Retroperitoneal fibrosis associated with IgG4-related disease diagnosed by prostate biopsy developed with acute post-renal renal failure: A case report

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Inflammation and Infection

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Retroperitoneal fibrosis is an uncommon disorder of unknown etiology that encompasses several different pathophysiological entities and leads to fibrosis in the retroperitoneum that surrounds the aorta and ureters, and IgG4 related disease (IgG4RD) is thought to be one of the causes of retroperitoneal fibrosis. We report a case of retroperitoneal fibrosis associated with IgG4RD developed with acute post-renal renal failure.

Introduction

A 79-year-old male suffered from lower limb edema and appetite loss for three days and complained of dyspnea, and visited our emergency department and had an emergency hospitalization in June 2016. There were not any sign and symptom of pancreatitis. His initial laboratory findings revealed renal failure (Creatinin 8.36 mg/dl, eGFR 5.4 mL/min/1.73m²) and mild inflammatory reaction (white blood cell count 7.6 x 10³/mL, CRP 2.07 mg/dl), high BNP 621.9 pg/mL, and high serum IgG4 757 mg/dl (normal level: 4.8 x 10⁵ mg/dl). The cardiothoracic ratio increased to 56%. CT and MRI scans revealed soft tissue masses in the retroperitoneum and left renal pelvis, and bilateral hydronephrosis (Fig. 1). There was no finding of pancreatic lesion. He was diagnosed with heart failure due to acute post-renal renal failure and bilateral ureteral stentings were performed emergently. Diuresis was obtained promptly after the procedure and renal function improved (Cre 1.07 mg/dl, eGFR 51.2 mL/min/1.73m²). The respiratory condition was also relieved. The patient was suspected of IgG4RD because of serum high IgG4 (757 mg/dl) on admission. Diffusion-weighted MRI showed a high signal area on the ventral side of the left apex of the prostate. For the diagnosis, we underwent needle biopsies of the prostate. The immunohistochemical evaluation of the biopsy specimens showed positive for IgG4 immunostaining; however, IgG4/IgG positive cell ratio was as low as 25% (Fig. 2). Cancer was not detected in the specimen. He was diagnosed with retroperitoneal fibrosis associated with IgG4-related disease, and was considered to develop acute post-renal renal failure. Steroid therapy was started with prednisolone (P LS) 35 mg/day. The tissue masses on the retroperitoneum and left renal pelvis were diminishing significantly after the treatment, and the serum IgG4 showed on a declining trend. The bilateral ureteral stents were removed. The renal function did not deteriorate after the removal without worsening of
hydromephrosis. DPP-4 inhibitor (alogliptin 12.5 mg/day) was started 1 week after the treatment because the pre-sleep hyperglycemia was observed after starting the steroid therapy. When PLS was tapered to 10 mg/day, the DPP-4 inhibitor was discontinued because of normalization of the pre-sleep blood glucose level. Currently, serum IgG4 is slightly high at 185 mg/dl, and PLS is tapered to and is being maintained at 10 mg/day.

Discussion

Retroperitoneal fibrosis is characterized by the development of extensive fibrosis throughout the retroperitoneum. The fibrosis leads to entrapment and obstruction of retroperitoneal structures, notably the ureters. Calculated annual incidence of retroperitoneal fibrosis was 1.3/100,000 inhabitants.1

IgG4RD is a novel clinical entity characterized by tissue infiltration of IgG4-positive plasma cells and an immune-mediated fibro-inflammatory condition that can affect multiple organs and lead to tumefactive, tissue destructive lesions and organ failure.2 Since Hamano et al. reported high serum IgG4 concentrations in autoimmune pancreatitis in 2001, the involvement of IgG4 in various diseases of the whole body has revealed.3 Since Hamano et al. reported complications of IgG4-associated autoimmune pancreatitis and retroperitoneal fibrosis, IgG4RD has listed as one of the causes of retroperitoneal fibrosis.3 In many cases, IgG4RD related multiple lesions are detected in addition to the retroperitoneum. The present case also has the lesions in the prostate and renal pelvis in addition to the retroperitoneum, however, did not have the findings of autoimmune pancreatitis. Definitive diagnosis of IgG4RD is obtained by pathological examination; however, tissues from deep organs such as retroperitoneal lesions are difficult to perform biopsy (Table 1). In comparison, samplings of prostate lesions are relatively easy and minimally invasive. For the definitive diagnosis of retroperitoneal fibrosis caused by acute post-ren al renal failure as in this patient, alternative prostate biopsy following the confirmation of the prostatic lesion by MRI is considered to be more useful than retroperitoneal biopsy. Pathological findings in the prostatic area of this case showed infiltration of IgG4 positive cells; however, the ratio of IgG4/IgG positive cells was as low as 25% (Fig. 2). The ratio of IgG4/IgG is not so high; however, this observation would be an evidence of IgG4RD from the point where IgG4 positive plasma cells that do not exist in normal prostate are conspicuous.

The first line of treatment for retroperitoneal fibrosis associated with IgG4RD is steroid therapy.2 This may reflect a concept of ‘acute phase’ of idiopathic retroperitoneal fibrosis in the past with higher infiltration of the immune-cells in the processes with evidence of inflammation.5 Indeed, elevation of the CRP level was observed in the present study. The starting dose of steroid is usually 30–40 mg/day (0.6 mg/kg per day) and the dose is tapered gradually thereafter. The goal of induction therapy is to discontinue glucocorticoid use 3–6 months after the start of treatment; however, many clinicians recommend the use of low-dose glucocorticoid maintenance therapy for up to 3 years because of often recurrence of the disease.2 Treatment at the time of recurrence has not been established. The present case has been in remission at the tapering dose of PLS 10 mg/day; however, strict follow-up is necessary because of slightly high level of serum IgG4 (185 mg/dl).

In conclusion, retroperitoneal fibrosis associated with IgG4RD is a systemic and chronic inflammatory disease involving multiple lesions. Because alternative prostate biopsy following the confirmation of the prostatic lesion by MRI is easy to perform, minimally invasive and useful for pathological confirmation for IgG4RD, this procedure is one of the options when affected organs are difficult to approach. Early diagnosis of this disease is clinically important to prevent irreversible organ damage, because most patients respond well to glucocorticoid.

![Fig. 1. CT before and after treatment and MRI images before treatment. a, b: CT images before treatment: A soft-tissue mass is uniformly imaged in the retroperitoneum with bilateral hydronephrosis. Lesions are also found along the wall of the left renal pelvis. c, d: CT images after treatment: All lesions diminish in size and the contrast effect decreases. e, f: MRI images before treatment: MRI findings at the lesions before treatment are moderate signal at T1WI, low signal at T2WI, high signal at DWI, and low value for ADC. DWI (b = 800) of the retroperitoneum (e) and prostate (f).](image-url)
Confl icts of interest
None.

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Table 1
The reported cases of retroperitoneal fibrosis with hydronephrosis associated with IgG4RD with pathological diagnosis.

| age | sex  | diagnostic lesion          | reference                           |
|-----|------|----------------------------|-------------------------------------|
| 1   | 49   | woman                      | renal pelvic tumor resection        | Med Mol Morphol. 2009; 42: 236-8. |
| 2   | 53   | man                        | right nephroureterectomy            | Pathol Int. 2010; 60: 779-83.  |
| 3   | 39   | man                        | left ureter partial reseetction      | Pathol Res Pract. 2011; 207: 712-4. |
| 4   | 80   | man                        | right nephroureterectomy            | Hinyokika Kiyo. 2012; 58: 613-6. Japanese |
| 5   | 71   | man                        | retroperitoneal mass reseetction     | Urol Int. 2013; 90: 365-8.    |
| 6   | 63   | woman                      | renal biopsy                        | Rheumatol Int. 2013; 33: 2141-4. |
| 7   | 70   | man                        | prostate biopsy                     | Hinyokika Kiyo. 2013; 59: 781-4. Japanese |
| 8   | 71   | man                        | intrapelvic mass reseetction         | World J Clin Cases. 2015; 3: 1000-4. |
| 9   | 70   | woman                      | ureteral biopsy                     | Hinyokika Kiyo. 2016; 62: 197–200. Japanese |
| 10  | 79   | man                        | prostate biopsy                     | The present case               |

Fig. 2. Pathological findings of the prostatic biopsy specimen. The biopsy specimen reveals prostatitis and few findings of fibrosis. Lymphocytes/plasma cells based chronic inflammatory cell infiltration is recognized. The immunohistochemical evaluation of the biopsy specimens shows positive for IgG4 immunostaining; however, IgG4/IgG positive cell ratio is as low as 25%. a. HE staining. (×10). b. HE staining. (×40) Focal inflammatory infiltrate with plasma cells. Immunostaining. (×20) c. IgG, d. IgG4.