Primary Localized Amyloidosis of the Ureter

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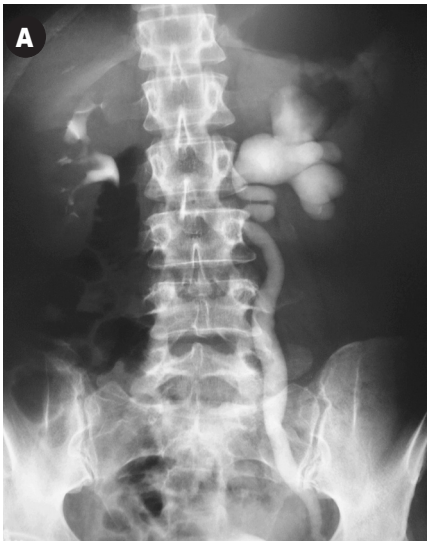
Amyloidosis is defined by the presence of insoluble protein deposits in tissues. It can be primary, when there is no underlying clinical condition; or secondary, due to a chronic inflammatory or neoplastic disorder, especially multiple myeloma. Amyloidosis is also classified as systemic (90–95%), or localized (6–9%) when affecting specific organs [1-3]. Localized amyloidosis is a rare condition and the bladder is the most commonly affected site. Clinically it appears as microscopic hematuria [4,5].

Few cases of ureteral amyloidosis have been described. We present here an additional case of primary amyloidosis of the ureter.

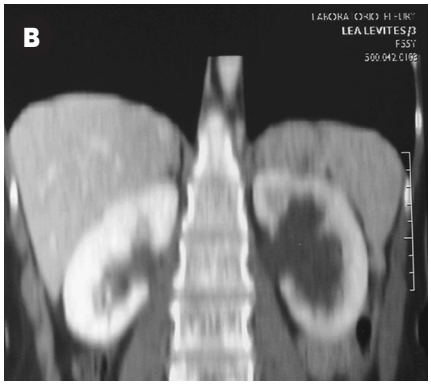
Patient Description

A 59 year old woman was admitted with a 3 month history of malaise, fatigue and increasing frequency of micturition, and episodes of urinary infection. Clinical examination was unremarkable. Blood cell count, blood biochemical investigation and urine culture were normal. Urinalysis demonstrated hematuria. Her previous history was positive for diabetes mellitus type 2 with good control of glycemia by means of insulin, and Hashimoto's thyroiditis with adequate levels of thyroid-stimulating hormone and free thyroxine using hormone replacement.

Renal ultrasound scanning and excretory urography demonstrated a left pelvicaliceal and ureteral dilatation reaching 2 cm from the ureterovesical junction [Figure A]. In addition, computed tomography revealed a dilatation of left renal calices and pelvis [Figure B]. No change in the urinary bladder was seen in the mictional urethrocystography. Surgical resection of the thick ureteral segment near junction with the bladder was performed, followed by end-to-end anastomosis. Histopathological analysis revealed an increase in thickness of the ureter wall. Congo-red staining was positive, and tumoral cells were not visible. Immunostaining for kappa and lambda light chains were positive, proving the lesion to be primary amyloidosis. Additional investigation excluded secondary causes such as serum protein immunoelectrophoresis. Serologies for human immunodeficiency virus, hepatitis B and C, cytomegalovirus, mononucleosis, syphilis, purified protein derivative tuberculosis skin test, autoantibodies (antinuclear antibody, anti-dsDNA, anti-Ro/SSA and anti-La/SSB), and serum cryoglobulins were negative. Investigation of systemic involvement of amyloidosis was also negative (patient's history, physical examination, heart echocardiography, 24 hour proteinuria, beta-2 microglobulin, serum amyloid A, upper endoscopy, thorax, abdominal and pelvis tomography).



Excretory urography showing dilatation of left renal calices, pelvis and ureter up to approximately 2 cm from ureterovesical junction



Computed tomography showing middle dilatation of left renal calices and pelvis

The patient is currently well, asymptomatic and a new abdominal and pelvis CT scan performed 5 years after her surgery did not show evidence of recurrent disease.

Comment

The first case of localized amyloidosis of the ureter was described by Lehmann in 1937 [4]. Since then fewer than 50 cases have been reported. Seventy-five percent of these cases were women aged 40–60, mostly from Japan, suggesting the importance of Asian ancestry in the incidence of the disease [4,5].

The primary form of disease is characterized by thick ureter walls due to deposition of light chains of immunoglobulin (type AL amyloidosis) [1], the distal third of ureter being the most common site

involved [4,5]. Bilateral lesions are an uncommon finding [4]. The pathogenesis is unknown, although there have been reports of monoclonal plasma cell infiltrate surrounding amyloid deposits, like a local immune cell dyscrasia. Association with chronic urinary infection has also been described, which would account for the persistent inflammation and local production of immunoglobulins [5].

Clinically, genitourinary amyloidosis usually manifests as symptoms of urinary obstruction. The patient described here complained of increased frequency of micturition, followed by malaise and fatigue, suggesting a urinary tract infection.

Radiological examinations like CT scan and excretory urography did not indicate a specific etiology, although they can detect ureteral narrowing and hydronephrosis [2]. Some authors consider the presence of submucosal calcifications in the ureter as a pathognomonic sign. However, these radiological findings can also be present in tuberculosis and schistosomiasis [5]. The correct diagnosis is confirmed by histopathological examination using Congo-red staining and the exclusion of other etiologies [3].

Nephro-ureterectomy is considered the optimal treatment, since the macroscopic aspect of the ureter may be indistinguishable from urothelial carcinoma. However, since localized amyloidosis is a benign condition, conservative surgical treatment is usually performed and allows renal preservation. A frozen section examination during the surgical procedure is advised [5].

Treatment with corticosteroids, with significant regression of ureter stenotic injury, has been reported [4]. However, well-designed therapeutic trials with a large number of patients with ureteral amyloidosis do not exist.

With this report we wish to alert physicians to the diagnostic possibility of localized amyloidosis in patients with persistent urinary irritative symptoms that do not respond to the usual therapies. Localized amyloidosis should be considered in women between age 40 and 70, particularly those of Japanese descent. In all likelihood, the extremely low incidence of localized disease could be explained, at least in part, by the fact that the diagnosis is often missed.

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