the presentation of primary amyloidosis of the urethra mimics carcinoma and treatment of this condition should be conservative.

Christie and Weingarten [48] reported a 38-year-old man who presented with a 2-week history of intermittent bloody urethral discharge which was accompanied discomfort in the terminal portion of his urethra. His symptoms had not responded to week's course of tetracycline therapy. Examination of his genitalia and prostate gland was normal. He underwent cystoscopy which revealed a segment with an irregular mucosal

surface with areas of reddening in the penile urethra. This abnormality extended from just within the fossa navicularis distally for about 1 cm proximal to it. The bladder appeared normal. The abnormal area was biopsied, pursuant to which a tentative diagnosis of amyloidosis was made. Biopsies of the urinary bladder and rectum were taken a number of days later and stained negatively for amyloid. Microscopic examination of the biopsied specimen from the abnormal area in the urethra revealed a pale staining material deep to the urethral epithelium and this stained positively with Congo red for amyloid, demonstrating lime green birefringence with polarized light and metachromasia with crystal violet. The amyloid was deposited in two patterns: (a) in solid globules and diffusely beneath the urethral epithelium, elevating and disrupting it, causing a squamous metaplasia, provoking a giant cell reaction and widening the spaces between connective tissue cells; and (b) in the walls of deeper blood vessels. Electron exhibited fibrils characteristic of amyloid. Christie and Weingarten [48] stated that a review by Fujima and associates [49] indicated that, unlike its more common counterpart in the bladder, which has been reported in both sexes, urethral amyloidosis presenting as a clinical entity has only been seen in males and up to the time of their publication amyloidosis of the urethra had not been associated with the presence of, or later development of, generalized or secondary amyloidosis, as occurs in some cases as stated by Missen and Tribe [50], this being an important potential prognostic difference. [48]

Christie and Weingarten [48] stated that amyloidosis is most commonly unifocal but it may be multifocal in the urethra, rarely also in the bladder as stated by Gerami and associates [51] and any portion of the urethra may be affected.

Primary amyloidosis of the lower ureter has been reported in the literature presenting as hydronephrosis secondary to ureteric stricture [52], [53], [54] and bilateral involvement presenting as anuria. [55] Treatment with ureteric stenting and occlusive dressing technique using dimethyl sulfoxide (DMSO) for 6 months leading to complete resolution of the lesion has been described. [52]

Amyloidosis can be classified according to their chemical fibril constituent as AL, AA, or ATTR (biochemical classification) or based upon clinical syndromes as localized and systemic. [56] Chitale and associates [56] stated that a combined biochemical-clinical or clinic-pathological classification is thought to be more practical as a given biochemical form of amyloid may be associated with diverse clinical settings. Chitale and associates [56] as well as Mitchell and associates [57] stated that:

- Clinically, the systemic/generalised and localised patterns could be sub-classified into primary amyloidosis when associated with some immunocyte dyscrasias (AL) and secondary amyloidosis when it

occurs as a complication of chronic inflammation or tissue destructive process (AA).

- Hereditary or familial amyloidosis constitutes a separate group of conditions with distinctive pattern of organ involvement.

Munikrishnan and associates [58] reported a 59-year-old man who presented with a one month history of painless haematuria. His clinical examination, urine cytology and routine blood tests were normal. He had intravenous urography which showed delayed excretion with obstruction in the right mid-ureter. He had a computed tomography scan and underwent a retrograde pyelogram and these confirmed a ureteric tumour obstructing the right ureter. Attempts at ureteroscopic biopsies were not successful but a presumed diagnosis of transitional cell carcinoma was made. During his operation, an extra-peritoneal approach to the ureter was used and local excision with end to end anastomosis over a JJ stent was carried out instead of nephroureterectomy. Histological examination of the specimen showed eosinophilic amyloid deposits in the lamina propria and inner muscle layer of the wall of the ureter, with Congo red positivity, characteristic of amyloidosis. No cause of secondary amyloidosis was found after further investigations. The ureteric stent was removed one month later and a retrograde pyelogram showed good drainage.

Munikrishnan and associates [58] commented that:

- Localized primary ureteric amyloidosis was rare and it is a benign condition which usually presents with haematuria and flank pain.
- Amyloidosis of the ureter is radiologically similar to transitional cell carcinoma.
- Ureteroscopic biopsies are advocated but often they are unsuccessful. Frozen section analysis may be helpful.
- Of the 31 cases reported at their time of publication, 21 cases had been reported in the Japanese literature [60], suggesting an eastern preponderance, and two thirds have been reported in women. [59] [60]
- The disease is common in the lower third but rare in the middle third of the ureter. [60]
- Most cases had been treated with nephrectomy or nephroureterectomy.
- Conservative surgery was performed in only 13 cases; nine local resections and anastomosis, three renal auto-transplantations and one extra-peritoneal segmental resection of the diseased ureter followed by mobilisation and simple anastomosis or ureteric substitution may be the treatment of choice.

Jang and associates, [62] reported a case of localized amyloidosis arising in the left upper ureter in a 77-year-old man who presented with painless visible haematuria and dysuria of 1 months duration. Urinalysis revealed haematuria and his urine cytology was normal. He had a computed tomography scan which an obstructing mass

with calcification in the left ureter. The differential diagnoses were a ureteric stone or malignancy. A left nephroureterectomy was performed. Macroscopic examination of the ureter showed segmental fibrotic thickening with luminal obstruction. Microscopic examination revealed deposition of pale-eosinophilic amorphous material with calcification and ossification. Congo red staining showed amyloid deposits with positive polarizing microscopic findings. They concluded that although amyloidosis of the ureter is rare it should be considered in the differential diagnosis of ureteral tumourous lesions in order to avoid unnecessary surgery. Jang and associates [62] stated that:

- The clinical significance of primary localized amyloidosis of the ureter is that it can often be mistaken for malignant disease.
- Hayashi and associates [63] reviewed 42 cases of primary amyloidosis of localized form in which they stated that more than 90% of the patients presented with visible haematuria or flank pain and their mean age was 55 years.
- It is worth noting that ureteral amyloidosis exhibiting osseous metaplasia and calcification can be indistinguishable from simple urolithiasis due to the peculiarity of the onset site.

Mark and associates [64] suggested that the common radiologic findings of amyloid deposition in the urinary tract are irregular ureteral narrowing, filling defects, and hydroureteronephrosis which closely resemble those of ureteral malignancy.

Three cases of primary localized amyloidosis of the ureter with osseous metaplasia were reported by Chung and associates [65] and Yamaguchi and associates. [66] Among these three cases Chung and associates [65] described on case in which the ureteral amyloidosis was misinterpreted as a ureteric stone.

Borza and associates [67] as well as Fushimi and associates [68] suggested that chronic and recurrent inflammation plays an important role in the localized amyloid deposition, because in a significant number of cases there is infiltration of plasma cells and lymphocytes around the amyloid deposits. Some authors [2], [68] stated that the amyloid deposits in localized amyloidosis are predominantly of lambda light chain. Borza and associates [67] as well as Fushimi and associates [68] stated that after the migration of of plasma cells and lymphocytes, localized monoclonal lympho-plasmacytic proliferation may induce exuberant production of the lambda immunoglobulin light chain light chain, which is a precursor of AL type protein.

Lee and associates [69] reported 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 who had left flank pain

and intermittent visible haematuria (case 2). The first patient (case 1) had an intravenous pyelography which revealed multiple filling defects in the entire right ureter, and in the case of the second patient (case 2) retrograde pyelography showed diffuse narrowing in the mid and lower portions of the left ureter. Localized amyloidosis was diagnosed in the two cases, and both had amyloid deposit in the renal pelvis and the urinary bladder in case 1, and in the contralateral ureter and the renal pelvis in case 2. Right nephroureterectomy was performed in case 1, however, a segmental resection of the ureter with preservation of the kidney was performed in case 2. Lee and associates [69] stated that:

- 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.

Davis and associates [70] reported a case of primary amyloidosis which involved the ureter and renal pelvis. They stated that histological examination was required to distinguish amyloidosis of renal pelvis from transitional cell carcinoma. They stated that intra-operative diagnosis of amyloidosis by frozen section may allow for a conservative surgical approach.

Shi and associates [71] reported a 68-year-old man with a space-occupying lesion in the left renal pelvis which was found by computed tomography scan. He was suspected of having malignancy before ureteroscopy. Histological examination of biopsy specimens taken from the lesion revealed amyloidosis. He was not given any treatment for the primary renal pelvis amyloidosis. New lesions were found in the urinary bladder 10 months later and in the left ureter 21 months later respectively. Shi and associates [71] stated that their case was the first primary renal pelvis AA type amyloidosis in which the patient had been monitored for the progress of lesions in renal pelvis, ureter and bladder.

Murphy and associates [72] reported a case of primary amyloidosis localized to the inferior renal pelvis of a kidney with a duplex collecting system. The patient presented with visible haematuria and mild flank pain which necessitated investigations which yielded a clinical impression of tumour within the lower pelvis of a duplex collecting system. At laparotomy a grossly haemorrhagic appearing mass in the lower pelvis was observed and a left ureteronephrectomy was performed. Histological examination of the surgical specimen revealed amyloid deposition within the inferior pelvis, the corresponding distal portions of the papillae, and the most proximal ureter. Amyloid was not present elsewhere within either the renal parenchyma or the superior collecting system.

Pan and Na [73] reported a 70-year-old man who had routine follow-up ultrasound scan of the renal tract as part of his follow-up assessment for a right partial nephrectomy he had undergone about a year earlier for angiomyolipoma. The ultrasound scan revealed what was considered to be a tumour in his left renal pelvis without any abnormality in the bladder or ureter. He was asymptomatic. There was evidence of non-visible haematuria on analysis of his urine otherwise all his routine blood test results were normal. His urine cytology was also normal. He next had computed tomography scan which revealed multiple soft tissue dense lesions with a maximum diameter of about 3 cm in the left renal pelvis and ipsilateral upper and middle calyces. He also had intravenous pyelogram which revealed a filling defect in the pelicalyceal system but no hydroureter in the left kidney. He underwent cystoscopy which revealed a normal bladder left ureteric urine revealed normal cytological examination. Left retrograde pyelogram images were consistent with intravenous urography. He underwent ureteroscopy which revealed one reddish tumour of 3 cm in diameter with a smooth surface. A biopsy was taken of the apparent tumour and the specimen was sent for histological examination. The ipsilateral ureteral mucosa looked smooth and normal. Histological examination of the biopsy specimen revealed urothelial hyperplasia and islands of amorphous eosinophilic material in the epithelium of some regions and small vessels. Staining with Congo red exhibited a characteristic birefringence. The patient declined to have any surgical intervention and preferred to have regular follow-up computed tomography scans because of benignity of amyloidosis and fear of surgical damage to his left kidney. He had a computed tomography scan six months after the diagnosis of his left renal pelvis amyloidosis which was similar to his previous scan with no change in the appearance of his left renal pelvis amyloidosis. He had another computed tomography scan about one year after the initial diagnosis of the left renal pelvis amyloidosis and this revealed no change in the appearance of the left renal pelvis amyloidosis but this time there was an irregular 1 cm diameter tumour at the posterior wall of the urinary bladder. Enhanced computed tomography scan showed a nodular enhanced lesion in the bladder with a thin pedicle to combine with the posterior wall of the bladder. He then had ultrasound scan of the renal tract which showed a mid-echo nodule about 2.4 cm x 2.2 cm x 1.9 cm protruding into the cavity of the urinary bladder with blood current signal at its base. He subsequently underwent cystoscopy which revealed a tumour with a smooth surface on the posterior wall of the bladder looking like a group of grapes with a diameter of 1 cm. He underwent trans-urethral resection of the bladder lesion and left ureteric urine collection for cytological examination which was negative. Haematoxylin and eosin staining of the resected bladder lesion revealed islands of amorphous eosinophilic material suggestive of amyloidosis of urinary epithelium, and this had involved lamina propria and small blood vessel wall, and it stained positively with

Congo red. The patient refused any post-operative prophylactic medical treatment to prevent recurrence of his bladder amyloidosis. About 25 months after the initial diagnosis of left renal pelvis amyloidosis he had another computed tomography scan which revealed no change in the size and appearance of the left renal pelvis mass, however, it revealed three new papillary tumours in his bladder. He then underwent cystoscopy and trans-urethral resection of the bladder lesions. He at the same sitting underwent left ureteroscopy which revealed a papilloma with a thin pedicle in the upper segment of the left ureter and this was resected, by means of laser. He also had biopsy of the left renal pelvis lesion. Histological examination of the ureteric lesion and the renal pelvis biopsy specimen were consistent with amyloidosis again. The resected bladder lesion was also that of amyloidosis. Pan and Na [74] stated that:

- Amyloidosis of the urinary system is a rare condition and few cases have been reported with simultaneous or successive multi-organ urothelial amyloidosis.
- According to the involved frequency rate of involvement of the urinary tract by amyloidosis, the urinary bladder is the commonest, then the ureter and renal pelvis, and the urethra which is the least involved.
- About 200 cases of amyloidosis of the urinary tract have been reported in the literature by September 2011 in the literature including 10 patients with more than two urinary organs involved (4 cases with renal pelvis and ureter, 4 with ureter and bladder, 2 with bilateral ureter) [2], [4], [20], [22], [36], [74], [75], [76], [77], [78], [79], [80], [81], but there was no reported case with renal pelvis involved successively or simultaneously.
- They had reported 1 patient with amyloidosis which had involved unilateral renal pelvis, bladder and ureter successively.

Conclusion

Primary amyloidosis involvement of the urinary tract is a rare clinical entity. Biopsy of the lesion is required to establish a diagnosis by means of the characteristic histological of eosinophilic amorphous appearance and positive Congo red staining with birefringence.

In view of the benign biological behaviour of amyloidosis conservative treatment is the best modality of treatment however, radical surgical excisions have been undertaken when a definitive diagnosis had not been established and these surgical treatments have been carried out based upon a presumptive diagnosis of a malignant tumour.

Surgical resection of the amyloid tumour is considered the first-line therapeutic method (TUR resection of bladder lesion; biopsy/resection or local segmental resection of a ureteric amyloid tumour; resection of urethral amyloid lesion). Pharmacotherapy can be used when the lesion is difficult to completely resect, or when a patient is unable tolerate surgery. Colchicine or

dimethyl sulfoxide may be beneficial for the control of the progression or recurrence of amyloidosis.

In view of reported recurrences of primary amyloidosis of the urinary bladder and other parts of the urinary tract careful surveillance protocol is necessary to identify local recurrent amyloid lesions as well as metachronous lesions that may develop elsewhere in the urinary tract.

References

1. Alcides Chaux Bladder Acquired non-neoplastic anomalies Amyloidosis. Pathology Outlines.com 2011 March; can be found at: www.pathologyoutlines.com/topic/bladderamyloidosis.html
2. Merrimen J L, Alkhudair W K, Gupta R. Localized amyloidosis of the urinary tract: case series of nine patients. *Urology* 2006 May; 67(5): 904 – 909
3. Tirzaman O, Wahner-Roedler D L, Malek R S, Sebo T J, Li C Y, Kyle R A. Primary localized amyloidosis of the urinary bladder: a case series of 31 patients. *Mayo Clin Proc* 2000 December; 75(12): 1264 – 1268
4. DeSouza M A, Rekhi B, Thyavihally Y B, Tongaokar H B, Desai S B. Localized amyloidosis of the urinary bladder, clinically masquerading as bladder cancer. *Indian J Pathol Microbiol* 2008 July- September; 51(3): 415 – 417
5. Andrade M J. lower urinary tract dysfunction in familial amyloidotic polyneuropathy, Portuguese type. *Neurourol Urodyn* 2009; 28(1): 26 – 32
6. Lipper S, Kahn L B. Amyloid tumor: A clinicopathologic study of four cases. *Am J Surg Pathol* 1978 June; 2(2): 141 – 145]
7. Garcia-Escudero Lopez A, Arruza Echevarria A, Leunda Saizar J, Infante Riano R, Padilla Nieva J, Ortiz Barredo E. Secondary Amyloidosis of the bladder and massive hematuria. *Actas Urologicas Espanolas* 2010; 34(1): 111 -115]
8. Fugita O E, Delatorre C G, Kavoussi L R. Primary localized amyloidosis of the ureter. *J Urol* 2001; 58: 281
9. Lance N J, Curran J J. Amyloidosis in a case of ankylosing spondylitis with a review of the literature. *J Rheumatol* 1991; 18: 100 – 103
10. Auge B K, Haluszka MM. Primary amyloidosis of the urinary bladder. *J Urol.* 2000; 163: 1867 – 1868
11. Huang C Y, Shun C T, Huang K H, Chen J, Pu Y S. Primary amyloidosis of the urinary bladder. *J Formos Med Assoc.* 2006; 105: 164 – 167
12. Malek R S, Wahner –Roedler D L, Gertz M A. Primary localized amyloidosis of the bladder: experience with dimethyl sulfoxide therapy. *J Urol.* 2002; 168: 1018 – 1020
13. Caballero Gine J M, Borrat Font P, Marti Picas L, Ristol Pont J. Amyloidosis vesical: presentación de dos casos. *Actas Urol. Esp.* 2000; 24: 413 – 415

14. Bender L M, Nelly C H. Secondary amyloidosis of the bladder: a case report. *J Urol*. 1969; 102: 60 – 62
15. Numi M J, Ekfors T O, Puntala P V. Secondary amyloidosis of the bladder: a cause of massive hematuria. *J Urol*. 1987; 138: 44 – 45
16. Tesedo Cubero J, Ristol R M, Fernandez Zuazu J. Hematuria masiva y perforación vesical, complicación de una amyloidosis sistémica. *Arch Esp Urol*. 1991; 44: 862 - 864
17. Bielsa O, Romero J A, Alcaraz A. Amiloidosis vesical secundaria. Una rara causa de hematuria. *Actas Urol Esp*. 1990; 14: 76 - 77
18. Sanz-Jaka J P, Arrinda Yeregui J M, Mendibil Dakal J. Afectación vesical en la amyloidosis sistémica. *Actas Urol Esp*. 1988; 41: 325 - 328
19. Palmero Martí J L, Budia Alba S, Ariandis Guzman S, Benedicto Redón A, hernández Martí M, Jiménez Cruz J F. Amiloidosis vesical secundaria. *Actas Urol Esp*. 2004; 28: 238 - 242
20. Gómez Garcia I, González Chamorro F, Fernández Fernández E, Palacio España A, Molina Burgos R, Alvarez E, et al. Hematuria y fracaso renal agudo como debut de amyloidosis vesical secundaria. Presentación de un Nuevo caso y revision de la literature. *Actas Urol. Esp*. 2005; 29: 603 - 606
21. Fariña Pérez L A, Ortiz Rey J A. Haematuria grave recidivante por amyloidosis secundaria. Mikulicz trasuretral como opción hemostática. *Arch. Esp. Urol*. 2005; 58: 665 – 668
22. Jain M, Kumari N, Chhabra P, Gupta R K. Localized amyloidosis of urinary bladder: A diagnostic dilemma. *Indian Journal of Pathology and Microbiology CASE REPORT* 2008; 51(2): 247 - 249
23. Wilkinson M, Fanning D M, Flood H. Rare disease Primary bladder amyloidosis *BMJ Case Reports* 2011; doi. 10.1136/bcr.05.2011.4211
24. Caldamone A A, Elbadawi A, Moshtagi A, Frank I N. Primary localized amyloidosis of urinary bladder. *Urology* 1980 February; 15(2): 174 – 180
25. Biewend M L, Menke D M, Calamia K T. The spectrum of localized amyloidosis: a case series of 20 patients and review of the literature. *Amyloid* 2006 September; 13(3): 135 -142
26. Khan S M, Birch P J, Bass P S, Williams J H, Theaker J M. Localized amyloidosis of the lower genitourinary tract: a clinicopathological and immunohistochemical study of nine cases. *Histopathology* 1992 august; 21(2): 143 – 147
27. Agarwal S K, Walmsley B H, Marley N J E. Primary amyloidosis of urinary bladder. *J R Soc Med* 1995 March; 88(3): 171 P – 172 P
28. Fujihara S, Glenner G G. Primary amyloidosis of the genitourinary tract: Immunohistochemical study of eleven cases. *Lab Invest*. 1981; 44(1): 55 -59
29. Glenner G G. Amyloid deposits and amyloidosis: the beta fibrillosis. *N Engl J Med* 1980; 302: 1283
30. Nurmi M J, Ekfors J O, Rajala P O, et al. Intravesical dimethylsulphoxide instillation in the treatment of secondary amyloidosis of the bladder. *J Urol*. 1990; 143: 808 – 810
31. Livingstone R B, Sarenbock L A, Barnes R D, et al. Colchicine therapy in primary amyloidosis of the bladder: a case report. *J Urol*. 1989; 142: 1570 – 1571
32. Malek R S, Greene L F, Furrow G M. Amyloidosis of the urinary bladder. *Br J urol* 1971; 43:189 – 200
33. Gupta P, Hanashetti S, Kulkarni J N. Primary amyloidosis with high grade transitional cell carcinoma of bladder: A rare case report. *J C R T* 2012; 8(2): 297 - 299
34. Biyani C S, Fitzmaurice R J, Upsdell S M. *BJU Int*. 1999 April; 83(6): 722 – 723
35. Srinath N, Sandhu A S, Bharadwa R, Sood R, Gupta S K, Pradharn A A, Madhusoodanan P. Primary amyloidosis of the urinary bladder: A case report. *Indian Journal of Urology* 2003; 19(2): 157 – 159
36. Patel S, Trivedi A, Dholaria P, Dholakia M, Devra A, Gupta B, Shah S A. Recurrent Multifocal Amyloidosis of Urinary Bladder. *Saudi Journal of kidney Diseases and Transplantation* 2008; 19(2): 247 – 249
37. Goswami A K, Vaidyanathan S S, Rao M S, Malik A K, Mathur R P, Sen T K. Primary localised amyloidosis of urinary bladder (a case report). *Journal of postgraduate Medicine* 1984; 30(4): 253 – 254
38. Kamoi T, Hanika S, Inagaki T, Kimura Y, Hirahara N, Sou J, Nakagawa S, Kawachi A, Miki T. *Acta urologica Japonica (Hinyokika Kiyō)* 2011 August; 57(8): 439 – 443
39. Altwairgi A. Primary amyloidosis of the urinary bladder presenting as painless haematuria. *International Journal of Health Sciences, Qassim University* 2011 July; 5(2): (July 2011/Rajab 1432H) can be found as: 181 Case Report Primary amyloidosis of the urinary bladder: ijhs.org.sa/index.php/journal/article/download/409/190
40. Williams O E, Kynaston H, Dixon G, Aryn O P. Amyloid tumour of the urethra presenting as non-specific urethritis. *Genitourin Med* 1992 October; 68(5): 332 - 333
41. Ullmann A S, Fine G, Johnson A J. Localized amyloidosis (amyloid tumour) of the urethra. *J Urol* 1964; 92: 42 – 44
42. Van Albertinck A. Local amyloid of urethra. *Frankfurter Zeitschrift fur Pathologie* 1925; 33: 248 – 257
43. Geram S, Easley C W, Payan H. Primary localized amyloidosis of the urethra and bladder. *Am Surg* 1970; 36: 375 – 377
44. Tilp A. Uber lokales tumor formiges Amyloid de Hambohe. *Zentralbl Allg Pathol* 1909; 20:913 - 916
45. Karisary A V. Primary localized amyloidosis of the urethra. *Eur urol* 1985; 11: 209
46. Ichioka K, Utsunomiya N, Ueda N, Matsui Y, Yoshimura K, Terai A. Primary localized amyloidosis of urethra: magnetic resonance imaging findings. *Urology* 2004 August 64(2): 376 – 378

Venyo A K G, Ahmed K. (September 2013) Amyloidosis of the urothelium (bladder, ureter, renal pelvis and urethra): A review of the literature. *Jour of Med Sc & Tech*; 2(3); Page No:

47. Provet J A, Mennen J, Sabatini M, Rakhman J, Golimbu M. Primary amyloidosis of urethra. *Urology* 1989 August; 34(2): 106 – 108
48. Christie A J, Weingarten C J. Amyloidosis presenting in the urethra. *Journal of Royal Society of Medicine* 1988 March; 81: 174 - 175
49. Fujima M, Tajima A, Minowada S, et al. Localized amyloidosis of urethra: Report of two cases. *Eur Urol*. 1981; 7: 189 – 192
50. Missen G A K, Tribe C R. Catastrophic haemorrhage from the bladder due to unrecognized secondary amyloidosis. *Br J Urol* 1970; 42: 43 - 49
51. Gerami S, Easley G W, Payan H. Primary localized amyloidosis of the urethra and bladder. *Am Surg* 1970; 38: 375 – 377
52. Kato Y, Sue Y, Fuji H, Numara A, Yachiku S. Localized amyloidosis of the ureter and bladder treated effectively by occlusive dressing technique therapy using dimethyl sulfoxide: a case report. *Hinyokika Kyo* 2000; 46: 421 – 424
53. Andreas B F, Oosting M. Primary amyloidosis of the ureter. *J Urol*. 1958; 79: 929 – 931
54. Kitsukawa S, Hoseda S, Otsuru N, Natsumoto T, Yamamoto Y, Matsumoto T. Localized amyloidosis of the ureter: a case report. *Hinyokika Kyo* 2006; 52:131 – 134
55. Paraskevas K I, Anagnostou D, Bouris C. anurea caused by primary amyloidosis of the lower third of the ureters, the ureterovesical junction and the urinary bladder: a case report and review of the literature. *Int Urol Nephrol* 2004; 36: 339 - 342
56. Chitale S, Morsey M, Peat D, Webb R. Amyloidosis of Lower genitourinary Tract: A Review. *EAU EEU Update Series* 2007; 5: 70 – 76
57. Mitchell R N, Kumar V. Diseases of immunity. In: Kumar V, Cotran R S, Robbins S L, editors. *Robbin's Basic Pathology*. 7th ed. Philadelphia W B Saunders 2003; P. 103 – 164
58. Munikrishnan V, Kennedy C, Al-Rufiae H. Primary Amyloidosis of the ureter. *BJU International* 2000; 85(6): 776
59. Awakura Y, Mizutani T, Kakehi Y et al. A case of localised amyloidosis of the ureter. *Hinyokika Kyo - Acta. Urol. Jap.* 1996; 42: 135 - 138
60. Gulmi F A, Mooppan U M M, Gomez-Leon G et al, Primary localised amyloidosis of ureter. *Urology* 1988; 32: 161 - 164
61. Farrands P a, Tribe C, Slade N. Localised amyloid of the ureter – a case report and review of the literature. *Histopathology* 1983; 7: 613
62. Jang S M, Han H, Jun Y J, Sim J, Ahn H I, Lee T Y, Jang K S, Park S S. Primary localized amyloidosis of the ureter presenting as a ureteral stone. *Basic and Applied Pathology* 2012; 5: 68 – 71]
63. Hayashi T, Kogima S, Sekine H, Mizuguchi K. Primary localized amyloidosis of the ureter. *Int J Urol*. 1998; 5: 383 – 385
64. Mark I R, Goodlad J, Lloyd-Davies R W. Localized amyloidosis of the genito-urinary tract. *J.R. Soc. Med.* 1995; 88: 320-324
65. Chung H S, Kwon S W, Kung D K, et al. Primary localized amyloidosis of the ureter associated with osseous metaplasia. *Korean J Urol*. 2004; 45: 189 – 191
66. Yamaguchi K, Kitagawa N, Kotake T, Matsuzaki O, Nagao K, Ito H. Primary localized amyloidosis of the ureter associated with osseous metaplasia. *Urol Int* 1991; 47:164 - 166
67. Borza T, Shah R H, Faerber C J, Wolf J S Jr. Localized amyloidosis of the upper urinary tract: a case series of three patients managed with reconstructive surgery or surveillance. *J endourol* 2010; 24: 641 -644
68. Fushimi T, Takei Y, Touma T et al. Bilateral localized amyloidosis of the ureters: clinicopathology and therapeutic approaches in two cases. *Amyloid* 2004; 11: 260 - 264
69. Lee H J, Song D E, Joo J E, Kim D H, Kim E K, Ro J Y. The Korean Journal of Pathology 2004; 38: 184 – 187.
70. Davis P S, Babaria A, March D E, Goldberg R D S. Primary amyloidosis of the ureter and renal pelvis. *Urologic radiology* 1987/1988; 9(1): 158 - 160
71. Shi L X, Li G, Zhang L, Cong B, Zhang X. primary localized AA type amyloidosis of the renal pelvis, ureter and bladder. *J Pak Med Sci*. 2012 April – June; 28(3): 530 - 532
72. Murphy M N, Alguacil-Garcia A, MacDonald R G. Primary amyloidosis of renal pelvis with duplicate collecting system. *Urology* 1986 May; 27(5): 470 - 473
73. Pan D L, Na Y Q. Amyloidosis of the Unilateral Renal Pelvis, Ureter and Urinary Bladder: a Case Report. *Chinese Medical Sciences Journal* 2011 September; 26(3): 197 - 200
74. Slavov C H, Vlahova A, Khristova S, et al. Amyloidosis of the urinary tract-case report and review of the literature. *Khirurgia (Sofia)* 2006; 2: 47 – 49
75. Nagasaka T, Togashi S, Watanabe H et al. Clinical and histopathological feature of progressive-type familial amyloidotic polyneuropathy with TIR Lys54. *J Neurol Sci* 2009; 276: 88 – 94.
76. Hajji K, Martin L, Deveney J M, et al. Rheumatoid arthritis-induced pseudotumoral AA amyloidosis of the bladder with vesico-peritoneal fistula. *Clin Nephrol* 2007; 67: 38 – 43.
77. Kirkpantur A, Baydar D E, Alton b, et al. Concomitant amyloidosis, renal papillary carcinoma and ipsilateral pelviccalyceal urothelial carcinoma in a patient with familial Mediterranean fever. *Amyloid* 2009; 16: 54 – 59.
78. Eccher A, Brunelli M, gobo S, et al. Subepithelial pelvic hematuria (Antopol-Goldman lesion),

Venyo A K G, Ahmed K. (September 2013) Amyloidosis of the urothelium (bladder, ureter, renal pelvis and urethra): A review of the literature. *Jour of Med Sc & Tech*; 2(3); Page No:

- simulating renal neoplasm: report of a case and review of the literature. *Int J Surg Pathol* 2009; 17: 264 – 267
79. Korkumaz C, Kebapci M. Addison's disease associated with widespread abdomino-pelvic visceral calcification due to secondary amyloidosis: a case report. *Acta Radil* 2004; 45: 800 – 802
80. Savareux L, Guy L, Essamet W, et al. Pyelo-ureteric amyloidosis. *Prog Urol* 2004; 14: 406 – 410
81. Iida S, Chujyo T, Nakata Y, et al. A case of amyloidosis of the renal pelvis. *Hinyokika Kyo* 2003; 49: 423 – 426
82. Heras M, Sanchez R, Saiz A, et al. Renal amyloidosis in a female with familial Mediterranean fever: clinical response to treatment with colchicine and infliximab. *Nefrologia* 2009; 2009: 373 – 375.
83. Azzabi S, Ben Hassine L, Cherif E, et al. Renal amyloidosis during Behcets disease, Study of one case. *Tunis med* 2009; 87: 213 – 214
84. Summerton D J, Hall I S, Tulloch D N. Primary amyloidosis of the urinary bladder and ureters. *Br J Urol* 1998; 81: 935.
85. Mccammon K A, Lentzner A N, Moriarty R P, et al. Intra-vesical dimethyl sulfoxide for primary amyloidosis of the bladder. *Urology* 1998; 52: 1136 – 1138

MD CRACK
THE ONLINE LECTURE SERIES FOR MEDICAL STUDENTS!
www.mdcrack.tv

No need to travel long hours ...
Lecture series at your door step!

Useful For :
▶ **PG Entrance Exams** (MD/MS/DNB)
▶ **MCI Screening Test** (Foreign Medical Graduates)
▶ **MBBS Students**

For 6 months : *INR 3199
For 12 months : *INR 5199

*HURRY!
DON'T MISS THE EARLY BIRD OFFER!

▶ 250 HOURS VIDEO LECTURES
▶ COVERS 19 MEDICAL SUBJECTS

Go to www.mdcrack.tv
Watch free demo videos

info@mdcrack.tv
www.facebook.com/Mdcrack