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신우 종괴 형성과 췌장 침범을 동반한 IgG4 연관 경화성 질환 1예

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A Case of IgG4-Related Pancreas and Kidney Disease Mimicking a Renal Pelvic Malignancy

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IgG4-related sclerosing disease is a disease entity that has recently attracted attention, manifesting as a multiorgan disease characterized by high serum IgG4 levels, extensive IgG4-positive plasma cells and lymphocyte infiltration of the affected organs, with the pancreas (autoimmune pancreatitis) and kidney as representative targets. In cases of renal involvement, parenchymal lesions are predominant, such as renal cortical lesions or diffuse renal enlargement. However, mass-like lesions involving the renal pelvis are very rare, and mass forming or pelvic involvement types should be distinguished from lymphomas, metastatic cancers and other genitourinary malignancies to avoid unnecessary surgery. Herein, we report a case of IgG4-related sclerosing disease involving the kidney as an unusual involvement pattern presenting as a mass-like lesion with pelvic and perirenal involvement. (Korean J Med 2014;87:710-715)

Keywords: IgG4-related kidney disease; Autoimmune pancreatitis; Renal pelvic mass

INTRODUCTION

IgG4-related sclerosing disease is a systemic condition characterized by elevated serum IgG levels, extensive IgG4-positive plasma cells and T-lymphocyte infiltration of various organs. The affected organs include the pancreas, biliary duct, lacrimal or salivary glands, retroperitoneum, central nervous system, thyroid gland, lung, liver, gastrointestinal tract, kidneys, prostate gland and lymph nodes [1]. Renal involvement has been described in approximately one-third of the reported cases [2,3] and presents with various radiological patterns. Usually, round or wedge-shaped cortical nodules, multiple and bilateral peripheral cortical lesions and diffuse renal enlargement patterns are reported; however, mass-like lesions or renal pelvic involvement

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patterns are relatively rare [3,4]. Differentiating IgG4-related sclerosing disease involving the kidney as a mass-like lesion from renal malignancies is difficult; therefore, many cases are diagnosed after surgical removal of the renal masses [5,6].

Herein, we report a case of IgG4-related sclerosing disease appearing as an autoimmune pancreatitis and bilateral renal pelvic masses. This is the first reported domestic case of unusual renal masses mimicking malignancy successfully diagnosed and treated without surgery, unlike other previous cases confirmed after invasive surgical intervention.

CASE REPORT

A 52-year-old male with a medical history of diabetes visited our department with intermittent left flank pain for 3 months. On admission, his blood pressure was 130/80 mmHg, body temperature 36.5℃, pulse rate 65/minute and respiration rate 20/minute. Left flank tenderness was observed on physical examination. Laboratory results showed a white blood cell (WBC) 7,470/mm^3; hemoglobin, 15.6 g/dL; platelet, 290,000/mm^3; aspartate aminotransferase, 14 IU/L; alanine aminotransferase, 5 IU/L; blood urea nitrogen, 9 mg/dL; creatinine, 1.0 mg/dL; total bilirubin, 0.6 mg/dL; direct bilirubin, 0.2 mg/dL; alkaline phosphatase, 199 IU/L; gamma glutamyl transferase, 5 IU/L; amylase, 191 IU/L; lipase, 277 IU/L and C-reactive protein, 0.63 mg/dL. Viral markers for type A, B and C were negative. Serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) measurements were 1.32 ng/mL and 5.28, respectively.

The abdominal computed tomography (CT) scan showed diffuse pancreatic enlargement with irregular strictures of the main pancreatic duct (Fig. 1A) and multiloculated cystic mass in the pancreatic tail portion (Fig. 1B). The CT also showed bilateral renal masses with mild contrast enhancement infiltrating both the renal pelvis and left renal sinus (Fig. 1C and 1D). We performed magnetic resonance imaging for further evaluation of the renal lesions and the renal masses showed low signal intensity on T1-weighted images with minimal enhancement, suggesting hypovascularity of the masses (Fig. 1E). Endoscopic retrograde cholangiopancreatography showed typical pancreatic duct findings of autoimmune pancreatitis (AIP) and branched- type intraductal papillary mucinous neoplasm on the tail portion was suspicious (Fig. 1F).

Serum IgG was 1,640 mg/dL (normal range 800-1,700 mg/dL) and IgG4 was 47.8 mg/dL (normal range 3.9-86.4 mg/dL). Despite the normal serum IgG and IgG4 levels, the autoimmune pancreatitis simultaneously involving the kidney was highly suspicious, and thus ultrasound-guided pancreatic head biopsy was performed. The pathological result revealed chronic dense lymphoplasmacytic inflammatory infiltration and strong positivity in the IgG4 immunohistochemical stain (Fig. 2).

Autoimmune pancreatitis involving the kidney as part of the IgG4-related sclerosing disease was diagnosed and the patient

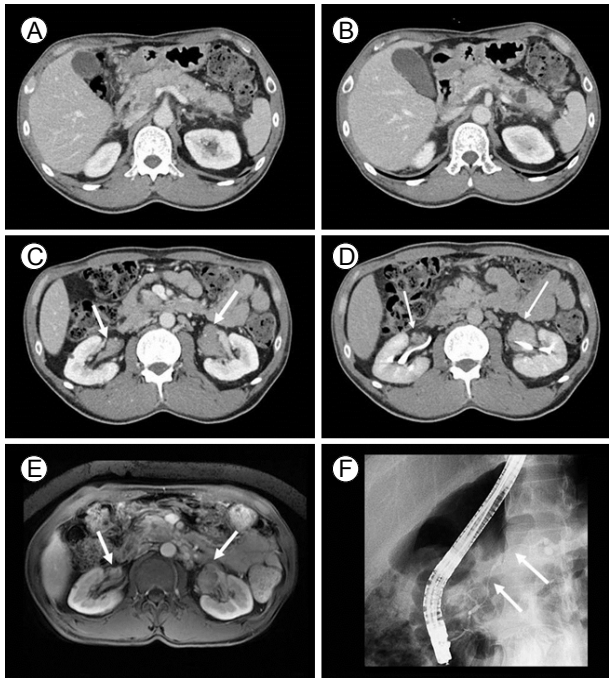

Figure 1. Initial evaluation using contrast-enhanced abdominal computed tomography (CT). (A) CT scan showing diffuse enlargement of the pancreas and peripancreatic fluid collection. (B) CT scan showing multiple cystic lesions without main pancreatic duct dilatation. (C, D) Homogenous masses (arrows) in bilateral renal sinuses and pelvis showing mild enhancement in the nephrographic and excretory phases. Magnetic resonance imaging findings of renal masses. (E) Contrast enhanced T1-weighted image reveals hypovascular renal masses (arrows) showing minimal contrast enhancement. Endoscopic retrograde cholangiopancreatography findings. (F) Pancreatic duct with multifocal irregular strictures (arrows).

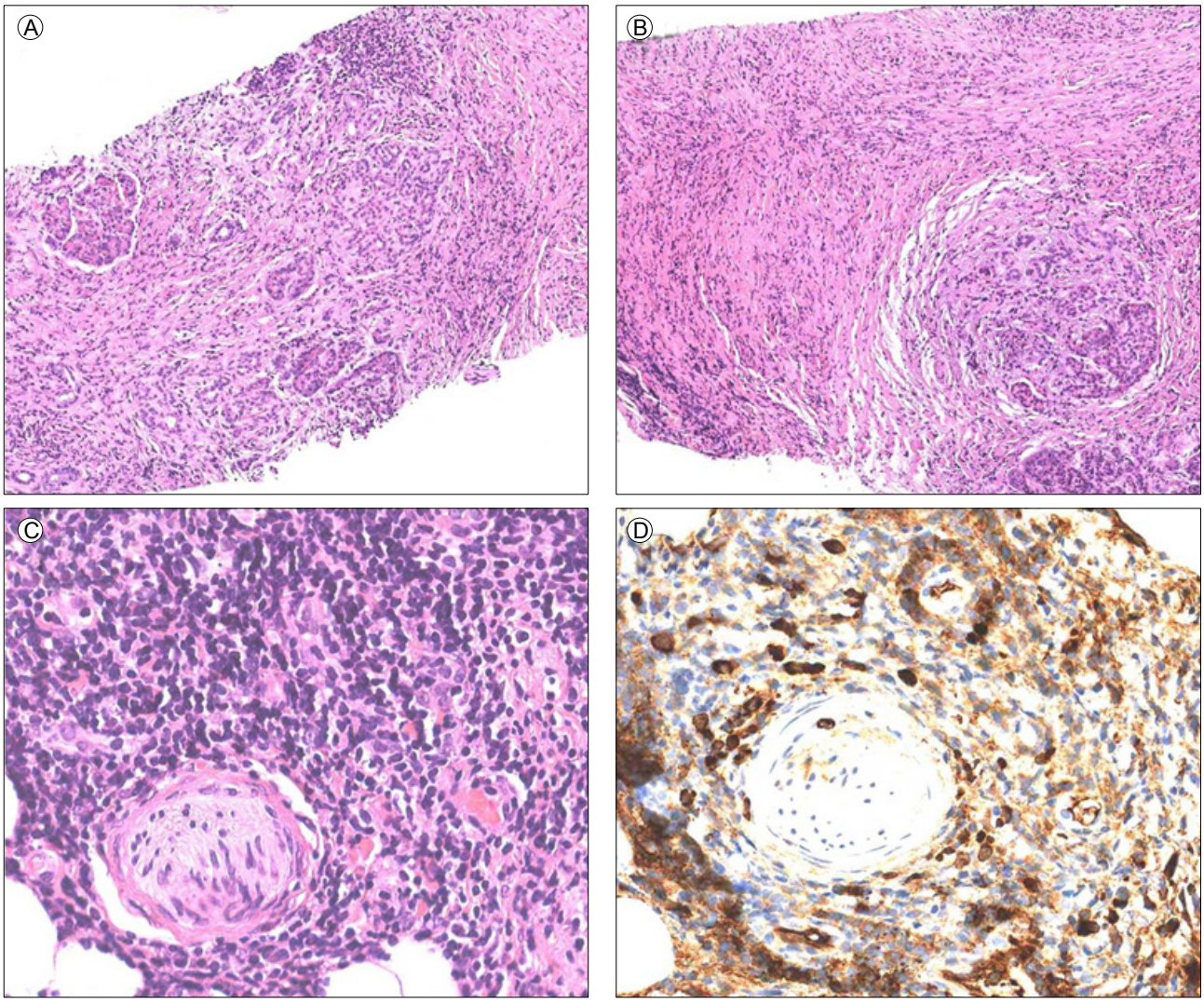

Figure 2. Histological findings of biopsy tissue from the pancreatic head. (A) The pancreas is replaced by fibrous tissue with diffuse infiltrates of chronic inflammatory cells. The pancreatic acini are atrophied and absent and the ducts are relatively well preserved (hematoxylin and eosin, H&E, ×40). (B) The proliferated fibrous tissue shows storiform appearance around the pancreatic parenchyma (H&E, ×100). (C) The chronic inflammatory cells are composed of lymphocytes and some plasma cells (H&E, ×400). (D) The immunohistochemical stain for IgG4 shows many positive cells in 50 high-power fields (HPF, ×400).

was initially treated with 40 mg of oral prednisolone daily for 4 weeks with a subsequent decrease in the dosage by 5 mg every week; he continued taking 5 mg of the steroid for 6 months. Currently, the patient is taking 5 mg of the steroid every other day for 6 months as a maintenance regimen. Follow-up serum IgG and IgG4 levels remained within the normal ranges. The pancreatic swelling showed marked improvement on the follow-up CT scan after 2 months of oral steroid therapy and the cystic lesion in the pancreatic tail portion was considered a pancreatic pseudocyst due to decreased size and invisibility. On regular follow-up CT scan at 3-month intervals (Fig. 3), the renal masses decreased steadily in size and the patient maintained a stable medical condition.

DISCUSSION

Kamisawa et al. [1] proposed the concept of IgG4-related sclerosing disease and suggested that autoimmune pancreatitis is

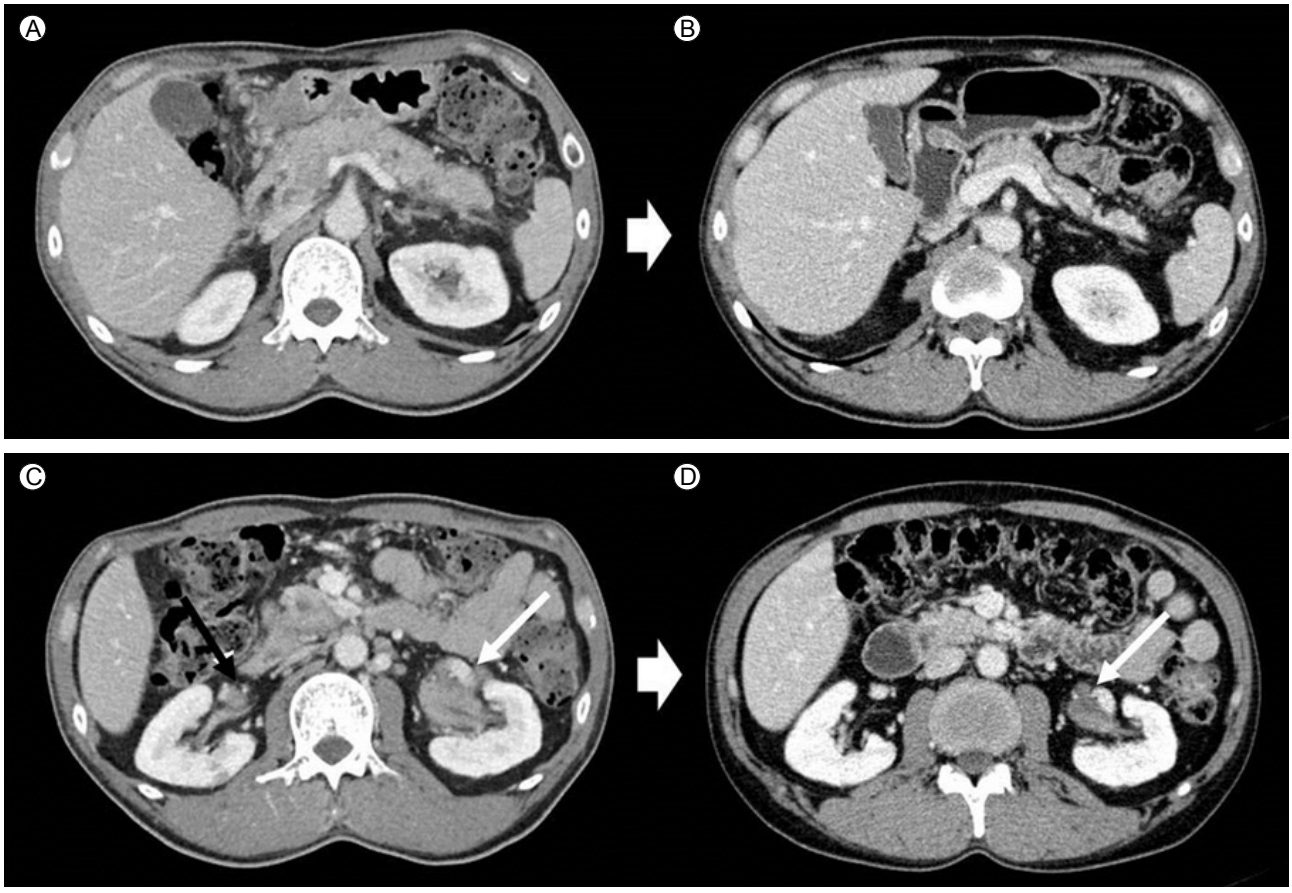

Figure 3. Follow-up CT scans at 12 months after oral steroid therapy. Compared with the initial images (A, C), pancreatic swelling and the cystic lesion in the tail portion are markedly improved (B), the left renal mass shows decreased size (white arrow), and the right renal pelvic mass has disappeared (black arrow) (D).

a component of that disease spectrum, recently recognized as a distinct disease entity. The disease is characterized by a high level of serum IgG4 and dense infiltration of IgG4-positive plasma cells into multiple organs and can affect a number of organ systems commonly manifesting as autoimmune pancreatitis.

Currently, the clinicopathological features of IgG4-related sclerosing disease remain unclear and globally established diagnostic criteria or treatment guidelines are unavailable. In our case, the CT scan showed diffuse enlargement of the pancreas and bilateral renal masses, but the serum IgG4 level was normal. For the diagnosis of IgG4-related sclerosing disease, the raised serum IgG4 level (> 135 mg/dL) is helpful but not essential because 79-90% of the patients show elevated levels [7].

In this case, we performed percutaneous ultrasound-guided pancreatic biopsy rather than endoscopic ultrasound-guided fine needle aspiration because the pancreas showed diffuse whole enlargement without a specific location. Pancreatic biopsy revealed marked infiltration of lymphocytes and plasmacytes with fibrosis and infiltration of IgG4-positive plasmacytes.

The renal lesions satisfied the criteria of "probable diagnosis" according to the 2011 diagnostic criteria for IgG4-related kidney disease [8], thus renal biopsy was not performed due to a high risk of serious complications. Renal masses were not cortical lesions but located at the renal pelvis, therefore the approach to the target mass was technically difficult with a high risk of vascular injury such as formation of aneurysm or arteriovenous fistula which can lead to hemorrhagic shock and urinary obstruction.

The final diagnosis of autoimmune pancreatitis involving the kidneys as a part of the systemic IgG4-related sclerosing disease

was made according to the 2009 clinical diagnostic criteria for IgG4-related disease proposed by the Japanese Research Committee [9].

As a representative target, renal involvement is present in approximately one-third of patients with autoimmune pancreatitis [2,3]. Currently, IgG4-related kidney disease is a new clinical entity in the field of nephrology emerging as an extrapancreatic manifestation of AIP [8].

The usual clinical manifestation of IgG4-related sclerosing disease involving the kidney is tubulointerstitial nephritis, but is not pathognomic. Therefore, distinguishing radiological findings plays an important role in the diagnosis. Characteristic CT findings of IgG4-kidney disease are as follows: multiple low-density cortical lesions, diffuse kidney enlargement, hypovascular mass and hypertrophic infiltration of the renal pelvic wall [4,5]. According to previous studies, renal parenchymal lesions are common, predominantly involving the renal cortex or presenting as a diffuse renal enlargement pattern, conversely, mass-like lesions or pelvic involvement patterns are relatively rare [3,4]. Particularly, mass forming or pelvic involvement types should be distinguished from lymphomas, metastatic cancer and other genitourinary malignancies to avoid unnecessary surgery. Khalili et al. [2] suggested that the coexistence of pancreatic and cortical renal lesions could be used as an indication for the differentiation of AIP from pancreatic adenocarcinoma, and thorough knowledge of the different patterns of autoimmune renal involvement is essential.

Unfortunately, differentiating autoimmune renal involvement disease with a malignant mass is difficult using radiological criteria alone. Autoimmune kidney disease has been mistaken for a malignant mass in many reports and diagnosed only after invasive operations [5,6]. To date, a total of four domestic cases of IgG4-related disease involving the kidney have been reported, and two patients who presented with a renal mass underwent nephrectomy due to the unclear differential diagnosis with malignancy. The patients were diagnosed with IgG4-related sclerosing disease involving the kidney after several years [6].

Glucocorticoids appear to be effective in the majority of patients with IgG4-related disease. The typical dosage is 40-60 mg/d with stepwise tapering of 5 mg every 1-2 weeks and continued maintenance therapy with prednisolone 5 mg/d without complete discontinuation of steroids is sometimes required to prevent relapse; however, clear evidence for the standardized regimens is lacking [10]. In summary IgG4-related sclerosing disease is a systemic disorder that can involve almost every organ. The kidney can be a representative target; however, renal pelvic involvement with mass-like lesions is very rare and should be distinguished from lymphomas and malignancies. In cases with normal serum IgG4 levels, histological results from the targeted organ are necessary and recognizing radiological findings of IgG4-related sclerosing disease is important to avoid unnecessary invasive interventions.

중심 단어: 면역글로불린 G4 연관성 신장 질환; 자가면역성 췌장염; 신우 종괴

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