



# Ureteral amyloidosis in the context of lymphoplasmacytic lymphoma and systemic amyloidosis

María Rianza Montes<sup>\*</sup>, Beatriz Teresa Antón Eguia, Garazi Letamendi Madariaga, José Antonio Gallego Sánchez

Department of Urology, Galdakao-Usansolo Hospital, Labeaga Auzoa, 48960, Galdakao, Vizcaya, Spain

## ARTICLE INFO

### Keywords:

Amyloidosis  
Macroglobulinemia  
Ureter  
Treatment

## ABSTRACT

Ureteral amyloidosis is a rare entity and of interest to urologists, hematologists, radiologists, and pathologists because it mimics urothelial cell carcinoma clinically, endoscopically and radiologically. A pre-operative ureteroscopy or surgical biopsy is required, and it is essential to exclude systemic amyloidosis.

We report a male who was diagnosed with IIIA stage lymphoplasmacytic lymphoma associating systemic amyloidosis with concomitant hematuria. Urine cytology was negative and computerized tomography urography (CTU) scan evidenced bilateral, proximal and medium, ureteral stenosis and wall thickening. Diagnosis of suspected amyloidosis was confirmed with laparoscopic biopsy due to ureteral stenosis, being positive for Congo red stain. Patient underwent systemic chemotherapy.

## 1. Background

Amyloidosis is a heterogeneous group of disorders caused by extracellular deposition of amyloid substances. It can be systemic or localized when affecting specific organs.<sup>1–3</sup> Localized urinary tract amyloidosis is a rare pathological entity, especially of the ureter. It can be clinically and radiologically confused with a neoplasm, being very difficult to diagnose it preoperatively.<sup>1</sup> We present a case of ureteral amyloidosis in a patient with lymphoplasmacytic lymphoma and a review of the literature.

## 2. Case presentation

A 59-year-old male was referred to the Urology department for presenting monosymptomatic self-limited macroscopic hematuria. He had history of smoking and IgM monoclonal gammopathy of undetermined significance but no urologic disorders. Physical examination, blood test, urine culture and cytology were normal except for hematuria. Abdominal ultrasound was performed without relevant findings. On computerized tomography urography (CTU), bilateral urothelial wall thickening was presented on both proximal and medium ureters associating right hydronephrosis (Fig. 1).

MRI was performed, due to concomitant left foot pain, revealing a soft tissue density mass in the fourth metatarsal with irruption of the

cortical bone. Biopsy showed an infiltrate of IgM+ and CD20+ lymphoplasmacytes surrounding a Congo-red positive amorphous tissue, indicative of amyloidoma. Positron emission tomography/CT demonstrated evidence of supra- and infra-diaphragmatic adenopathies and pathological bone enhancements in both femurs, tibiae and fibulae with MRI of the lower extremities confirming that these bone lesions were similar to those seen in the left foot and therefore also consistent with amyloidomas.

Lymph node biopsy presented infiltration by clonal lymphoplasmacytes and bone marrow biopsy showed immunophenotype, karyotype, and molecular markers, such as MYD88 y CXCR4, free of tumor infiltration. Echocardiogram was normal, ruling out cardiac amyloidosis, as well as subcutaneous fat biopsy (Congo-red stain negative).

Given these findings, IIIA stage lymphoplasmacytic lymphoma with kappa systemic amyloidosis was diagnosed, including multiple bone amyloidomas and bilateral ureteral stricture under study. Treatment was started with 14 Gy radiation therapy in the left foot with slow but progressive improvement in pain and functional mobility.

In order to determine the cause of ureteral stricture, ureterorenoscopy was subsequently performed being impossible to progress above the fifth vertebral level due to critical stricture. Bilateral retrograde pyelography revealed bilateral obstruction from this level to ureteropelvic junction and right grade-3 hydronephrosis. Cytologies were normal and bilateral double J stents were placed.

<sup>\*</sup> Corresponding author.

E-mail addresses: [maria.riazamontes@osakidetza.eus](mailto:maria.riazamontes@osakidetza.eus), [hospital.galdakao-usansolo@osakidetza.eus](mailto:hospital.galdakao-usansolo@osakidetza.eus) (M. Rianza Montes).



**Fig. 1. Venous phase CTU scan.** Concentric and diffuse urothelial wall thickening which affects proximal and medium ureters with right retrograde hydronephrosis. Absence of filling defects and lithiasis in the whole urothelial tract.

Study was completed with MR urography which showed infiltrative and bilateral periureteral lesion, predominantly in right ureter, extended from renal pelvis to distal ureter. Given the bilateral obstructive uropathy and the suspected systemic amyloidosis, the patient underwent exploratory laparoscopy for tissue biopsy.

Histological examination and immunohistochemical (IHC) techniques showed fibrofatty tissue with positive Congo red amyloid deposits; some foreign multinuclear giant cells; monoclonal B lymphocytes (CD20 +); aberrant plasma cells (CD38<sup>+</sup>, CD138<sup>+</sup>) and lymphoplasmacytocytes MYD88<sup>+</sup> and negative CXCR4. Amyloid was positive for P component with a predominance of Kappa light chains (Fig. 2).

After confirming ureteral amyloidosis, his disease was restaged as IIIA lymphoplasmacytic lymphoma and kappa systemic amyloidosis with bone and medium and proximal bilateral ureteral involvement. Treatment was based on immunochemotherapy with VR-CAP-MYOCET (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) and patient was scheduled to bilateral ureteral stents periodic exchanges. At present, he has received 3 cycles with good tolerance and

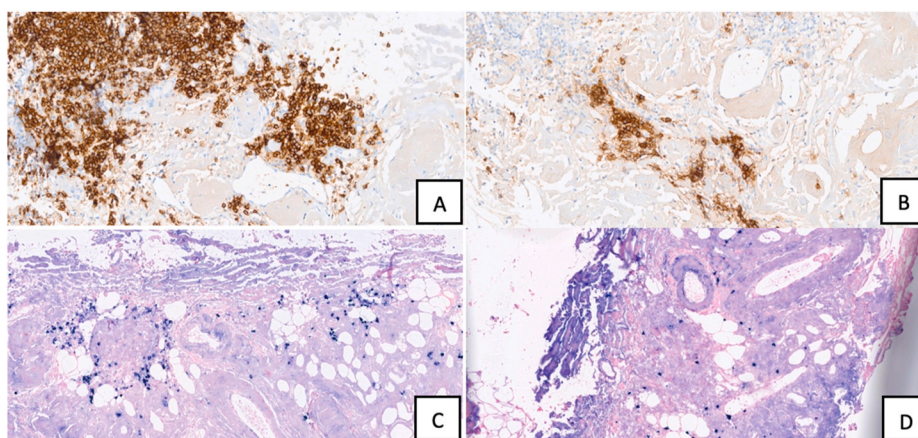
is currently waiting to complete another three and subsequently undergo autologous hematopoietic stem cell transplant.

### 3. Discussion and conclusion

Lymphoplasmacytic lymphoma is a malignant disorder of plasma cells in which B lymphocytes produce excessive amounts of M proteins causing IgM related symptoms (hyperviscosity, hemorrhage, thrombosis, headache, seizures, stupor, etc) or lymphoplasmacytic infiltration symptoms (recurrent infections, generalized adenopathies or B symptoms). 2–5% is associated with amyloidosis being classified as localized when involving one organ or systemic when involving multiple sites.<sup>1–3</sup> The therapeutic management and prognostic implications are different. Systemic amyloidosis is progressive and usually fatal, requiring systemic treatment. On the contrary, localized amyloidosis has good prognosis and can be managed with close observation or non-surgical treatments.

Localized amyloidosis of the urinary tract is a rare condition and usually involves the bladder and prostate. Less frequently it affects the ureter, urethra and renal pelvis. Its pathogenesis is unknown; however, abnormal protein metabolism and chronic urinary tract infections or repeated inflammation of the mucosa associated with hematologic immune-related disorders are the best pathogenetic theories.<sup>1,2,4</sup> The first case of ureteral amyloidosis was described by Lehmann in 1937.<sup>2</sup> Around 53 cases have been published, three of them from Spanish authors. Most of the literature is Japanese and Korean, meaning there might be a racial predisposition in the Far East. It mainly affects women and the age at diagnosis is between 50 and 70 years.<sup>2</sup> Clinically, it presents with loin pain and hematuria. Urine cytology is usually negative since most amyloid deposits are subepithelial and CTU scan findings are unspecific.<sup>1,3</sup> Ureteral stricture and wall thickening, mostly distal and unilateral, lead to retrograde hydronephrosis which can be confused with ureteral neoplasm. Some authors consider submucosal ureteral calcifications as a typical sign; however, they can also be present in tuberculosis and schistosomiasis.<sup>2</sup>

Diagnosis must include biopsy via an ureteroscope. Characteristically, the amyloid deposit shows apple-green birefringence under polarized light when stained with Congo red. Moreover, IHC is used to further classify the type of amyloidosis. It is essential to exclude systemic amyloidosis performing a subcutaneous fat or rectal biopsy. If confirmed, early treatment with systemic chemotherapy is important given the worst prognosis. Although localized disease has better clinical course, systemic dissemination must be avoided, therefore, surveillance imaging and routine follow-up are necessary. In some cases, dimethyl sulfoxide instillation through nephrostomy is an option. If obstructive uropathy with worsening kidney function is presented, early conservative surgery with ureterectomy is indicated.<sup>2,3</sup>



**Fig. 2. Microscopic findings of ureteral amyloidosis.** IHC showed CD20<sup>+</sup> equivalent to type B lymphocytic infiltrate and CD38<sup>+</sup> to plasma cells (A and B). In situ hybridization technique corresponding to kappa and lambda light chains showed a predominance of the former (C and D).

The case we report is an unusual one due to the diagnosis of a lymphoplasmacytic lymphoma as well as a systemic amyloidosis affecting infrequent sites such as bone, with multiple amyloidomas, and both ureters. Diagnosis was performed by laparoscopic ureteral biopsy due to stenosis and indicated treatment was systemic chemotherapy.

Ureteral amyloidosis is a rare entity, and its diagnosis is difficult and usually not suspected in these patients based only on clinical, endoscopic and radiologic findings.<sup>1</sup> Therefore, it is important to consider it in the differential diagnosis of patients with hematuria and ureteral thickening. Histological examination is a requirement for definitive diagnosis, and it is essential to exclude systemic amyloidosis for early therapeutic management with systemic chemotherapy. Localized disease has benign clinical course and relatively good prognosis.

### Ethics approval and consent to participate

All procedures were followed in accordance with the ethical standards of the Human Research Ethics Committees (“HREC”) and the Declaration of Helsinki of 1975.

### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

### Availability of data and materials

The references are shown below.

### Funding

The authors have no funding to disclose.

### Authors’ contributions

RM has made substantial contributions to the creation and design of the work. ABT and GJA have reviewed this report and have approved the

submitted version (and any substantially modified version that involves the author’s contribution to the study); and to have agreed both to be personally accountable for the author’s own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even the ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

### Declaration of competing interest

The authors have no conflicts of interest to disclose.

### Acknowledgements

The authors thank the patient for allowing them to publish the case report and the images taken. They would also like to extend their gratitude to the Departments of Urology, Radiology, Hematology and Pathological Anatomy.

### List of abbreviations

CTU	computerized tomography urography
Ig	immunoglobulin
MRI	magnetic resonance imaging
IHC	immunohistochemical
VR-CAP-MYOCET	bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone

### References

1. Zhou F, Lee P, Zhou M, Melamed J, Deng F-M. Primary localized amyloidosis of the urinary tract frequently mimics neoplasia: a clinicopathologic analysis of 11 cases. *Am J Clin Exp Urol.* 2014;2(1):71–75.
2. Ding X, Yan X, Ma X, et al. Localized amyloidosis of the ureter: a case report and literature review. *J Can Urol Assoc.* 2013;7(11–12).
3. Lu W, Wang Y, Zhang M, et al. Primary localized amyloidoma of the renal pelvis: a case report and literature review. *Oncol Lett.* 2016;11(2):1095–1100.
4. Kim SH, Park WS, Joung JY, Lee KH, Chung J, Seo HK. A surgically treated case of ureterovesical amyloidosis of the bladder in a patient with idiopathic thrombocytopenia. *Case Rep Urol.* 2018;2018:1–4.