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Original contribution

IgG4-associated inflammatory pseudotumor of ureter: clinicopathologic and immunohistochemical study of 3 cases

Sun A. Kim MD[a], Sang-Ryung Lee MD[a], Jooryung Huh MD, PhD[a], Steven S. Shen MD, PhD[b], Jae Y. Ro MD, PhD[a,b,*]

[a]*Department of Pathology, Asan Medical Center, Seoul, 138-736 Korea*
[b]*The Methodist Hospital and Weill Medical College of Cornell University, Houston, TX 77030, USA*

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Summary Inflammatory pseudotumors are lesions characterized by proliferation of fibroblasts/myofibroblasts with variable chronic inflammatory cell infiltration. Recent studies have suggested that inflammatory pseudotumor with abundant IgG4-positive plasma cells may be a unique entity associated with systemic IgG4-related sclerosing disease and should be distinguished from other similar lesions such as inflammatory myofibroblastic tumor and fibrohistiocytic-type inflammatory pseudotumor. Localized inflammatory pseudotumor has been rarely reported in the ureter, and IgG4-associated inflammatory pseudotumor of ureter has not been described. We describe herein 3 cases of ureteral inflammatory pseudotumor of IgG4-associated lymphoplasmacytic type, focusing on density of IgG4-positive plasma cells; infiltration pattern of eosinophils and histiocytes; presence of obliterative phlebitis; and immunohistochemical profiles of smooth muscle actin, anaplastic lymphoma kinase, and CD68. Three patients, 45- and 47-year-old men and 84-year-old woman, all presented with flank pain and ureteral narrowing by a mass effect. Microscopic examination of the resected ureters showed suburothelial masslike lesions with fibroblasts/myofibroblasts without atypia, abundant plasma cells, and scattered eosinophils and histiocytes. The lesion of the 47-year-old man showed obliterative phlebitis in addition to the above findings. The lesion of the 84-year-old woman was accompanied by urothelial carcinoma in situ in the overlying urothelium. Spindle cells were diffusely or focally positive for smooth muscle actin but negative for anaplastic lymphoma kinase in all 3 cases. For each case, respectively, an average of 154, 112, and 50 plasma cells per high-power fields were immunoreactive for IgG4, a diagnostic feature of IgG4 inflammatory pseudotumor. We described 3 cases of IgG4-associated inflammatory pseudotumor of ureter with pathologic and immunohistochemical features that are compatible for lymphoplasmacytic type of inflammatory pseudotumor. Further study is needed to characterize any relationship between this entity and systemic sclerosing disease and/or urothelial carcinogenesis.

1. Introduction

Inflammatory pseudotumor (IPT) is a generic term for a wide range of lesions sharing similar histologic features. It is characterized by the proliferation of fibroblasts or myofibroblasts in a background of myxoid to collagenous stroma

* Corresponding author. The Methodist Hospital and the Weill Medical College of Cornell University, Houston, TX 77030, USA.
E-mail address: jaero@tmhs.org (J. Y. Ro).

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and variable chronic inflammatory infiltrate [1,2]. IPT has been described under a variety of names such as fibroxanthoma, inflammatory myofibroblastic tumor (IMT), inflammatory myofibrohistiocytic proliferation, pseudosarcomatous fibromyxoid tumor, visceral form of nodular fasciitis, or plasma cell granuloma [1-8]. It appears that IPT is a heterogeneous disease that can occur throughout the body. Recently, a number of recent studies have shown that IPT with abundant IgG4-positive plasma cells may be a unique disease distinct from other lesions in the IPT category, and instead, it may belong to systemic IgG4-related sclerosing disease, which is characterized by a plasma cell–rich histologic pattern, abundant IgG4-positive plasma cells, and high serum IgG4 levels [8-12].

IPT was originally described in the lung, and subsequently, it has been reported in various other locations including urinary tract [3-7]. IPT in the ureter is extremely rare, and only 8 cases have been described. We herein describe 3 additional cases of IPT of ureter, which showed abundant IgG4-positive plasma cells. We focus on the histologic and immunohistochemical features that are known to be helpful in differentiating IgG4-related IPT from other types of IPTs [8]. This present study is not only a report of additional IPTs in this rare site but also is the first description of IgG4-associated IPTs of the ureter.

2. Materials and methods

We identified 3 cases of IPT originating from the ureter at 2 institutes from January 2002 to May 2009. Clinical information was obtained from the review of patients' medical records. Gross specimens and hematoxylin and eosin–stained slides were examined. The inflammatory infiltrate were divided into 3 patterns, that are, nodular, scattered, or mixed. Immunohistochemical studies were performed for IgG4 (1:2000; Dako, Glostrup, Denmark), anaplastic lymphoma kinase (ALK; 1:50, Dako), smooth muscle actin (SMA, 1:200; Dako), and CD68 (1:2000; Dako) for all 3 cases. We estimated the average number of IgG4-positive plasma cells per high-power field (HPF; ×10 eyepiece and ×40 objective lens) by counting 10 HPFs in areas with marked inflammation within the tumor. SMA immunoreactivity of spindle cells was classified as negative, focally positive (less than 50% cells staining), and diffusely positive (50% or more cells staining). ALK immunoreactivity was estimated as presence or absence. The morphology of the histiocytes was evaluated by both hematoxylin and eosin staining and CD68 immunostaining.

3. Results

3.1. Clinical findings

There were 2 male (cases 1 and 2) and 1 female (case 3) patients. The 2 male patients were 45 and 47 years old, and the female patient was 84 years old. All 3 patients presented with flank pain. Patient 1 presented with left flank pain of several years duration with recent exacerbation. Patient 2 presented with left flank pain for 1 month. Patient 3 presented with right flank pain as well as intermittent hematuria and a palpable right lower abdominal mass. None of the patients had other significant medical problems or any history of urinary tract instrumentation. Laboratory tests were unremarkable in all patients, and serum IgG level was either not checked (cases 1 and 3) or normal (case 2, serum IgG was 855.0 mg/dL; reference range, 700.0-1600.0 mg/dL). Serum IgG4 measurement was not performed in any of the cases. Urine cytology revealed no malignant cells in cases 1 and 2. In case 3, urine cytology demonstrated urothelial carcinoma, but cystoscopic examination of urinary bladder was negative.

In case 1, abdominopelvic computed tomography (APCT) revealed a well-defined mass with homogenous enhancement in the left midureter, accompanied by dilatation of the proximal ureter and renal pelvis. On retrograde pyelogram, a mass shadow in the midureter delayed the excretion of contrast and resulted in partial obstruction (Fig. 1). In case 2, a 3.0-cm infiltrative mass was identified at the level of the left distal ureter on APCT. Retrograde pyelogram showed segmental narrowing of the left distal ureter with contrast passage disturbance, suggestive of extrinsic compression. In case 3, APCT scan demonstrated hydronephrosis of the right kidney, questionable right proximal ureteral narrowing with a mass effect, and a 2-cm adrenal cystic mass.

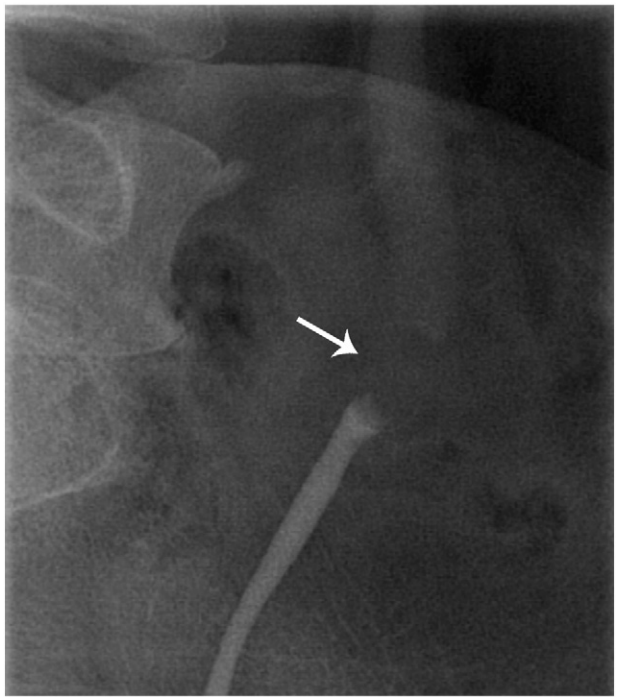

Fig. 1 Retrograde pyelogram shows a filling defect in the left midureter (arrow) in case 1.