Clinical Case Report

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A case of immunoglobulin G4-related lung disease with bilateral diffuse infiltration

A case report

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Abstract

Rationale: Immunoglobulin (Ig) G4-related disease (IgG4-RD) is a rare and chronic progressive autoimmune disease. It is a novel clinical entity characterized by elevated serum IgG4 concentration and tissue infiltration by $IgG4^+$ plasma cells. IgG4-related lung disease (IgG4-RLD) has been described as interstitial pneumonia and inflammatory pseudotumor, with various abnormal radiographic patterns. We report a case of IgG4-related lung disease with bilateral diffuse infiltration.

Patient concerns: A 65-year-old woman was admitted to our hospital because of cough, sputum, and fever. Chest computed tomography (CT) revealed multifocal areas of consolidations, nodules, and ground glass opacities in both lungs. She still had fever after anti-infective therapy.

Diagnoses: Bronchial bronchoscopy and percutaneous lung biopsy were performed, resulted in a pathological diagnosis of IgG4-RLD.

Interventions: The patient was started on oral prednisolone 30 mg/day for 28 days, and then was gradually tapered.

Outcomes: After one week treatment, the temperature was stable, CT showed significant improvement in the areas of consolidations and nodules.

Lessons: It is a typical case of IgG4-RLD. This case indicated that suggestive evidence, radiological appearances, serum tests, pathological characteristics, and classic therapy IgG4-RLD. It is a rare disease that needs our more attention in future.

Abbreviations: AIP = autoimmune pancreatitis, CRP = C-reactive protein, CT = computed tomography, HPF = high-power field, IgG4 = immunoglobulin (Ig) G4, IgG4-RD = immunoglobulin (Ig) G4-related disease, IgG4-RLD = immunoglobulin (Ig) G4-related lung disease, PCT = procalcitonin, WBC = white blood cell.

Keywords: IgG4-related disease, IgG4-related lung disease, pulmonary infection

1. Introduction

Immunoglobulin (Ig) G4-related disease (IgG4-RD) is a novel clinical entity characterized by elevated serum IgG4 concentration and tissue infiltration by IgG4+ plasma cells. IgG4-RD has been of interest since 2001, when Hamano et al[1] reported infiltration of IgG4-positive plasma cells in the pancreas. Over the past decade, the disease has emerged as a unified systemic disease that links many individual organ conditions once considered to be unrelated.[2,3] Involvement of nearly every anatomic site has been reported, but the most commonly affected organs or anatomic sites are the pancreas, biliary tract, major salivary glands (submandibular, parotid), lacrimal glands, retroperitoneum, and lymph nodes.[4,5] IgG4-related lung disease (IgG4-RLD) has been described as interstitial pneumonia and inflammatory pseudotumor.[6,7] IgG4-RLD is known to present with various abnormal radiographic patterns.[8]

Here, we report a case of IgG4-RLD with bilateral diffuse infiltration.

2. Case report

A 65-year-old woman was admitted to our hospital because of cough, sputum, and fever. No particular personal and family medical history was reported, and she never smoked. Physical examination showed moist rales on both sides, and no other abnormal vital signs.

Blood examination showed white blood cell (WBC) 7.95×10^9/L, procalcitonin (PCT) 0.073 ng/mL, C-reactive protein (CRP) 31.2 mg/L, IgG 23.3 g/L, IgG 942 IU/mL, and normal levels of IgA, IgM, G test, and GM test.

Chest computed tomography (CT) revealed multifocal areas of consolidations, nodules, and ground glass opacities in both lungs, with cervical and axillary lymph node swelling and a little pleural effusion (Fig. 1). After 7 days treatment of moxifloxacin, she still had fever. Bronchial bronchoscopy and percutaneous lung biopsy were performed. All the bronchia were unobstructed, and a lot of purulent secretions and punctate hemorrhages were found. No neoplasm or caseous lesions were seen (Fig. 2).The pathological findings from the

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The authors have no conflicts of interest to declare.

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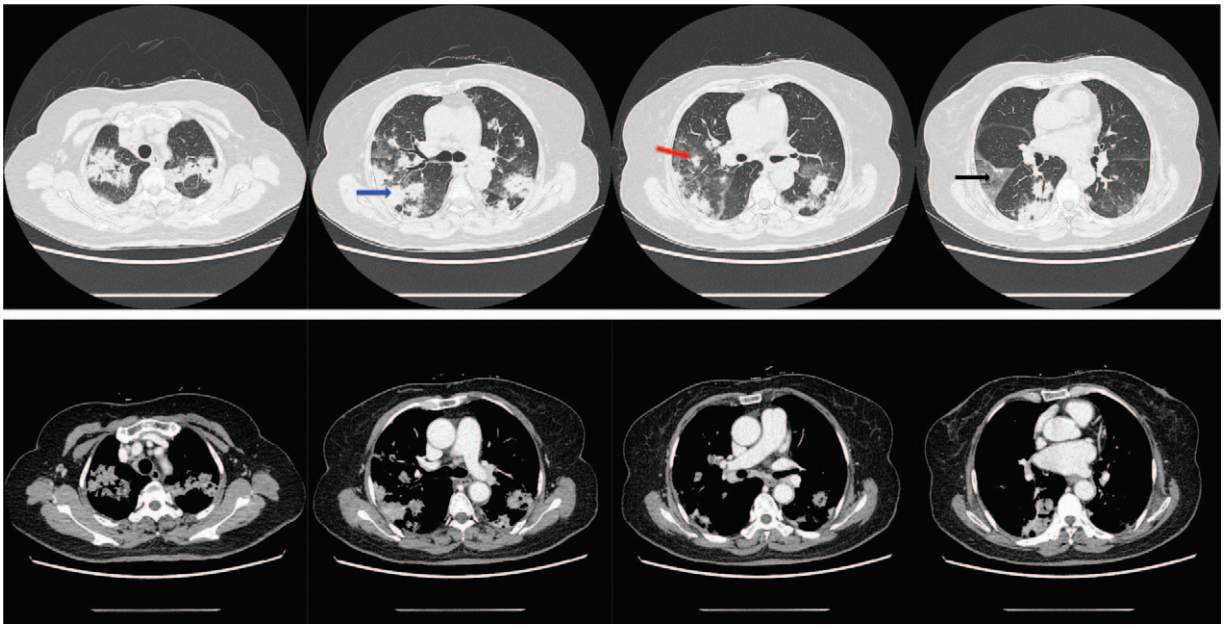

Figure 1. Computed tomography (CT) images at admission. At admission, CT scan showed multifocal areas of consolidations (blue arrow), nodules (red arrow), and ground glass opacities (black arrow) in both lungs, with cervical and axillary lymph node swelling and a little pleural effusion.

biopsy showed infiltration of lymphocytes and plasma cells (Fig. 3). Persistent fever did not improve. Chest CT was performed again, and indicated progression of the lesions (Fig. 4).

The patient and her family went to Peking Union Medical College Hospital with her percutaneous lung biopsy specimens. Immunohistochemistry showed more than 40% of the total plasma cells were IgG4-positive, and >50 IgG4-positive plasma cells/high-power field (HPF). Serum levels of IgG4 were elevated to 10,200 mg/L.

We diagnosed the case as IgG4-RLD. The patient was started on oral prednisolone 30 mg/d for 28 days, and then was gradually tapered. After 1 week of treatment, the temperature was stable, and CT showed significant improvement in the areas of consolidations and nodules (Fig. 5). As of the time of writing, the patient has remained well without disease progression.

Informed consent was signed by the patient.

3. Discussion

The most accurate assessment of IgG4-RD is based on a full clinical history, physical examination, selected laboratory investigations, and appropriate radiology studies.[9] A detailed review of past medical problems often reveals unrecognized manifestations of IgG4-RD.[10] The symptoms, physical examination, and routine blood test of IgG4-RLD, are usually not specific. Cough, sputum, and fever were the main symptoms of this case, and blood test just showed inflammation. According to the symptoms, physical examination, and routine blood test, we diagnosed pneumonia initially, and gave antibiotic treatment. So it is important to do further test and think of more possible diagnoses after initial treatment failure.

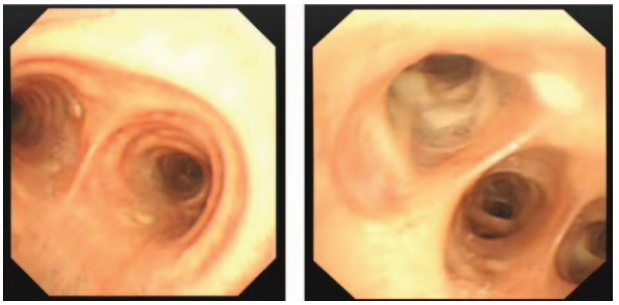

Figure 2. Bronchoscopy. All the bronchia were unobstructed, a lot of purulent secretions and punctate hemorrhages were found. No neoplasm or caseous lesion was seen.

In 2001, type 1 autoimmune pancreatitis (AIP) was associated with an elevated serum IgG4 concentration.[11] Elevated serum IgG4 concentration was included in both IgG4-RD and type 1 (IgG4-related) AIP diagnostic criteria.[12–14] Other studies have demonstrated variability in the sensitivity of serum IgG4 elevation for the diagnosis of IgG4-RD. Between 3% and 30% of IgG4-RD patients had normal serum IgG4 concentrations.[12–16] The serum levels of IgG4 of this patient were elevated to 10,200 mg/L, which is more than 1350 mg/L. This is the specific evidence to indicate the diagnosis of IgG4-RD, but the test is not developed in every hospital; the patient went to Peking Union Medical College Hospital to do further test. Also, we should recognize that the serum level of IgG4 is only 1 of the diagnostic criteria of IgG4-RD, and it could be normal in some IgG4-RD cases.

IgG4-related disease, which is a newly recognized fibroinflammatory condition characterized by several features and previously referred to as IgG4-related sclerosing disease or hyper-IgG4 disease, may occur in the lung, and involve the alveolar parenchyma, airways, and pleura.[17] Inoue et al[18] found that the radiologic features of IgG4-related lung disease could be classified into 4 types: solid nodular, round-shaped ground glass opacity, alveolar interstitial, and bronchovascular. Furthermore, Umeda et al[8] reported the following 8 patterns of pulmonary findings in IgG4-RRD: bronchial wall thickening;

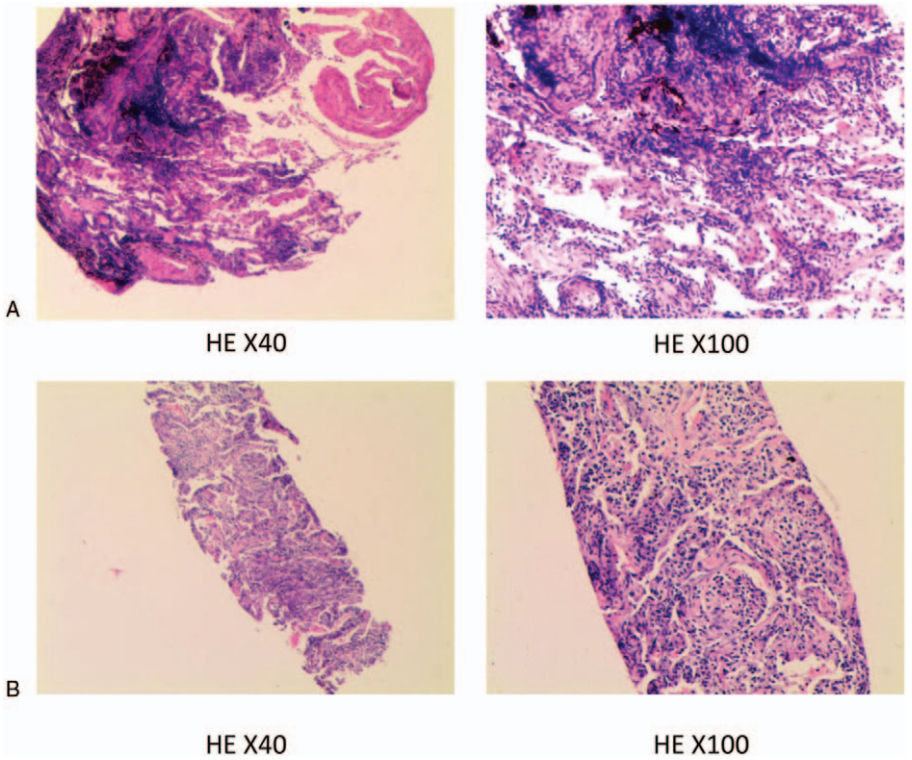

Figure 3. Biopsy pathology. (A) Bronchial bronchoscopy showed a large number of interstitial inflammatory cells, the alveolar septa were slightly wider, and the alveolar epithelial cells proliferated. (B) Percutaneous lung biopsy showed a lot of plasma cells and lymphocytes infiltration, alveolar septum slightly widened, hyperplasia of fibrous tissue, and pink exudate in some alveolar space.

consolidation; nodule; ground glass opacity; interlobular thickening; honeycombing; pleural thickening/effusion; and mediastinal lymphadenopathy. A few cases of IgG4-related interstitial pneumonia have been newly reported.[18,19–22] Bilateral ground glass opacities were the most common radiological findings, followed by reticular shadows.[18,22] This case was accompanied by bilateral diffuse infiltration, and interstitial pneumonia was found in CT scan. But, as mentioned

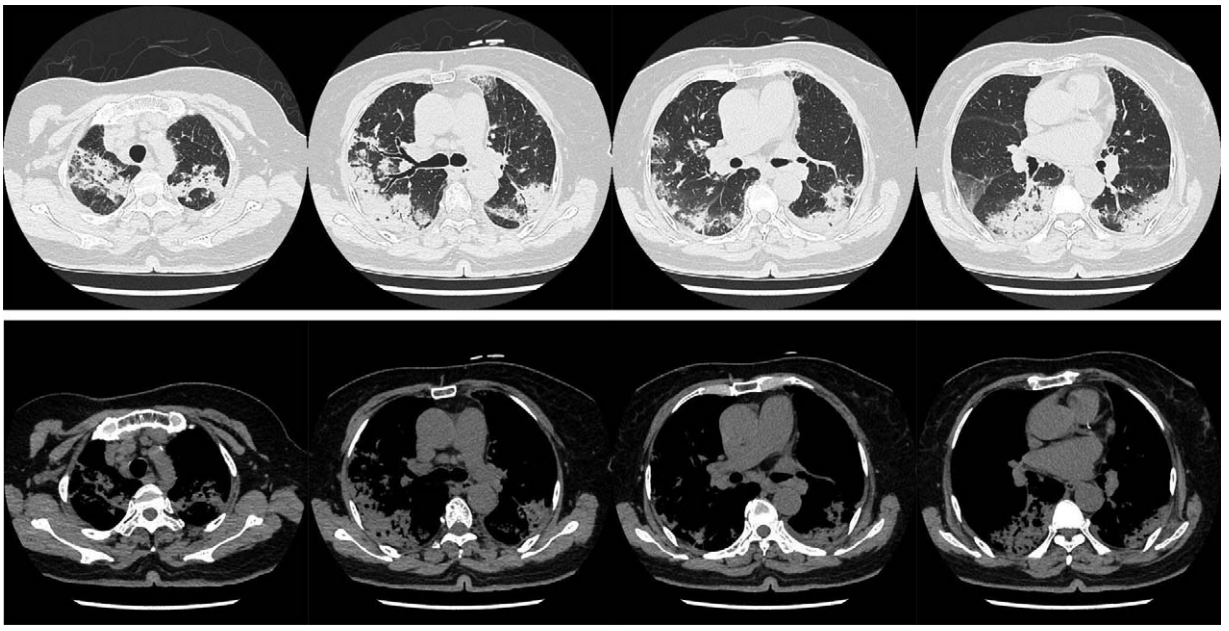

Figure 4. Computed tomography (CT) images after antibiotic treatment. After 7 days treatment of moxifloxacin, chest CT was performed again, and indicated progression of the lesion.

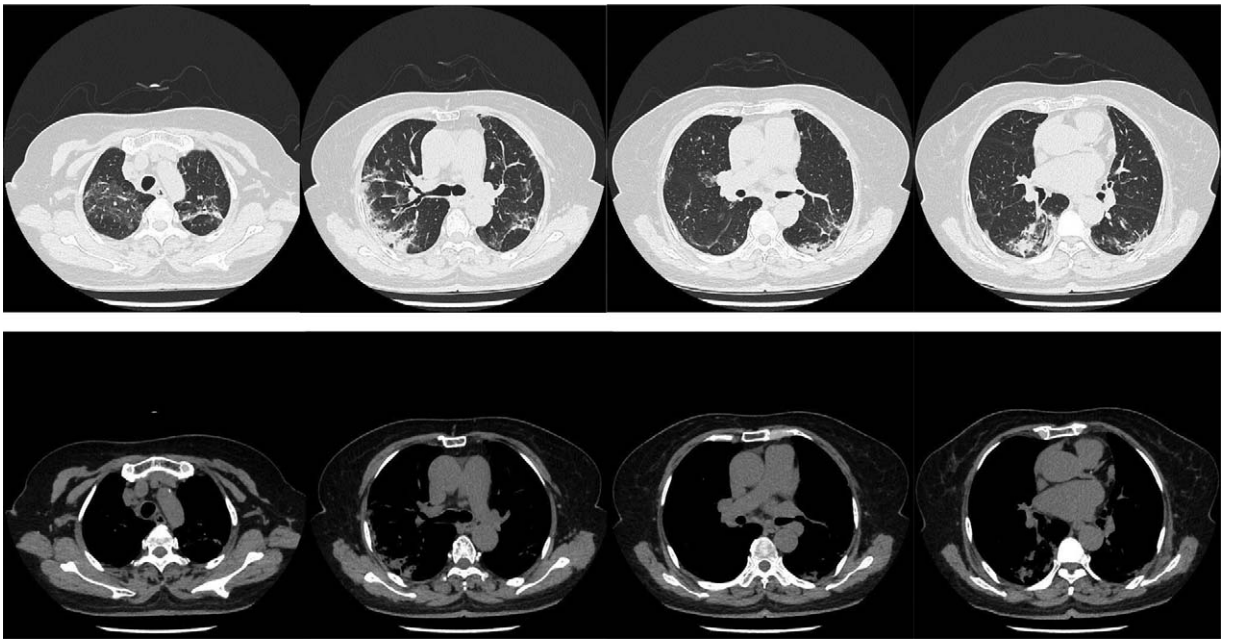

Figure 5. Computed tomography (CT) images after glucocorticoids treatment. We diagnosed the case as IgG4-RLD. The patient was started on oral prednisolone 30 mg/d. After 1 week of treatment, CT showed significant improvement in the areas of consolidations and nodules.

above, there was no specificity in CT imaging. The diagnosis needs more indications and evidences.

Diagnostic confirmation by biopsy is strongly recommended for the exclusion of malignancies and other IgG4-RD mimics. Biopsy is typically necessary to exclude malignancy. Although there are comprehensive diagnostic criteria for IgG4-RD, the clinical assessment, laboratory evaluation, and imaging characteristics are often unable to distinguish the tumefactive lesions of IgG4-RD from cancer. International consensus guidelines outline the histopathologic and immunohistochemistry features that support the diagnosis of IgG4-RD, and, in the proper clinical setting, can be viewed as diagnostic.[23,24] Typical infiltration of plasma cells and lymphocyte, more than 40% of the total plasma cells were IgG4-positive, and >10 IgG4-positive plasma cells/ HPF, these are pathological characteristics of IgG4-RD.[25] The pathological findings from the biopsy showed infiltration of lymphocytes and plasma cells. Immunohistochemistry showed more than 40% of the total plasma cells were IgG4-positive, and >50 IgG4-positive plasma cells/ HPF. The immunohistochemistry were done outside our hospital, it was a pity that we were not able to obtain the pathological pictures.

All patients with symptomatic, active IgG4-RD require treatment, some urgently. Glucocorticoids are the first-line agent for remission induction in all patients with active, untreated IgG4-RD unless contraindications to such treatment are present.[9] This patient was started on oral prednisolone 30 mg/d for 28 days, and then was gradually tapered. After 1 week of glucocorticoids treatment, CT showed obvious improvement of lesions. There are many diseases that respond well to glucocorticoids, such as eosinophilic pneumonia, organized pneumonia, and so on. However, there must be sufficient evidence to warrant treatment with glucocorticoids, and this was only available after additional biopsies and IgG4 measurements were performed.

4. Conclusions

This is a typical case of IgG4-RLD. This case indicated the suggestive evidence, radiological appearances, serum tests, pathological characteristics, and classic therapy of IgG4-RLD. It is a rare disease that needs more of our attention in future.

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