Immunoglobulin G4-related sclerosing disease presenting as a rare cause of renal pelvic mass mimicking malignancy

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Immunoglobulin G4-related sclerosing disease is a recently recognized disease entity most commonly associated with autoimmune pancreatitis. This condition can also manifest as extra-pancreatic disease involving the bile ducts, kidney, lung, and retroperitoneum. The disease entity consists of elevated serum IgG4 levels, extensive IgG4-positive plasma cells, and lymphocyte infiltration of the affected organs. We describe the clinical and radiographic presentation and pathologic findings in a patient with isolated renal involvement in IgG4-related sclerosing disease.

Case report
A 71-year-old Caucasian male with a history of gout and type 2 diabetes mellitus presented with proteinuria, eosinophilia, and lymphocytopenia. He denied any weight loss and anorexia. CT of the abdomen demonstrated a heterogeneous, low-attenuating, right renal pelvis soft-tissue mass with indistinct borders and no significant enhancement (Fig. 1). Malignancy such as lymphoma or invasive transitional-cell carcinoma was suspected. The patient underwent ureteroscopy with biopsies of the right kidney and proximal right ureter. Both revealed benign urothelial mucosa with subacute eosinophilic inflammation. Both were negative for malignant cells.

A CT-guided biopsy was then performed, with multiple 18-gauge core biopsy specimens obtained, which demonstrated acute and chronic inflammatory cells, reactive lymphoid follicles, plasma cells, eosinophils, and scattered multinucleated giant cells compatible with an inflammatory process. Flow cytometry was negative for lymphoma. Bone marrow biopsy revealed a mild increase in eosinophils. Follow-up CT 5 months later showed no significant change in appearance.

The patient clinically began to deteriorate, with weight loss and hypoalbuminemia, and underwent a right nephrectomy two months later. The surgical pathology from the right nephrectomy demonstrated a fibroinflammatory process with acute and chronic inflammatory infiltrate, lymphoid aggregates, plasma cells, macrophages, and rare multinucleated giant cells (Figs. 2-3). There was a mixture of kappa- and lambda-positive plasma cells. CD3, CD4, and CD20 highlighted B and T lymphocytes (Fig. 4). Findings were consistent with IgG4-related sclerosing disease as well as stage II membranous nephropathy and tubulointerstitial nephritis.

Discussion
IgG4-related sclerosing disease is a systemic condition causing elevation of serum IgG4 concentration and abundant IgG4-positive plasma-cell infiltration. It can affect a number of different organ systems and most commonly manifests as autoimmune pancreatitis. However, involvement has been reported in many other organ systems, including the biliary system (sclerosing cholangitis), kidneys (tubulointerstitial nephritis), retroperitoneum (retroperitoneal fibrosis), salivary glands (sclerosing sialadenitis), thyroid, lung (inflammatory pseudotumors), mediastinum,
mesentery (sclerosing mesenteritis), and breast and prostate gland (prostatitis) (1). There are many common features in patients with IgG4-related sclerosing disease, including predominance in middle-aged to elderly men, hypergammaglobulinemia, negativity for anti SS-A and anti SS-B antibodies, hypocomplementemia, eosinophilia, elevated serum IgG4 level, and abundant infiltration of affected organs by IgG4-positive plasma cells. There is often marked improvement after corticosteroid therapy (2).

Renal involvement has been described in approximately one-third of patients with autoimmune pancreatitis with four patterns of involvement: round or wedge-shaped cortical nodules, multiple and bilateral peripheral cortical lesions, masslike lesions, and renal pelvic involvement (3). Renal parenchymal lesions are mostly bilateral and multiple, predominantly involving the renal cortex, and are composed of lymphoplasmacytic infiltrate. Round or wedge-shaped nodules usually suggest a differential diagnosis including pyelonephritis, lymphoma, infarct, or metastases (4). As seen in this case, this entity can present as a solitary mass mimicking a neoplasm. Other presentations that have been described include a diffuse soft-tissue rim surrounding the kidney, diffuse wall-thickening of the renal pelvis, or irregular nodules in the bilateral renal sinuses. On CT, renal lesions typically are hypoattenuating on early-phase contrast-material-enhanced images, with mild enhancement on delayed-phase images. Thus, distinguishing renal lesions from lymphoma based on imaging findings alone is impossible. Renal lesions can progress to cortical scarring (5).

Gross pathologic evaluation revealed extensive infiltrative involvement of the kidney extending into the adjacent perinephric tissue and involving the peripelvic and periureteral soft tissues. As is characteristic of IgG4-related sclerosing disease, histologic evaluation revealed that the infiltrate consisted of plasma cells, lymphocytes, and eosinophils. An
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Figure 3. 71-year-old male with IgG4-related sclerosing disease. (A) Low-power H&E stain shows diffuse infiltration of the renal interstitium by eosinophils, plasma cells, and lymphocytes. (B) High-power H&E stain shows eosinophils, lymphocytes, and plasma cells. (C) H&E stain of perinephric adipose tissue shows the same infiltrate of eosinophils, plasma cells, and lymphocytes.

Figure 4. 71-year-old male with IgG4-related sclerosing disease. Immunochemical stains show plasma cells with (A) IgG kappa (B) IgG lambda, and (C) an excess number of IgG4-positive stains compatible with IgG4-related sclerosing disease.
excess of plasma cells were IgG-positive, with a mixture of both kappa- and lambda-positive plasma cells compatible with a polyclonal process. This suggested an inflammatory process rather than a monoclonal infiltrate typical of a neoplastic process. The most common findings are tubulointerstitial nephritis with IgG4+ plasma-cell-rich inflammatory infiltrate. In most cases, the glomeruli are usually spared; however, this patient had thickening of the glomerular basement membrane and findings consistent with stage II membranous nephropathy. Tubulointerstitial nephritis has a high degree of steroid sensitivity, whereas steroid treatment with membranous nephropathy is variable (6).

The radiographic findings are variable, making this diagnosis difficult with imaging alone, and pathologic correlation may be necessary. However, heightened awareness of this disease entity and its clinical and radiographic presentations may alert one to consider the diagnosis. Laboratory and histologic evaluation may help support the diagnosis once it is entertained. Since this condition is often highly responsive to corticosteroid therapy, accurate diagnosis and treatment may have a positive impact on the clinical course and prevent unnecessary surgery. The pathogenesis and etiology are yet unknown, and further research remains necessary.

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