

A rare case of localised AA-type amyloidosis of the ureter with spheroids of amyloid

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ABSTRACT We present a case of localised AA-type amyloidosis of the ureter with spheroids of amyloid. Localised AA-type amyloidosis of the urogenital tract is uncommon and extremely rare as a cause of ureteric obstruction, with only two such cases described in the literature to date. Most previously described cases at this site are related to primary AL-type amyloidosis. Another interesting finding in this case is the presence of spheroids of amyloid, which to the best of our knowledge, has not been previously reported at this site, and is also unusual at other sites.

Keywords: AA amyloidosis, spheroids of amyloid, ureter
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INTRODUCTION

Localised AA amyloidosis of the urogenital tract is rare, and is even more uncommon as a cause of ureteric obstruction. Most previously described cases are related to primary amyloidosis (AL type). We present a case of localised secondary amyloidosis of the ureter with spheroids of amyloid, an interesting finding, which to the best of our knowledge, has not previously been reported at this site and is also unusual at other sites.

CASE REPORT

A 32-year-old Chinese woman with no significant past medical history first presented with right loin pain to the Accident and Emergency Department, Singapore General Hospital in April 2007. Abdominal radiography and subsequent computed tomography of the kidneys, ureters and bladder showed small calculi in the lower pole of the right kidney, while ultrasonography of the kidney showed mild right hydronephrosis. The patient underwent right ureteroscopy (URS), retrograde pyelogram (RPG) and right double-J stent insertion. She was advised concerning the need for subsequent surveillance of the mild right hydronephrosis, which worsened by July 2007 when she underwent right URS and RPG, and right ureteric re-implantation with psoas hitch. Right RPG revealed a long segment of ureteric stricture, while the URS did not reveal any intraluminal stones or tumour.

During ureteric re-implantation, a 4 cm segment of the patient's ureter was submitted for intra-operative frozen section. This showed a thickened ureteric wall without evidence of malignancy. In addition, two other segments of the ureter measuring 2 cm and 1.5 cm in greatest dimension were received in 10% formaldehyde in the histopathology section for routine histology. Grossly, the segment of the ureter was diffusely thickened and rigid. Histology of the cross-section of the ureter in both specimens revealed markedly thickened ureteric walls due to the presence of amorphous, pale eosinophilic, extracellular nodular deposits

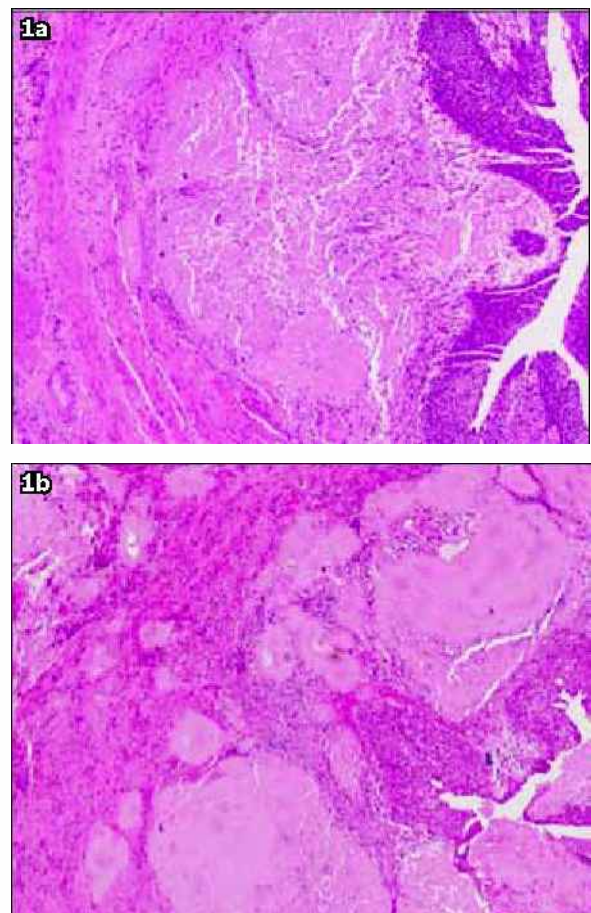


Fig. 1 (a & b) Photomicrographs show large nodular deposits of amorphous, pale eosinophilic extracellular material in the lamina propria (Haematoxylin & eosin, × 100).

expanding the lamina propria and extending patchily into the muscularis propria as well as focally into the adventitia (Figs. 1 a & b). These deposits resulted in thickening of the blood vessel walls and urothelial basement membrane. Narrowing of the ureteric lumen was apparent, while foci of mild chronic inflammation

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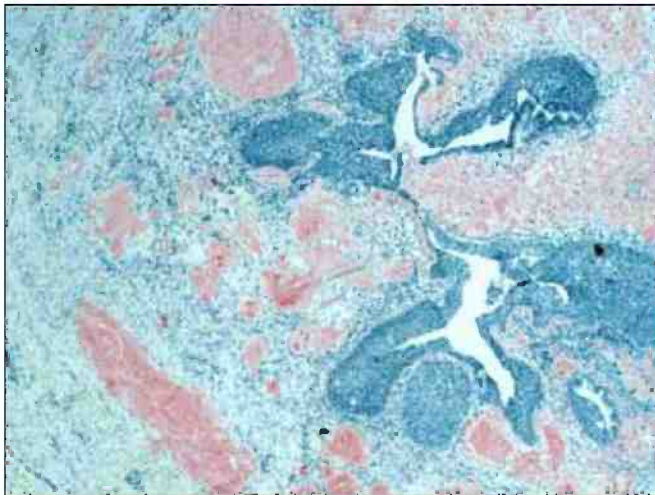


Fig. 2 Photomicrograph shows positive salmon red colouration of the pale eosinophilic deposits (Congo red stain, $\times 40$).

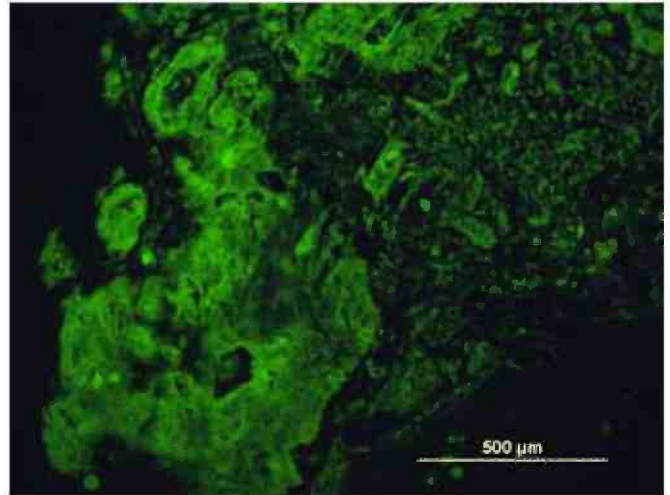


Fig. 4 Photomicrograph shows immunofluorescence of the amyloid deposits (Thioflavin-T stain, $\times 200$).

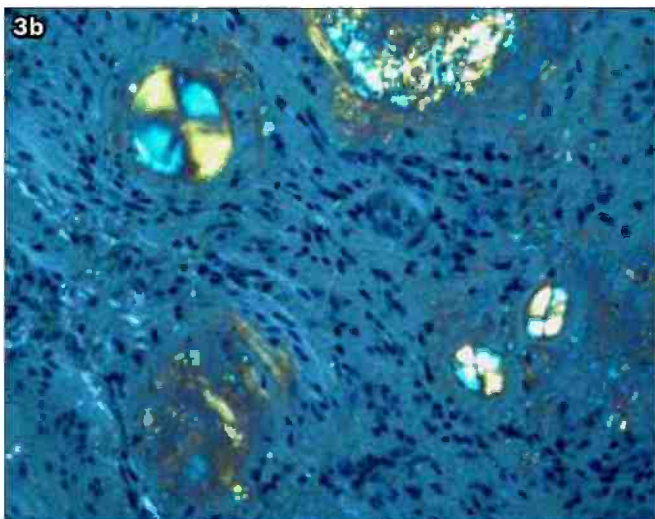
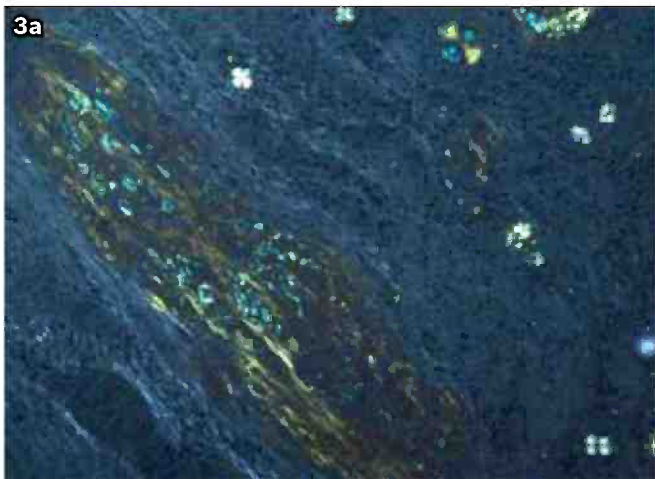


Fig. 3 Photomicrographs show (a) apple green birefringence of the amyloid deposits upon polarisation, with globular polarised deposits seen in the right upper half of the image (Congo red stain, $\times 100$); and (b) spheroids of amyloid deposits (Congo red stain, $\times 400$)

incorporating lymphocytes and plasma cells in the lamina propria were observed. The overlying urothelium was free of dysplasia or malignancy. There were neither epithelioid granulomas nor any evidence of endometriosis.

Congo red stain imparted a salmon red colour to the amorphous pale eosinophilic deposits, proving the amyloidogenic nature of the deposits (Fig. 2). Interestingly, upon polarisation, along with the characteristic apple-green birefringence, there were also spheroids of amyloid, an occurrence that was rarely seen (Figs. 3 a & b). There was loss of reactivity to Congo red staining after pre-treatment with acidified potassium permanganate, suggesting the possibility of an AA-type amyloid. Thioflavin T immunofluorescence was also strongly positive (Fig. 4). A diagnosis of amyloidosis of the ureter, likely AA-type, was rendered.

Subsequent serum and urine immunofixation electrophoresis tests did not show a monoclonal band with anti-IgG, anti-IgA, anti-IgM, anti-kappa and anti-lambda antibodies. Protein electrophoresis of the urine and serum did not show any M-band. Other investigations done simultaneously showed negative rheumatoid factor, anti-nuclear antibody and anti-cyclical citrullinated peptide antibody enzyme-linked immunosorbent assay tests. Erythrocyte sedimentation rate was mildly elevated at 23 mm/hour, while C-reactive protein (CRP) was normal at 5.8 mg/L. The patient had remained asymptomatic three years later with normal renal function.

DISCUSSION

The term 'amyloid', which means 'starch-like', was coined by Virchow to describe tissue deposits that stain with iodine solutions.⁽¹⁾ Amyloidosis is a generic term for a heterogeneous group of disorders characterised by a common finding of extracellular accumulation of fibrillar protein deposits. Amyloidosis can be primary, which is usually the result of plasma cell dyscrasia such as multiple myeloma (AL-type with kappa or lambda light chain restriction) or secondary, which is caused by the deposition of acute-phase proteins (such as serum amyloid A) synthesised by the liver (AA-type).⁽¹⁾ Serum amyloid A is an apolipoprotein of high-density lipoprotein, which like CRP, is synthesised by the liver under the transcriptional regulation of cytokines, including IL-1, IL-6 and TNF- α , which typically

increase during inflammation.^(2,3) Moreover, amyloid deposition may be confined to one organ (localised) or may involve multiple organ systems (systemic).⁽⁴⁾ As amyloidosis appears insidiously and mysteriously, it is generally not suspected pre-operatively, and recognition of the entity ultimately depends on its morphological identification in appropriate biopsies.

In 1937, Lehmann reported the first case of ureteral amyloidosis.⁽⁵⁾ Its usual presenting symptoms are pain, haematuria and obstruction, which are commonly confused with a neoplasm or endometriosis.^(6,7) It mainly involves the lower portion of the ureter, as in the present case, with very few cases of bilateral involvement.^(6,7) A review of the literature reveals that amyloidosis of the urogenital tract, particularly of the ureter, is very rare, and that these deposits are mostly of the AL-type even when localised.^(1,4,6-8) So far, only two cases of AA or secondary amyloid deposits in the ureter are found in our literature search.^(2,8) Neither of the two cases is associated with globular spheroids of amyloid, which is the finding in our case. Thus, our case appears to represent an even more uncommon presentation, being likely the first to show nodular AA amyloidosis with globular spheroids of amyloid. Globular spheroids of amyloid have been reported in a few other sites, e.g. the jejunum, liver, uterine cervix, breast, medullary carcinoma of the thyroid, pancreatic islet cell tumours and pituitary

adenoma,⁽⁹⁾ but none has been described in the ureter with AA amyloidosis.

In conclusion, localised AA amyloidosis of the ureter is extremely rare, and only two such cases have been found in the literature to date. A unique and interesting finding in our case is the presence of spheroids of amyloid, which to the best of our knowledge, has not been reported at this site and is also extremely rare elsewhere.

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