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A Case of IgG4-Related Disease with Mikulicz' Disease, Pancreatitis, Ascending Aortitis, Membranous Nephropathy and Tubulointerstitial Nephritis

Tong Vincent Aw[1,2] and Adel Ekladious[1,3*]

[1]*Acute Medical Unit and General Medicine Department, Canberra Hospital, Canberra, ACT, Australia.*

[2]*ANU Medical School, Australian National University, Canberra, ACT, Australia.*

[3]*Faculty of Health and Medical Sciences, University of Western Australia, Perth, WA, Australia.*

***Correspondence:**

Adel Ekladious, Faculty of Health and Medical Sciences, University of Western Australia, 35 Stirling Highway Perth, WA, and Royal Hobart Hospital, 48 Liverpool Street, Hobart TAS 7000, Tel: 61499449905, Australia.

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Keywords

Abdominal pain, Diarrhea, Fatty stools.

Introduction

IgG4 related disease (IgG4-RD) is an insidiously progressive, multisystem autoimmune and fibrotic disease characterised by the presence of organ-infiltrating IgG4+ plasma cells and an elevated IgG4 level [1]. As a relatively recently described entity with lack of familiarity amongst clinicians in general, formal diagnosis is often delayed with a mean symptom duration of five years until diagnosis [1,2]. We present a prototypical case of IgG4RD in a patient with a subacute history of gastrointestinal and sicca symptoms, where prompt-targeted investigations led to rapid diagnosis of IgG4-RD with multiorgan involvement and subsequent steroid therapy lead to a good outcome with disease resolution.

Case Presentation

A 67 year-old woman presented to hospital with a six-week history of intermitted abdominal pain and diarrhea with fatty stools, along with bilateral parotid gland enlargement and ocular sicca symptoms. She did not have any significant medical history and did not take regular medications. She never smoked, did not drink alcohol nor ever used illicit drugs. She had a family history of systemic lupus erythematosus in her mother.

On examination, she was hemodynamic stable and afebrile. She had bilateral palpable parotid enlargement, but no cervical lymphadenopathy. Abdominal examination revealed a mildly ender epigastrium without signs of peritonism nor organomegaly. Her cardiorespiratory examination was unremarkable.

She had elevated inflammatory markers with an erythrocyte sedimentation rate (ESR) of 100 mm/hour and a C-reactive protein of 39 mg/L. Lipase and amylase levels were mildly elevated at 190 U/L and 200U/L respectively. Blood glucose level and HbA1c were elevated at 12 mmol/L and 8% respectively. Stool analysis revealed unformed stools with fat globules and reduced faecal elastase of 20 µg/g. Stool culture was negative for infectious pathogens. Serum chromogranin A was not elevated at 16ng/L.

Computerised Tomography of the abdomen with contrast revealed a diffusely enlarged, hypodense, sausage-shaped pancreas with sharp and smooth borders with decreased enhancement in the early and delayed phase. Furthermore, there was concurrent radiological evidence of ascending aortitis. Magnetic resonance cholangio-pancreatogram revealed pancreatic enlargement with abnormal signal intensity on T1 and T2-weighted suggestive of autoimmune pancreatitis. Endoscopic ultrasound and pancreatic biopsy revealed diffuse lymphoplasmacytic infiltration with IgG4+ plasma cells accompanied by storiform fibrosis and obliterative phlebitis securing the diagnosis of IgG4-RD with autoimmune pancreatitis. Radiological evidence of aortitis suggests concurrent IgG4-RD with aortitis.

Creatinine was elevated at 212 µmol/L with 6.0 grams of proteinuria in 24 hours and no dysmorphic white cells or red cells. Anti-glomerular basement membrane antibodies and Anti-phospholipase A2 receptor antibodies were negative. Renal tract

ultrasound did not reveal any structural abnormality. Renal biopsy showed thickened capillary walls and mesangial hypercellularity, and glomerular basement membrane features consistent with membranous nephropathy, as well as eosinophilic infiltrate with tubulitis in keeping with concurrent acute tubulointerstitial nephritis. There was positive IgG4 staining in the tubules and glomerular basement membrane – securing the diagnosis of IgG4-RD with membranous nephropathy and tubulointerstitial nephritis.

Parotid gland biopsy was performed to investigate the parotid gland enlargement. Histopathology revealed storiform fibrosis with lymphoplasmacytic infiltration of IgG4+ plasma cells securing the diagnosis of Mikulicz' disease in the setting of ocular sicca symptoms suggesting concurrent lacrimal gland involvement. Serum IgG4 levels were markedly elevated at 9.9 g/L. Full blood count, liver function test, electrolytes, troponin, thyroid function tests and haematinic studies were unremarkable. Hepatitis B, Hepatitis C, HIV and Syphilis serology were negative. Autoimmune serology was negative including Anti-nuclear antibodies, Anti-dsDNA antibodies, Anti-neutrophil cytoplasmic antibodies, Rheumatoid factor and Complement studies.

Upper and lower gastrointestinal endoscopy were unremarkable. Serum protein electrophoresis did not reveal a monoclonal band and serum free light chain levels were normal with a normal kappa/lambda ratio. Peripheral blood immunophenotyping excluded an underlying monoclonal hematological malignancy.

Outcome and follow up

The patient was diagnosed with IgG4-RD – more specifically, Mikulicz' disease with systemic involvement including autoimmune pancreatitis, membranous and tubulointerstitial disease and ascending inflammatory aortitis.

She was treated with high-dose steroid therapy for 6 weeks with slow tapering, followed by Rituximab. On 6 week follow-up, symptoms had fully resolved and patient was eating well and gaining weight. IgG4 levels had normalized to 0.5 g/L. Proteinuria had improved to 200 mg per 24 hours. Inflammatory markers lipase, amylase and serum creatinine all resolved to normal levels.

Discussion

IgG4-RD is a rare multisystem autoimmune disease first described two decades ago, with ever-increasing awareness of this disease amongst clinicians [1,3]. We present a case of IgG4-RD in a middle aged patient with multiorgan involvement and good response to steroid therapy. The diagnosis of IgG4-RD is often significantly delayed due to the typically insidious progression of symptoms and lack of familiarity of this disease amongst clinicians [1,2]. In our patient, symptoms were subacute and diagnosis was made promptly.

A large cross-sectional analysis of IgG4-RD patients revealed four clinically-distinct phenotypes – Pancreato-hepato-biliary disease, Retroperitoneal fibrosis and/or aortitis, Head and neck-limited disease, and classic Mikulicz disease with systemic involvement. Our patient best fits into the latter case of Mikulicz disease with systemic involvement including kidneys, lacrimal and parotid glands, pancreas and thoracic aorta – a rare manifestation for this phenotype of IgG4-RD. Although patients with IgG4-RD typically develop multisystem disease, extensive multiorgan involvement of more than three organs is relatively uncommon [4], with only few case reports of extensive involvement of up to ten organs [5,6]. Our patient had five organs involved – all of which were classic manifestations of IgG4-RD.

Conclusion

In summary, we present a prototypical case of IgG4-RD with classic multiorgan manifestations, which was promptly diagnosed and treated with a good outcome. We hope this case will help familiarize clinicians with IgG4-RD and lead to future prompt diagnosis and treatment of this rare disease.

References

1. Perugino CA, Stone JH. IgG4-related disease an update on pathophysiology and implications for clinical care. Nat Rev Rheumatol. 2020; 16: 702-714.
2. Wallace ZS, Deshpande V, Mattoo H, et al. IgG4-Related Disease Clinical and Laboratory Features in One Hundred Twenty-Five Patients. Arthritis Rheumatol. 2015; 67: 2466-2475.
3. Kamisawa T, Funata N, Hayashi Y, et al. A new clinicopathological entity of IgG4-related autoimmune disease. J Gastroenterol. 2003; 38: 982-984.
4. Chen Y, Zhao JZ, Feng RE, et al. Types of Organ Involvement in Patients with Immunoglobulin G4-related Disease. Chin Med J Engl. 2016; 129: 1525-1532.
5. Higashioka K, Yoshida K, Oryoji K, et al. A Case of Immunoglobulin G4-Related Disease with Extensive Multiorgan Involvements. Case Rep Rheumatol. 2015; 2015: 392893.
6. Tarte NN, Ravipati CS, Leon de la Rocha JA, et al. IgG4-related disease with multiorgan involvement a case-based review. Rheumatol Int. 2021; 41: 1169-1174.