Clinical Case Reports International

Case Report
Published: 09 Sep, 2023

IgG4-Related Disease with Pancreas and Skin Involvement: Case Report and Review of Literature

*Xiao C, Lu T and Huang X**

Department of Rheumatology, Tongji University School of Medicine and Shanghai East Hospital, China

Abstract

Immunoglobulin G4-Related Disease (IgG4-RD) is an autoimmune inflammatory disease characterized by infiltration of IgG4+ plasma cells, which can affect multiple organs such as pancreas, biliary tract, kidneys, salivary glands, lymph nodes, aorta, and retroperitoneum, et al. Cutaneous lesion involvement is a rare clinical manifestation of IgG4-RD. We report a case of IgG4-RD presenting with cutaneous lesions in combination with autoimmune pancreatitis and subacute thyroiditis. A skin biopsy pathology confirmed the diagnosis of IgG4-RD. Here we present an uncommon case of IgG4-RD with subacute thyroiditis with pancreatic and skin involvement and provide a brief literature review of skin manifestations and treatment.

Keywords: Autoimmune pancreatitis; IgG4-related disease; Rash Skin pathology

Case Presentation

A 78-year-old woman was presented to the rheumatology clinic a year ago for scattered rashes on her lower extremities and pain in. The skin lesion began to be pinpoint-like and gradually merged, with clear boundaries, no pruritus, and hyperpigmentation (Figure 1). Six years before this presentation, she was treated for diarrhea and anorexia in another hospital. Pancreas Magnetic Resonance Imaging (MRI) was performed which revealed suspected pancreatic cancer (Figure 2). Endoscopic Ultrasonography (EUS) revealed a 2.5 cm × 1.6 cm round mass in the pancreatic tail. The EUS of a fine-needle aspiration of pancreatic mass showed clumps of acinus and ductal epithelium, and no malignant cells and atypical epithelial cells were discovered. The serum IgG4 concentration was 4.78 g/L. Treatments such as supplementation of pancreatic enzymes, inhabitation of retinoic acid and protection of the gastric mucosa were initiated. But the patient is still suffering from recurrent diarrhea. Autoimmune pancreatitis was presumed after CT angiography of the pancreas was administrated with contrast material. Treatment with prednisone at an initial dose of 25 mg per day was started in April 2015, and the dosage was gradually reduced to 5 mg per day. After half a year of treatment, the diarrhea had not significantly abated, so the therapy was withdrawn. The pancreas lesion did not no progress at the 6-year follow up confirmed by CT scan, however IgG4 level increased to 7.01 g/L.

Three years before this presentation, the patient was evaluated by colonoscopy due to abdominal pain and a submucosal eminence lesion was detected in the ascending colon. The right hemicolectomy was performed to remove the cancer. The biopsy demonstrated a partial mass-like lesion in which all mucosa infiltrated with lymphocytic clusters, fibrous tissue hyperplasia, twisted blood vessels, and no granulomatous lesions was found. The distribution of T lymphocyte and B lymphocyte infiltration was proportional. No medication was administrated to her. The patient also had a history of hypertension and thrombocytopenia. On examination, she was found to have cutaneous lesion on her lower extremities and tenderness in her neck. The polymorphic eruption consists of multiple, scattered, dark brown rashes, varying in size up to 5 cm on both lower extremities, with no desquamation or raised lesions. Hemoglobin was 109 g/L (reference range 115-150 g/L), C-reactive protein was 26.37 mg/L (reference range 0-10 mg/L), erythrocyte sedimentation rate was 50 mm/H (reference range 0-20 mm/H), procalcitonin was 0.051 ng/mL (reference range <0.046 ng/mL), creatinine was 90 umol/L (reference range 41-81 umol/L), IgG4 was 2.56 g/L (reference range 0.03-2.01 g/L), serum thyroglobulin was more than 500 ng/mL (reference range 3.5-77 ng/mL). Coagulation, complement, thyroid function and tumor markers were normal. Autoantibodies were positive for antinuclear antibody with titer 1:300 (Immunofluorescent pattern: Granular type). Antinuclear antibody profiles, rheumatoid factor, anti-CCP antibody, anticardiolipin antibody, and antineutrophil antibody were all negative. B-ultrasound of peripheral lymph nodes revealed enlarged

OPEN ACCESS

Correspondence:
Xinfang Huang, Department of Rheumatology, Tongji University School of Medicine and Shanghai East Hospital, 150 Jimo Road, Shanghai, 200120, China, Tel: (+86) (021) 38804518; Fax: (+86) (021) 58798999

Received Date: *21 Aug 2023*
Accepted Date: *05 Sep 2023*
Published Date: *09 Sep 2023*

Citation:
Xiao C, Lu T, Huang X. IgG4-Related Disease with Pancreas and Skin Involvement: Case Report and Review of Literature. Clin Case Rep Int. 2023; 7: 1607.

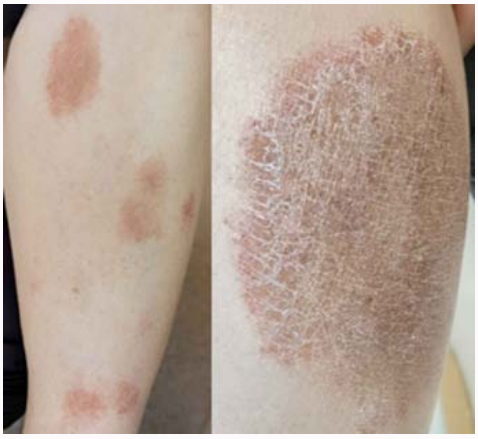

Figure 1: Morphology of rash on lower extremity of the patient.

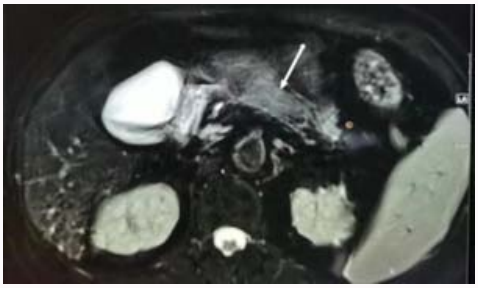

Figure 2: Upper abdominal MRI shows pancreas space-occupying (arrow).

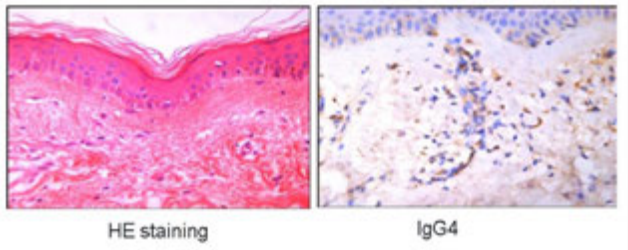

Figure 3: Skin pathology HE staining (Left): Microscopically, a small amount of plasma cells and lymphocytes infiltrated in the papillary dermis and beside small blood vessels, collagen fibers hyperplasia with hyaline degeneration in the dermal reticular layer, and reduced adnexa, consistent with IgG4-related diseases. Immunohistochemistry (Right): CD4(+)>CD8(+), IgG (+), IgG4(12-14/HPF, +), Ki67 (basal cell+).

inguinal and axillary lymph nodes. Thyroid B-ultrasound suggested an abnormal echo in the right lobe of the thyroid, and subacute thyroiditis was considered. Magnetic Resonance Cholangiopancreatography (MRCP) showed splenomegaly and esophagogastric varices. Skin pathology was necessary for the differential diagnosis and a skin biopsy was performed. The pathological manifestation demonstrated a small amount of plasma cells and infiltrated lymphocytes in the papillary dermis and adjacent to small blood vessels, collagen fibers hyperplasia with hyaline degeneration in the dermal reticular layer, adnexa reduced, IgG4+ plasma cell staining, 12 to 14 IgG4+ plasma cells per high magnification (Figure 3).

The clinical manifestations involved multiple organs and combined with increased serum IgG4 concentration and the biopsy results, the patient was diagnosed with IgG4-RD associated with subacute thyroiditis. Accordingly, the patient was prescribed oral prednisone 30 mg daily. Her rash and diarrhea gradually improved after treatment. After two months, IgG4 was reduced to 1.24 g/L, the rash had completely subsided, and the diarrhea had improved significantly. The prednisone was reduced to 5 mg per day as a maintenance therapy, and there was no rash and diarrhea recurred during the subsequent 1-year follow-up.

Discussion

IgG4-RD is a unique clinical pathological disorder characterized by elevated circulating IgG4 levels and tissue infiltration of IgG4+ plasma cells. Various organs are involved in IgG4-RD including the pancreas, salivary glands, lacrimal glands, bile ducts, peritoneum, kidneys, pituitary glands, lungs, and thyroid glands. Thus, symptoms and signs vary depending on the organs involved and the severity of the disease [1].

This case provided a patient with IgG4-RD involving the pancreas, skin and subacute thyroiditis. The cutaneous pathology facilitated a definitive diagnosis for this patient and allowed her to respond well to therapy. Only a few dozen cases of skin lesions associated IgG4-RD had been reported so far. Skin lesions can present as erythema, subcutaneous nodules, or papules, and are mostly distributed around the ears, face, and limbs, and are often combined with dacryoadenitis and sialadenitis, with infrequent involvement of the pancreas, liver, and biliary tract. Given this patient's previous history, clinical presentation, and constellation of symptoms, we suspect that subacute thyroiditis is secondary to IgG4-RD [2].

The specificity of skin lesions related to IgG4-RD is very poor. At present, the skin lesions can be classified into seven subtypes: 1) cutaneous plasmacytosis (multiple papulonodules or indurations on the trunk and proximal part of the limbs), 2) pseudolymphoma and angiolymphoid hyperplasia with eosinophilia (plaques and papulonodules mainly on the periauricular, cheek and mandible regions), 3) Mikulicz disease (palpebral swelling, sicca syndrome and exophthalmos), 4) psoriasis-like eruption (strikingly mimicking psoriasis vulgaris), 5) unspecified maculopapular or erythematous eruptions, 6) hypergammaglobulinemic purpura (bilateral asymmetrical palpable purpuric lesions on the lower extremities) and urticarial vasculitis (prolonged urticarial lesions occasionally with purpura) and 7) ischemic digit (Raynaud phenomenon and digital gangrene). Most of the lesions are subacute and it often takes months or years to be diagnosed. Regardless of the organ involved, the key histologic features are dense lymphoplasmacytic infiltration, storiform fibrosis, and thrombophlebitis. Among skin lesions, however, thrombophlebitis is rarely observed and occurs clinically in IgG4-RD [3-7].

Not all patients with skin lesions require treatment, but without treatment, skin lesions are at risk of persistence or enlargement, whether treated or not, depending on symptoms and the extent of organ involvement. IgG4 levels can often be used as a marker to monitor therapeutic response. Steroids are usually effective in treating IgG4-RD, but immunosuppressants such as methotrexate, azathioprine, and mycophenolate mofetil are also effective. In addition, rituximab also has some effect on IgG4-RD treatment. After this patient was treated with a moderate dose of prednisone monotherapy, the rash did not recur, thyroid pain and diarrhea significantly resolved, and the levels of serological marker IgG4 returned to the normal range. Imaging findings on the pancreas is still under follow-up. While

patients respond well to glucocorticoids, relapse rates remained high during reduction and maintenance therapy. Currently, the optimal therapy is still being explored [8-10].

This patient also had a mucosal protrusion in the ascending colon. She received a diagnosis of suspected Crohn's disease by a gastroenterologist at another hospital. The diagnosis was ruled out after a multi-disciplinary team discussion. We speculate that the mucosal lesion in the ascending colon may be related to IgG4-RD.

In conclusion, we have described an infrequent patient with IgG4-RD involving the skin and pancreas who was definitively diagnosed and effectively treated with the help of skin pathology. Importantly, it has been recognized that many different morphological rashes can also occur in IgG4-RD. Correct diagnosis relies on serum IgG4 levels and histological and immunohistochemical analysis.

Funding

This work was supported by Shanghai Municipal Health Commission under Grant numbers 202150013.

References

1. Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. Comprehensive diagnostic criteria for IgG4-Related Disease (IgG4-RD), 2011. Mod Rheumatol. 2012;22(1):21-30.
2. Maritati F, Peyronel F, Vaglio A. IgG4-related disease: A clinical perspective. Rheumatology (Oxford). 2020;59(Suppl 3):iii123-31.
3. Cheuk W, Lee KC, Chong LY, Yuen ST, Chan JK. IgG4-related Sclerosing disease: A potential new etiology of cutaneous pseudolymphoma. Am J Surg Pathol. 2009;33(11):1713-9.
4. Khosroshahi A, Carruthers MD, Deshpande V, Leb L, Reed JI, Stone JH. Cutaneous immunoglobulin G4-related systemic disease. Am J Med. 2011;124(10):e7-8.
5. Sato Y, Takeuchi M, Takata K, Ohno K, Iwaki N, Orita Y, et al. Clinicopathologic analysis of IgG4-related skin disease. Mod Pathol. 2013;26(4):523-32.
6. Yamada K, Hamaguchi Y, Saeki T, Yagi K, Ito N, Kakuchi Y, et al. Investigations of IgG4-related disease involving the skin. Mod Rheumatol. 2013;23(5):986-93.
7. Tokura Y, Yagi H, Yanaguchi H, Majima Y, Kasuya A, Ito T, et al. IgG4-related skin disease. Br J Dermatol. 2014;171(5):959-67.
8. Stone J H, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med. 2012;366(6):539-51.
9. Kamisawa T, Okazaki K, Kawa S, Shimosegawa T, Tanaka M; Research Committee for Intractable Pancreatic D. Japanese consensus guidelines for management of autoimmune pancreatitis: III. Treatment and prognosis of AIP. J Gastroenterol. 2010;45(5):471-7.
10. Ghazale A, Chari ST, Zhang L, Smyrk TC, Takahashi N, Levy MJ, et al. Immunoglobulin G4-associated cholangitis: Clinical profile and response to therapy. Gastroenterology. 2008;134(3):706-15.