Urology Case Reports 51 (2023) 102563

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Oncology

Localized Amyroid A amyloidsis of ureter: A case report

Kaori Yamashita [a,*], Keita Yoshida [b], Tadao Nakazawa [b], Takahiro Shiseki [a], Eri Sekido [a], Satoshi Kubota [a], Masashi Inui [a]

[a] Department of Urology, Tokyo Women's Medical University Yachiyo Medical Center, Japan
[b] Department of Pathology, Tokyo Women's Medical University Yachiyo Medical Center, Japan

A B S T R A C T

Amyloidosis of the ureter is a rare disease, distinguishing it from a neoplasm is difficult. A 64-year-old Japanese woman suffered from macrohematuria and left side hydronephrosis with ultrasound in 2014. Retrograde pyelography revealed no ureter tumor at that time. The patient had macrohematuria, left side hydronephrosis, and ureteral stenosis in the left ureter on retrograde pyelography. She was suspected of having a ureter tumor when she was 71 years old in 2021. The patient underwent ureteroscopy with biopsy. Pathological specimens contained the amyloid A component, based on immunohistochemistry staining. We diagnosed the patient with amyloid A amyloidosis of the ureter.

1. Introduction

The amyloidoses are a rare group of diseases that result from the extracellular deposition of amyloid. Amyloid deposits are composed of protein fibrils and can affect any organ system such as the heart, kidneys, liver, peripheral nervous system (i.e., peripheral neuropathy), soft tissue, or gastrointestinal system.[1] Localized amyloidosis of the ureter is rare—in particular, amyloid A (AA) amyloidosis of the ureter is very rare. However, amyloidosis of the ureter can be easily confused with a ureter tumor. We report a patient with a case of AA amyloidosis of the ureter that was detected via ureteroscopy with biopsy.

2. Case report

A 64-year-old Japanese woman had asymptomatic macrohematuria and left side hydronephrosis, detected with ultrasound, and was referred to our hospital in January 2014. She had hypertrophic cardiomyopathy and paroxysmal atrial fibrillation but she did not have rheumatoid arthritis, other rheumatic disease, neoplasms, inflammatory bowel disease, or chronic infection. She had no amyloidosis in her family history. Computed tomography revealed no ureter tumor or hydronephrosis. Retrograde pyelography revealed no ureter tumor, and urine cytology was class I in our hospital at that time. She thereafter sometimes had macrohematuria. However, urinalysis, urine cytology, and ultrasound were checked regularly, and the findings were within the normal range. The patient had asymptomatic macrohematuria and left side hydronephrosis, detected with ultrasound, when she was 71 years old in October 2021. Urinalysis revealed no proteinuria. Blood analysis findings were as follows: the serum creatinine level was 0.66 mg/dL and the C-reactive protein level was 0.06 mg/dL. All routine examinations were normal. Retrograde pyelography revealed hydronephrosis and a ureteral stenosis of approximately 3 cm in the lower ureter (Fig. 1A). Urine cytology was class II. Computed tomography revealed left side hydronephrosis and ureteral stenosis in the lower ureter (Fig. 1B). The patient underwent ureteroscopy with biopsy. Rigid ureteroscopy showed excrescences resembling urothelial carcinoma. The microscopic observation revealed the deposition of an eosinophilic amorphous material beneath the non-neoplastic urothelium in the hematoxylin and eosin (H&E)-stained specimen sections (Fig. 2A and B). The material scarcely contained a cellular component at high magnification (× 40) (Fig. 2B). The amorphous material was positive for Congo red staining, which indicated that it was composed of amyloid (Fig. 2C). Positivity for Congo red staining disappeared after the sample underwent the potassium permanganate ($KMnO_4$) process (Fig. 2D). Immunohistochemistry revealed that the material was positive for the amyloid A component (Fig. 2E). We diagnosed AA amyloidosis of the ureter. During 21 months of follow-up after ureteroscopy, biologics were not administered to this patient as the treatment of AA amyloidosis, she reported neither microhematuria nor hydronephrosis.

* Corresponding author. Department of Urology, Tokyo Women's Medical University Yachiyo Medical Center, 477-96, Owadashinden, Yachiyo-shi, Chiba, 276-8524, Japan.
E-mail address: kmurology@yahoo.co.jp (K. Yamashita).

https://doi.org/10.1016/j.eucr.2023.102563
Received 28 June 2023; Received in revised form 8 September 2023; Accepted 10 September 2023
Available online 13 September 2023

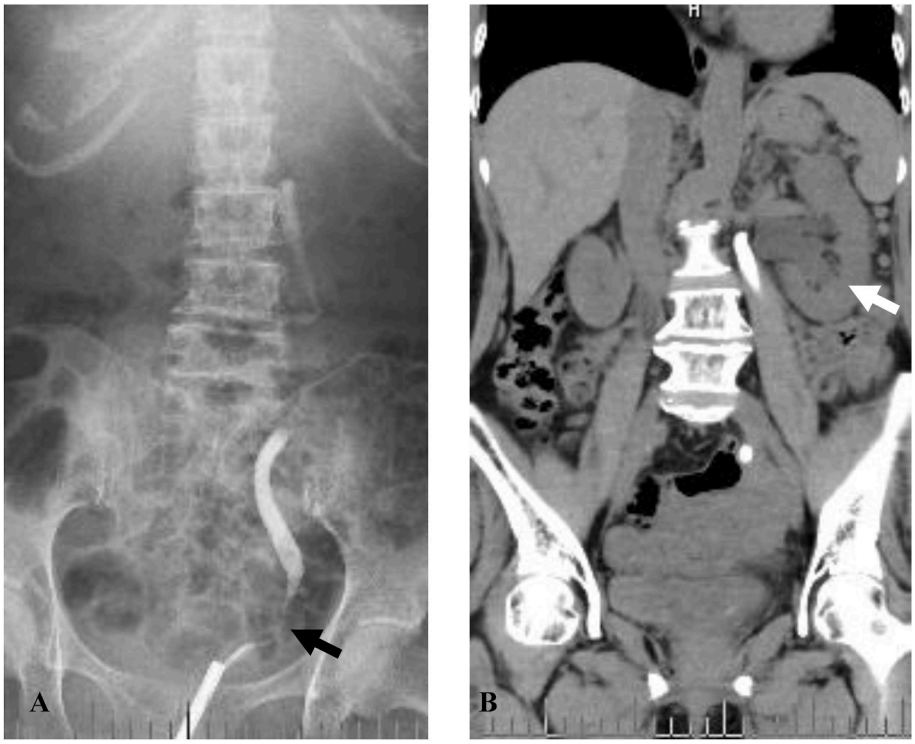

Fig. 1. Imaging findings.
A. Retrograde pyelography reveals hydronephrosis and ureteral stenosis (arrow) of approximately 3 cm in the left lower ureter.
B. The computed tomography image shows left side hydronephrosis (arrow) and ureteral stenosis in the left lower ureter.. (The contrast remains in the left upper ureter because this image was taken after retrograde pyelography.)

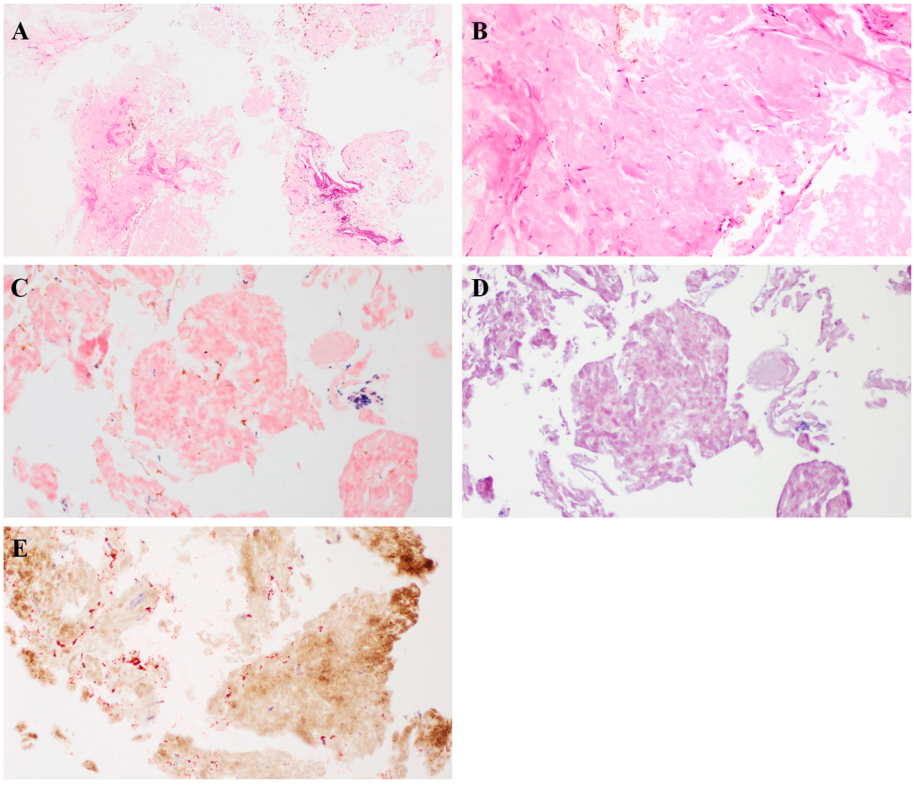

Fig. 2. Microphotographs of amyloid deposition.
A. Eosinophilic amorphous material is in the stroma (H & E, × 40).
B. Cells are scant in the area (H & E, × 200).
C. The material is positive for Congo red staining (× 200).
D. The positivity is impaired by potassium permanganate (KMnO4) process (× 200).
E. Immunohistochemically, the material is diffusely positive for amyloid A (× 200). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3. Discussion

The amyloidoses are a group of rare diseases that result from the extracellular deposition of amyloid. Major systemic types of amyloidosis include immunoglobulin light chain amyloidosis (AL amyloidosis), wild-type transthyretin (ATTRwt) amyloidosis, and AA amyloidosis. Wechalekar et al.[1] demonstrated that the frequency of AL amyloidosis, ATTRwt amyloidosis, and AA amyloidosis was 68%, 9.8%, and 12%, respectively. Most cases of amyloidosis may be defined as AL amyloidosis.

AA amyloidosis is one of the main types of systemic amyloidosis. Organ damage results from the extracellular deposition of the soluble

acute-phase reactant serum amyloid A protein as insoluble amyloid fibrils.[2] The kidneys, liver, heart and gastrointestinal system are the organs most commonly involved in AA amyloidosis.[1] AA amyloidosis of the urinary tract is rare—in particular, AA amyloidosis of the ureter is very rare. Mantoo et al.[3] have reported localized AA-type amyloidosis of the ureter with spheroid amyloid, as far as we are aware. Some cases of ureteral amyloidosis have not been classified in detail by the type of AL amyloidosis such as ATTRwt amyloidosis or AA amyloidosis. The number of AA amyloidosis cases may actually be greater. With regard to a diagnosis of amyloidosis, amyloid deposits have to be characterized histochemically, based on positive staining with Congo red.[2] Immunohistochemistry is available for diagnosing the fibril type of amyloid in AL amyloidosis, ATTRwt amyloidosis, AA amyloidosis, etc.[1]

Okuda et al.[4] reported that the median age among 199 people with AA amyloidosis in Japan was 65 years (age range, 22–90 years) and the male:female ratio was approximately 1:3. The characteristics in our 64-year-old female patient are commonly found in patients with AA amyloidosis.

AA amyloidosis is a secondary amyloidosis. The underlying diseases in patients with AA amyloidosis are rheumatic arthritis (60.3%), uncharacterized inflammatory disease (11.1%), neoplasms (7.0%), other rheumatic diseases (6.5%), inflammatory bowel disease (4.5%), chronic infection (4.5%), Castleman's disease (4.0%), and autoinflammatory disease (2.0%), based on a nationwide survey conducted in Japan.[4] To date, the patient has not had an underlying disease; however, we will continue assessing the patient for the development of underlying diseases such as rheumatic disease, inflammatory disease or neoplasms.

Okuda et al.[4] summarized the clinical manifestations at diagnosis among their 199 patients with AA amyloidosis, which were renal failure (76.4%), proteinuria (51.3%), serious gastrointestinal symptoms (39.7%), intractable diarrhea (32.2%), cardiac failure (11.6%), hypothyroidism (11.6%), and atrial fibrillation (3.5%), etc. Our patient did not have renal failure or proteinuria, but she had hypertrophic cardiomyopathy and paroxysmal atrial fibrillation. Thus, comorbid cardiac amyloidosis was suspected. Cardiac biopsy was not performed, a definitive diagnosis of cardiac amyloidosis has not been determined.

In this patient, diagnosing AA amyloidosis of the ureter took approximately 7 years. Hydronephrosis was initially detected with ultrasound at another hospital and the patient was referred to our hospital. However, at her first visit to our hospital, hydronephrosis was not detected with computed tomography and retrograde pyelography. At the time, we speculated that the cause of hydronephrosis that had been detected with ultrasound at the other hospital was a ureter stone in the lower ureter and that the stone may have passed before the patient was referred to our hospital. Thus, we hesitated evaluating the cause of hydronephrosis via ureteroscopy with biopsy. Seven years later, we detected hydronephrosis with ultrasound, computed tomography, and retrograde pyelography. We performed ureteroscopy, examined the pathology of specimens, and diagnosed the cause of hydronephrosis as AA amyloidosis. If we had evaluated the cause of hydronephrosis via ureteroscopy with biopsy at the first visit, we may have reached a definitive diagnosis of AA amyloidosis of the ureter earlier. In amyloidosis of the ureter, a speculation is that the extracellular deposition of amyloid in the ureter results in hydronephrosis. The extracellular deposition of amyloid depends on the state of benign amyloidosis; for this reason, hydronephrosis appears or disappears. A malignant ureter tumor is a differential diagnosis of amyloidosis of the ureter. Performing ureteroscopy and examining the pathology of specimens are necessary to distinguish amyloidosis of the ureter from a malignant ureter tumor before performing nephroureterectomy.

The treatment of AA amyloidosis involves suppressing inflammation[1] such as anti-interleukin 6 receptor antibody (tocilizumab), tumor necrosis factor inhibitor (etanercept, infliximab, adalimumab or golimumab) or selective T cell costimulation modulator (abatacept)[4] or using a therapy targeted to an underlying disorder.[5] However, the treatment for AL amyloidosis is chemotherapy or autologous stem cell transplant, and the treatment for ATTR amyloidosis is liver transplantation, diflunisal therapy, or supportive therapy.[1] The treatment depends on the type of amyloidosis.[1] Therefore, urologists and clinicians should diagnose the type of amyloidosis via biopsy.

In conclusion, AA amyloidosis of the ureter is very rare. However, AA amyloidosis of the ureter occurs with hydronephrosis or macrohematuria. Ureter tumor is a differential diagnosis of AA amyloidosis of the ureter. Urologists should perform ureteroscopy and check the pathology to distinguish AA amyloidosis of the ureter from a ureter tumor.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

References

1. Wechalekar AD, Gilmore JD, Hawkins PN. Systemic amyloidosis. *Lancet*. 2016;387:2641–2654.
2. Brunger AF, Nienhuis HLA, Bijzet J, Hazenberg BPC. Cause of AA amyloidosis: a systematic review. *Amyloid*. 2020;27:1–12.
3. Mantoo S, Hwang JSG, Chiang GSC, Tan PH. A rare case of localised AA-type amyloidosis of the ureter with spheroids of amyloid. *Singap Med J*. 2012;53:77–79.
4. Okuda Y, Yamada T, Ueda M, Ando Y. First nationwide survey of 199 patients with amyloid A amyloidosis in Japan. *Intern Med*. 2018;57:3351–3355.
5. Papa Riccardo, Lachmann HJ. Secondary, AA, amyloidosis. *Rheum Dis Clin N Am*. 2018;44:585–603.