Case Report

Immunoglobulin G4-Related Systemic Sclerosing Disease: A Case Involving the Ureter and Kidney

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Immunoglobulin (Ig) G4-related sclerosing disease is a newly defined clinicopathological entity characterized by lymphoplasmacytic infiltration of IgG4-positive plasma cells and varying degrees of fibrosis within affected tissues. Patients usually exhibit multisystem involvement and often respond well to steroid and immunosuppressive therapy. This report presents a case of IgG4-related sclerosing disease involving the ureter and kidney. We hope to bring IgG4-related sclerosing disease to the attention of urologists, because it is an uncommon disease that commonly responds to systemic corticosteroids.

Keywords: Immunoglobulin G; Sclerosis; Ureter

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Article History:

received 18 June, 2011

accepted 11 October, 2011

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INTRODUCTION

Immunoglobulin (Ig) G4-related sclerosing disease is an immunoglobulin deposition disease characterized by infiltration of organs by IgG4-positive plasma cells. Manifestations include retroperitoneal fibrosis, dacryoadenitis, sialadenitis, thyroiditis, pneumonitis, pancreatitis, sclerosing cholangitis, tubulointestinal nephritis, prostatitis, and hypophysitis [1,2].

Most patients exhibit multisystem involvement and often respond well to steroid therapy. Regardless of organ involvement, biopsy with review of histopathology and immunohistochemical staining for IgG4 are essential for diagnosis [3,4]. Herein we describe a case of IgG4-related sclerosing disease that involved the left pelvocaliceal system and extended to the level of the left ureter, thereby causing left hydronephrosis.

CASE REPORT

A 70-year-old man was transferred to Kyung Hee University Hospital at Gangdong for further evaluation of left hydronephrosis. He had recently visited a private clinic because of dyspepsia, and abdominal ultrasonography had shown left hydronephrosis. The physical examination re-

vealed no tenderness of the abdomen and no costovertebral angle tenderness.

His laboratory data showed a white blood cell count of $4.4 \times 10^3/\text{mm}^3$, hemoglobin of 14.3 g/dL, a platelet count of 164K, a serum creatinine level of 1.1 mg/dL, and an erythrocyte sedimentation rate of 6 mm/h. The results of a liver function test and electrolyte values were within the normal range. Urine analysis showed a white blood cell count of 0-1 and a red blood cell count of 0-1. The results of a urine gram stain were negative. His C-reactive protein concentration was 0.04 mg/dL. An abdominal computed tomographic (CT) scan revealed an enhanced soft tissue mass infiltrating the left renal pelvis of the left kidney and extending to the level of the left mid ureter, causing left hydronephrosis (Fig. 1A). A chest CT scan revealed a small, well-defined nodule in the left lower lobe, an enlarged right hilar lymph node, enlarged interlobar lymph nodes, and an enlarged left paraesophageal lymph node (Fig. 1B).

For pathological confirmation, laparoscopic biopsy of the periureteral lesion was performed by the same method as conventional laparoscopic partial nephrectomy [5]. There were adhesions between the hard mass lesions and the left ureter around the ureteropelvic junction. Several frozen biopsies of the periureteral mass were performed. No malignant cells were found, but heavy lymphoid cell infiltration

FIG. 1. (A) Infiltrating soft tissue mass involving left pelvocalyceal system and extending to the level of left mid ureter, causing left hydronephrosis (arrow). (B) A small well-defined nodule in left lower lobe, enlarged left paraesophageal lymph node (arrows).

FIG. 2. (A) Periureteral mass biopsy. Hematoxylin and eosin stain shows fibrosis with lymphoplasmacytic aggregation ($\times 400$). (B) Periureteral mass biopsy. Immunoglobulin (Ig) G immunohistochemical staining shows more than 50 IgG4-positive cell/high-powered field ($\times 400$).

was seen. The histological examination was negative for malignancy but showed soft tissue mixed lymphocytic infiltration with germinal centers (Fig. 2A). IgG4 immunostaining revealed numerous cells positive for IgG and more than 50 IgG4-positive cells per high-powered field (Fig. 2B). The patient's serum IgG level was increased to 1,839 mg/dL (normal range, 870 to 1,700 mg/dL). His serum IgG4 level was 0.420 g/L (normal range, 0.061 to 0.214 g/L). A diagnosis of IgG4-sclerosing disease was made. The patient was initially treated with 40 mg of oral prednisolone daily for 2 weeks with a subsequent decrease in the dosage by 5 mg every 2 weeks. He was maintained on steroid therapy for 3 months, and the follow-up ultrasonography showed minimal hydronephrosis. We plan to keep treating the patient with prednisolone therapy and to perform regular follow-up abdominal CT scans.

DISCUSSION

Lately, IgG4-related sclerosing disease has been proposed to describe the group of autoimmune disorders involving connective tissue. Prominent infiltration of IgG4-positive plasma cells in affected tissues is a characteristic feature of this disease. An increasing number of sclerosing diseases are recognized as part of the disease spectrum, such as autoimmune pancreatitis, sclerosing cholangitis, chronic cholecystitis, chronic sclerosing sialadenitis, retroperitoneal fibrosis, tubulointestinal nephritis, interstitial pneumonia, and lymphocystic hypophysitis.

In our case, fibrotic tissues around the left kidney and ureter resulted in hydronephrosis. A chest CT scan showed the left paraesophageal, right hilar, and both interlobar lymph nodes to be enlarged and the presence of a small nod-

ule in the left lower lobe. The abdominal CT showed an infiltrating soft tissue mass involving the left pelvocaliceal system and extending to the left midureter. The soft tissue mass was well enhanced on the CT. Our presumptive diagnosis was lymphoma. For definitive diagnosis, laparoscopic biopsy of the mass was performed. Immunohistochemical staining of the specimen showed more than 50 IgG4-positive cells per high-powered field.

IgG4-related systemic disease is a diagnostic challenge. Serum IgG and IgG4 levels are variable in patients with the disease. Imaging findings in IgG4-related systemic disease are not specific for the disease either. Histopathology and immunohistochemical staining for IgG4 are the most valuable diagnostic tools in IgG4-related systemic disease [6].

The standard treatment of IgG4-related sclerosing disease is systemic corticosteroids. The routine dosage is 40 to 60 mg/d with stepwise tapering. Immunosuppressive agents can be used in the case of corticosteroid-refractory disease. However, no standardized regimens for these agents exist. Thus, further randomized trials are needed. In our case, although hydronephrosis was present, the patient had no signs of renal functional impairment. If severe hydronephrosis and renal functional impairment are present, ureteral stent indwelling is needed [7].

In periureteral IgG4-related systemic sclerosing disease, differential diagnosis with other renal disease is essential. Biopsy should be regarded as a diagnostic option for diseases such as retroperitoneal fibrosis, retroperitoneal sarcoma, lymphoma, and retroperitoneal hematoma, which are difficult to differentiate with CT scans. Also, the relationship between IgG, IgG4, and perirenal masses

must be kept in mind. Urologists should be aware of the possibility of IgG4-related disease in the differential diagnosis of a periureteral mass.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

REFERENCES

1. Neild GH, Rodriguez-Justo M, Wall C, Connolly JO. Hyper-IgG4 disease: report and characterisation of a new disease. *BMC Med* 2006;4:23.
2. Chari ST. Diagnosis of autoimmune pancreatitis using its five cardinal features: introducing the Mayo Clinic's HISORt criteria. *J Gastroenterol* 2007;42 Suppl 18:39-41.
3. Lin YJ, Chen PC, Chen HA, Li CF. IgG4-related retroperitoneal fibrosis: the first reported case in a Chinese population. *Int J Rheum Dis* 2010;13:e70-3.
4. Minato N, Takayama H, Mukai M, Miyagawa Y, Tsujihata M, Nonomura N, et al. A case report of retroperitoneal fibrosis associated with IgG4-related sclerosing disease. *Hinyokika Kiyo* 2010;56:371-5.
5. Kim KY, Kim DK, Woo SH, Kim ET, Lee SB. Laparoscopic partial nephrectomy: an useful method of decision making for determining the approach and surgical method based on the systematic classification of tumor location. *Korean J Urol* 2008;49:1067-73.
6. Stone JR. Aortitis, periaortitis, and retroperitoneal fibrosis, as manifestations of IgG4-related systemic disease. *Curr Opin Rheumatol* 2011;23:88-94.
7. Van Moerkercke W, Verhamme M, Meeus G, Oyen R, Steenbergen WV. A case of IgG4-related sclerosing disease with retroperitoneal fibrosis, autoimmune pancreatitis and bilateral focal nephritis. *Pancreas* 2009;38:825-32.