IgG4-related Disease: A Mass Lesion in the Intrarenal Sinus near the Renal Pelvis

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Abstract

A 52-year-old Japanese woman was admitted to our hospital with a mass lesion in the renal pelvis detected on a health screening examination. The surgical specimen contained a mass exhibiting the histological features of immunoglobulin (Ig)G4-related disease, including lymphoplasmacytic infiltration and sclerosis with numerous IgG4-producing plasma cells. Postoperatively, an elevation of the serum IgG4 level was confirmed at 403 mg/dL; however, there was no evidence of tubulointerstitial nephritis or glomerulopathy, including membranous nephropathy, and the urothelium of the renal pelvis was intact without inflammation. We herein report this case in which IgG4-related disease of the renal pelvic region presented with a mass lesion in the intrarenal sinus near the renal pelvis, not ‘pyelitis’ (as described by Stone).

Key words: IgG4-related disease, IgG4-related kidney disease, IgG4-related pyelitis, mass lesion in the intrarenal sinus


Introduction

Immunoglobulin (Ig)G4-related disease is a systemic multi-organ disease characterized by elevation of the serum IgG4 level and the infiltration of various tissues by IgG4-producing plasma cells (1, 2). Kawano et al. reported that IgG4-related kidney disease has the following features: (1) kidney damage, (2) characteristic findings on computed tomography (CT), (3) a serum IgG4 level of ≥135 mg/dL and (4) renal histology showing (a) dense lymphoplasmacytic infiltration with IgG4-positive plasma cells and (b) characteristic ‘storiform’ fibrosis surrounding nests of lymphocytes and/or plasma cells (3). IgG4-related kidney disease includes tubulointerstitial nephritis (TIN) and membranous nephropathy secondary to IgG4-related disease, as well as renal pelvic lesions (3-5). Stone et al. proposed that involvement of the renal pelvis should be termed IgG4-related renal pyelitis (2), although there has been only one report of the pathology of IgG4-related pelvic lesions (6). We encountered a 52-year-old Japanese woman with a mass lesion in the renal pelvis. Surgical resection revealed that the mass had the histological features of IgG4-related disease, although there was no evidence of TIN or glomerulopathy affecting the renal parenchyma, and the renal pelvic urothelium was intact without inflammation. We herein report this case in which IgG4-related disease of the renal pelvic region did not cause pyelitis, but rather produced a mass lesion in the intrarenal sinus near the renal pelvis.

Case Report

In May 2011, a 52-year-old Japanese woman was admitted to our hospital for an evaluation of a mass lesion in the renal pelvis detected on a health screening examination. The patient had no relevant past medical history. On a physical...
examination, her temperature was 36.4°C and her blood pressure was 104/61 mmHg. Laboratory tests revealed a serum albumin level of 4.1 g/dL, total protein level of 7.9 g/dL, urea nitrogen level of 13 mg/dL, serum creatinine level of 0.5 mg/dL and C-reactive protein level of 0.0 mg/dL. The soluble interleukin-2 receptor (sIL-2R) concentration was 240 U/mL (normal range: 145 to 519). The level of urinary soluble interleukin-2 receptor (sIL-2R) concentration was markedly elevated at 70-80%. Periodic acid methenamine silver (PAM) staining demonstrated a “bird’s eye” swirling pattern of irregular fibers surrounding nests of inflammatory cells, known as storiform fibrosis (Fig. 3d). These findings suggested a diagnosis of IgG4-related disease in the intrarenal sinus near the renal pelvis.

**Diagnosis**

Based on the surgical findings, the following investigations were performed. Blood tests of the serum levels showed an IgG level of 1,732 mg/dL and IgG4 level of 403 mg/dL (normal <105 mg/dL), whereas the IgA level was 217 mg/dL and the IgM level was 163 mg/dL. Antinuclear antibodies and anti-Ro antibodies (SS-A) were negative. In addition, the serum C3 level was 98 mg/dL (normal >18 mg/dL), the C4 level was 39 mg/dL (normal >18 mg/dL) and the CH50 level was 53 U/mL (normal: >30 U/mL). Scintigraphy with 18F-FDG demonstrated uptake by the salivary glands, particularly in the right parotid gland and left submandibular gland. Moreover, magnetic resonance imaging (MRI) confirmed enlargement of the salivary glands, and salivary gland scintigraphy with 99mTcO4 demonstrated decreased secretion of saliva. No lesions were observed in the retroperitoneum, pancreas, biliary tract, lacrimal glands or lungs. Based on these findings, the patient was diagnosed with IgG4-related disease with multi-organ involvement.

**Clinical course**

Postoperatively, no immunosuppressive therapy, including steroids, was administered because the salivary gland swelling and other findings remained stable, although the serum

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**Figure 1.** Computed tomography (CT) reveals a mass (2.4×1.8×1.8 cm) with poor contrast enhancement occupying the renal sinus adjacent to the renal pelvis. There are no irregularities in the pelvic lumen.

**Figure 2.** Light microscopy reveals that the mass (large arrows) consists of numerous lymphoplasmacytic cells and many lymphoid follicles with germinal centers. The surrounding tissues, including the renal pelvis (small arrows) and renal parenchyma (*), are intact without the infiltration of inflammatory cells (×50).

Laparoscopic nephrectomy

In June 2011, laparoscopic left nephrectomy was performed. The surgical specimen contained a whitish mass with a smooth surface that occupied the renal sinus. Histologically, the mass featured numerous lymphoplasmacytic cells, including many lymphoid follicles with germinal centers. The surrounding tissues, such as the urothelium of the renal pelvis and the renal parenchyma, were intact, without infiltration by inflammatory cells (Fig. 2, 3a, b). Immunohistochemistry showed many of the inflammatory cells around the lymphoid follicles to be IgG-positive plasma cells (Fig. 3c), and the IgG4-positive/IgG-positive plasma cell ratio was markedly elevated at 70-80%. Scintigraphy with 67Ga-citrate showed uptake by the salivary glands, particularly in the right parotid gland and left submandibular gland. Moreover, magnetic resonance imaging (MRI) confirmed enlargement of the salivary glands, and salivary gland scintigraphy with 99mTcO4 demonstrated decreased secretion of saliva. No lesions were observed in the retroperitoneum, pancreas, biliary tract, lacrimal glands or lungs. Based on these findings, the patient was diagnosed with IgG4-related disease with multi-organ involvement.

**Clinical course**

Postoperatively, no immunosuppressive therapy, including steroids, was administered because the salivary gland swelling and other findings remained stable, although the serum
positive plasma cells were also positive for IgG4, and the infiltration of lymphocytic cells (Hematoxylin and Eosin staining). The mass consists of numerous lymphohistocytic cells, including many lymphoid follicles with germinal centers (arrows), c: Immunohistochemistry of the inflammatory cells around the lymphoid follicles shows IgG-positive plasma cells, with 70% to 80% of these cells also being positive for IgG4 (brown) (×200). d: Periodic acid methenamine silver (PAM) staining of the mass demonstrates a ‘bird’s eye’ appearance created by irregular fibers surrounding nests of inflammatory cells with pathognomonic swirling and storiform fibrosis (×400).

IgG4 remained persistently in the range of 300 to 400 mg/dL.

**Discussion**

Kawano et al. proposed three characteristic radiologic features of IgG4-related kidney disease: (1) multiple low-density areas on contrast CT, (2) diffuse bilateral enlargement of the kidneys in patients with a decreased renal function in whom the administration of contrast medium is inadvisable and (3) diffuse thickening of the renal pelvic walls with a smooth luminal surface. These findings are often detected incidentally during evaluations of patients with IgG4-related disease (3-5). Kuroda et al. reported the case of a 49-year-old Japanese woman with IgG4-related disease arising in the renal pelvis (6). In that case, left hydronephrosis and marked thickening of the left renal pelvic wall were detected on CT, and, histologically, there was prominent infiltration of lymphocytes beneath the urothelium of the renal pelvis. In addition, many lymphoid follicles were evident, with prominent sclerotic fibrosis and numerous plasma cells in the interfollicular areas. More than 50% of the IgG-positive plasma cells were also positive for IgG4, and the serum IgG4 level was elevated postoperatively. Furthermore, examinations identified swelling of the major and minor salivary glands and lacrimal glands. Therefore, chronic sclerosing pyelitis was diagnosed, although no inflammation was detected in the urothelium of the renal pelvis, and the authors suggested that the renal pelvis may have been involved in the IgG4-related disease.

Saeki et al. reported that, in their study, histological examinations identified swelling of the major and minor salivary glands and lacrimal glands. Therefore, chronic sclerosing pyelitis was diagnosed, although no inflammation was detected in the urothelium of the renal pelvis, and the authors suggested that the renal pelvis may have been involved in the IgG4-related disease.

In conclusion, previous reports regarding the involvement of the renal pelvis in IgG4-related disease have mentioned pyelitis that is characterized by diffuse thickening of the renal pelvic wall on radiological examinations. However, the current patient did not have pyelitis, and the involvement in the renal pelvic region was characterized by the formation of a mass lesion near the renal pelvic wall and in the intra-
renal sinus associated with lymphoplasmacytic infiltrates and sclerosis, while the surrounding tissues, such as the renal pelvic urothelium and renal parenchyma, were intact, without inflammatory cell infiltration. This case suggests that IgG4-related kidney disease and IgG4-related disease involving the renal pelvic region are independent conditions. While surgical therapy is often selected as a therapeutic option for mass lesions located in the pelvic region, the present case indicates that immunosuppressive therapy, such as steroids, may become a therapeutic option in cases involving pelvic mass lesions accompanied by elevation of the serum IgG4 level and/or systemic multi-organ disease.

The authors state that they have no Conflict of Interest (COI).

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References