

IgG4-related disease presenting as a pancreatic mass: A case report

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ABSTRACT

Immunoglobulin G4-related disease (IgG4-RD) is an increasingly recognized fibroinflammatory condition with characteristic clinical, serological, and histopathological features. It might involve any organ in the body with a special predilection for lymph nodes, salivary glands, the pancreas, and the retroperitoneum. Due to the non-specific features of the disease and the capability of mimicking many other medical conditions, the diagnosis of IgG4-RD could be delayed. Herin, we describe a case of a middle-aged man who presented with obstructive jaundice due to a pancreatic mass. Further evaluation revealed multiple cervical and inguinal lymphadenopathy, bilateral wedge-shaped lesions in the kidneys and substantial thickening of the aortic wall that was suggestive of aortitis/periaortitis. A histopathological examination of an inguinal lymph node showed increased infiltration of nodal immunoglobulin G4 (IgG4) plasma cells (>30/high-power field) with a high serum IgG4 immunoglobulin level. Based on that, the patient was diagnosed with IgG4-RD, and he was successfully treated with pulse steroid therapy with complete resolution of his symptoms and the radiological and laboratory findings. IgG4-RD is a protean condition with a large spectrum of clinical manifestations that could mimic many other serious medical conditions. Early recognition and management of immunosuppression are vital for complete recovery.

Key words: Autoimmune disease, Immunoglobulin G4-related disease, Lymphadenopathy, Pancreatic mass, Steroids

Immunoglobulin G4-related disease (IgG4-RD) is a recently described clinicopathological condition with a wide range of clinical manifestations. It commonly presents as neoplasms with characteristic histological features including dense lymphoplasmacytic infiltrates that are rich in immunoglobulin G4 (IgG4)-positive plasma cells, fibrosis arranged in a storiform pattern, obliterative phlebitis, and modest tissue eosinophilia in addition to elevated serum IgG4 antibody concentrations. [1]. This entity was first described in 2001, when autoimmune pancreatitis in a patient correlated with elevated serum IgG4 levels and numerous IgG4-rich lymphoplasmacytic cells [2,3]. In 2003, IgG4-RD was defined as a new systemic clinicopathological entity [4]. The term “IgG4-RD” was coined in 2012 [5]. In 2019, a group of experts from the American College of Rheumatology/European League Against Rheumatism proposed classification criteria for IgG4-RD that included a scoring system of a constellation of certain clinical, radiological, serological, and pathological features in the absence of specified exclusion criteria [6].

The most involved organs include the pancreas, major salivary glands, lacrimal glands, retroperitoneum, and lymphatic ducts, and the disease often presents as tumor-like swellings that

are detectable by imaging studies [6]. The presentation is usually subacute and could mimic many medical conditions, therefore, the diagnosis is usually delayed as in this case.

CASE PRESENTATION

A 47-year-old Egyptian man with a history of hypertension and diabetes mellitus presented to the emergency department with painless cervical lymphadenopathy of 1-month duration. There was no fever, night sweats, or weight loss. The patient visited several private clinics and received various antibiotics without improvement, which prompted him to visit our hospital.

Clinical examination showed a conscious and afebrile patient with a normal body build and normal vital signs. A neck examination revealed a palpable non-tender mass on the right side of the neck, whereas the remainder of his examination was unremarkable.

Initial laboratory tests revealed a hemoglobin level of 13 g/dL, a total leukocyte count of 10,000/mm³ with a normal differential, and a platelet count of 220,000/mm³. Other investigations including liver enzymes, renal function test, and coagulation profile were within the normal ranges. Quanti FERON test and human immunodeficiency virus enzyme-linked immunosorbent assay were both negative, whereas the C-reactive protein was

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slightly raised at 34 mg/L. His alpha-fetoprotein and cancer antigen (CA) 19-9 were within the normal range. The chest radiograph was normal. Ultrasound examination of the neck showed right-sided sizable lymphadenopathy. Cervical lymph node biopsy demonstrated follicular hyperplasia, but immunophenotyping by flow cytometry excluded lymphoma.

Six months later, the patient was admitted because of jaundice, dark urine, and pale stool. Clinical examination revealed yellowish discoloration of sclera with cervical and inguinal lymphadenopathies. Liver function tests were consistent with cholestatic jaundice. Viral and autoimmune hepatitis screen tests were negative, and computed tomography scan of the abdomen showed a 4 cm mass at the junction of the body and head of the pancreas without causing obstruction or dilatation of the pancreatic duct. Magnetic resonance cholangiopancreatography (MRCP) revealed pancreatic head mass obstructing the biliary ducts, peri-pancreatic lymph nodes, multiple wedge-shaped lesions in both kidneys, and significant aortic thickening suggestive of aortitis/periaortitis. These findings were suggestive of lymphoma, pancreatic malignancy, or autoimmune pancreatitis. Endoscopic ultrasound-guided fine needle aspiration biopsy samples taken from the pancreatic head mass and peri-pancreatic lymph nodes showed only a few atypical cells, with no evidence of malignancy or metastatic carcinoma.

Inguinal lymph node biopsy showed many lymphoid follicles with prominent germinal centers consistent with reactive follicular hyperplasia, while flow cytometry was negative for the immunophenotypes of lymphoma. However, histopathology examination of the lymph node showed increased nodal IgG4 plasma cells (>30/high-power field), consistent with IgG4-RD. Subsequently, the blood test showed elevated serum IgG-4 levels supporting the histological diagnosis of IgG4-RD.

The patient responded very well to intravenous steroid pulse therapy followed by oral steroid with complete resolution of jaundice and lymphadenopathy, whereas IgG4 antibody level dropped toward the normal range.

DISCUSSION

IgG4-RD is an immune-mediated fibroinflammatory condition, a recently described entity with a challenging diagnosis. This disease is increasingly considered in the differential diagnosis of a variety of symptoms of organ- or system dysfunction [7]. The exact etiology and pathogenesis are still not well understood.

In this case, the patient had subacute development of masses involving cervical and abdominal lymph nodes, the pancreas, and the kidneys. In a case series of 114 patients by Zen and Nakanuma, most cases had multifocal disease particularly in patients with renal lesions [8]. It must be noted, however, that although affected organs share common histopathological features in common, certain findings such as storiform fibrosis might not be seen in the affected lymph nodes as in our case. Moreover, high serum IgG4 levels and dense intranodal IgG4+ plasma cells can be found in many other mimicking conditions such as malignancy, Castleman disease, and granulomatous with

polyangiitis [9]. According to Mahajan *et al.*, IgG4 antibodies are unlikely pathogenic but produced as an epiphenomenon in response to cytokine release [10]. Elevated serum IgG4 levels are considered to have high sensitivity and positive predictive value for IgG4-RD (>90%) but with low specificity and negative predictive value [11]. Therefore, histopathological findings should be interpreted considering the clinical, radiological, and serological data of each patient.

Inflammatory involvement of the aorta in IgG4-RD is relatively common. In our case, the incidental finding of the significant abdominal aorta wall thickening during MRCP imaging of the pancreas helped in narrowing the differential diagnoses to inflammatory diseases that affect the aorta. Aortitis is inflammation of the wall of the aorta while periaortitis describes extended inflammation of the periaortic space. Both conditions could be considered a spectrum of inflammatory aorta involvement that could occur secondary to rheumatological diseases, neoplastic disorders, or infectious etiologies [12]. In IgG4-RD, aortitis affects more commonly the thoracic aorta whereas periaortitis is more frequently noticed in the abdominal part of the aorta. Interestingly, a histopathological review of a large number of thoracic aorta specimens in patients who underwent thoracic aorta resection found that three-quarters of patients with lymphoplasmacytic aortitis had other characteristic histopathological features of IgG4-RD highlighting the possibility of underdiagnosis of IgG4-related aortic disease [13]. It must be noted also that pathological examination of the affected vessels is not always feasible or indicated. Radiological evaluation of the vasculature alongside clinical and serological tests aids in establishing the diagnosis of IgG4-RD [12]. While the classical site of involvement in other forms of inflammatory vasculitis such as Takayasu arteritis or giant cell arteritis is the media, IgG4-RD predominantly affects the adventitia and periadventitial tissues and it is strongly associated with retroperitoneal fibrosis [14].

As in most other cases of IgG4-RD, the patient in our case responded well to glucocorticoid therapy alone. However, to date, there is no randomized controlled trial that guides treatment decisions in IgG4-RD while the available treatment guidelines depend mainly on observational studies and expert opinion. According to the 2015 international consensus guidance on IgG4-RD management, early recognition and initiation of therapy are necessary for all patients with symptomatic disease and some individuals with asymptomatic disease due to the indolent nature of IgG4-RD and to avoid the risk of progression from the treatable inflammatory stage to treatment-refractory fibrotic disease and end-organ damage [6]. Glucocorticoids remain the first line of management but many patients relapse with tapering the dose or even during the steroid therapy. Therefore, the use of steroid-sparing immunosuppressive therapy is warranted for some patients during the induction and/or maintenance phases [15]. The role of rituximab is highlighted in IgG4-RD that is refractory to glucocorticoids or relapses with dose tapering and in patients who have strong contraindications to glucocorticoid [16]. Nevertheless, rituximab use in IgG4-RD was not evaluated in

randomized controlled trials and its utilization is limited by cost, potential serious infections, and short-term effects. Therefore, the use of rituximab in IgG4-RD should be individualized taking into consideration multidisciplinary team input and patient preferences.

We presented a case of a middle-aged male who developed painless swelling of cervical lymph nodes followed 6 months later with painless jaundice, abdominal lymphadenopathy, and involvement of the aorta and kidneys raising the suspicion for malignancy. Subsequent tissue biopsy and serum IgG4 levels supported the diagnosis of IgG4-RD. The patient responded well to corticosteroid therapy alone and was kept under follow-up in the rheumatology clinic.

CONCLUSION

IgG4-RD should be considered in the differential diagnosis of patients presenting with tumorous swelling of multiple organs, especially with large vessel involvement. Establishing the diagnosis of IgG4-RD often necessitates a histopathological examination of affected tissues alongside other suggestive clinical, radiological, and serological findings. Clinical response to corticosteroids is characteristic but patients should be kept under active surveillance for potential disease relapse.

REFERENCES

- Wallace ZS, Zhang Y, Perugino CA, *et al.* Clinical phenotypes of IgG4-related disease: An analysis of two international cross-sectional cohorts. *Ann Rheum Dis* 2019;78:406-12.
- Stone JH, Zen Y, Deshpande V. IgG4-related disease. *N Engl J Med* 2012;366:539-51.
- Hamano H, Kawa S, Horiuchi A, *et al.* High serum IgG4 concentrations in patients with sclerosing pancreatitis. *N Engl J Med* 2001;344:732-8.

- Kamisawa T, Funata N, Hayashi Y, *et al.* A new clinicopathological entity of IgG4-related autoimmune disease. *J Gastroenterol* 2003;38:982-4.
- Stone JH, Khosroshahi A, Deshpande V, *et al.* Recommendations for the nomenclature of IgG4-related disease and its individual organ system manifestations. *Arthritis Rheum* 2012;64:3061-7.
- Wallace ZS, Naden RP, Chari S, *et al.* The 2019 American College of Rheumatology/European league against rheumatism classification criteria for IgG4-related disease. *Arthritis Rheumatol* 2020;72:7-19.
- Martínez-Valle F, Orozco-Gálvez O, Fernández-Codina A. Update in etiopathogeny, diagnosis and treatment of the IgG4 related disease. *Med Clin (Barc)* 2018;151:18-25.
- Zen Y, Nakanuma Y. IgG4-related disease: A cross-sectional study of 114 cases. *Am J Surg Pathol* 2010;34:1812-9.
- Deshpande V, Zen Y, Chan JK, *et al.* Consensus statement on the pathology of IgG4-related disease. *Mod Pathol* 2012;25:1181-92.
- Mahajan VS, Mattoo H, Deshpande V, *et al.* IgG4-related disease. *Annu Rev Pathol* 2014;9:315-47.
- Carruthers MN, Khosroshahi A, Augustin T, *et al.* The diagnostic utility of serum IgG4 concentrations in IgG4-related disease. *Ann Rheum Dis* 2015;74:14-8.
- Marvisi C, Buttini EA, Vaglio A. Aortitis and periaortitis: The puzzling spectrum of inflammatory aortic diseases. *Presse Med* 2020;49:104018.
- Stone JR. Aortitis, periaortitis, and retroperitoneal fibrosis, as manifestations of IgG4-related systemic disease. *Curr Opin Rheumatol* 2011;23:88-94.
- Xu J, Bettendorf B, D'Oria M, *et al.* Multidisciplinary diagnosis and management of inflammatory aortic aneurysms. *J Vasc Surg* 2022;78:231-42.e2.
- Khosroshahi A, Wallace ZS, Crowe JL, *et al.* International consensus guidance statement on the management and treatment of IgG4-related disease. *Arthritis Rheumatol* 2015;67:1688-99.
- Hart PA, Topazian MD, Witzig TE, *et al.* Treatment of relapsing autoimmune pancreatitis with immunomodulators and rituximab: The Mayo Clinic experience. *Gut* 2013;62:1607-15.

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