Isolated pulmonary manifestation of IgG4 disease with response to steroids and relapse: A rare case report

Sir,

IgG4-related disease is currently considered as a disease of unknown etiology, with commonly shared features that include an elevated serum concentration of IgG4-pronounced lymphocytes and IgG4-positive plasma cell infiltrates and fibrosis with consequent swelling of the involved organs, as well as nodulations and hyperplastic lesions. Clinical manifestations may include enlargement of involved organs, obstruction and pressure symptoms because of hyperplasia and dysfunction because of cell infiltration and fibrosis. Pathological features including the presence of marked lymphocyte, plasma cell infiltration, and fibrosis with IgG4-positive plasma cell infiltrates, that is, an IgG4/IgG ratio of >40%, and the occurrence of 10 IgG4-positive cells per high-power field (HPF) have been proposed.[1]

A 46-year-old, nonsmoking man, presented with a history of chest pain and hemoptysis since three months. He was diagnosed to have pneumonia at another hospital and was treated with oral antibiotics.

As the patient's symptoms did not abate with treatment, he was referred to our center for further management. On physical examination, his vital signs were within normal limits. He was not in obvious distress. The systemic examination was unremarkable.

On evaluation, his chest x-ray revealed nonhomogenous consolidation of the right upper zone, with an air bronchogram. His blood counts and routine biochemistries were normal. His Mantoux test and sputum smear and culture for *Mycobacterium tuberculosis* bacilli were negative. We proceeded to do computed tomography (CT) of the thorax, which revealed collapse and consolidation in the right upper lobe with adjacent areas of branching opacities [Figure 1]. With a wide range of differentials in mind, a battery of blood tests were further ordered. These revealed a serum IgG4 of 4264 mg/L (normal range 100 - 1400 mg/L). Serum antineutrophilic antibodies were not detected. Rheumatoid factor (RA) and C-reactive protein (CRP) were within normal limits. Hence, he was considered to have pulmonary IgG4 disease with differentials, such as, sarcoidosis, bronchogenic carcinoma, lymphoma, and Castleman disease.[2]

A CT-guided biopsy was performed to determine the etiology, which revealed a dense lymphoplasmacytic infiltrate, with entrapped bronchial glands (arrow) [Figure 2]. There were dense infiltrates of plasma cells and IgG4 immunostaining showed positive cytoplasm staining in most of the plasma cells. Quantifying, 60–80 IgG4 positive plasma cells per HPF were found. The ratio of IgG: IgG4 positive plasma cells were 60–80%. This confirmed the suspicion of IgG4 disease.

The patient was treated with a high dosage of corticosteroids. A dose of 0.5 mg/kg/body of prednisolone was prescribed for a month, with subsequent gradual tapering, at the rate of 4 mg per month. A follow-up CT of the chest after four months showed that the consolidation had reduced in size, with areas of scarring, and his serum IgG4 levels dropped significantly to 2881mg/l. The steroid dose was further reduced.

A review after six months from the start of treatment, revealed a recurrence of the consolidation [Figure 3] with a simultaneous increase in the IgG4 levels to 3352 mg/l. He was diagnosed with recurrence of pulmonary IgG4 disease. The prednisolone dose was hiked to 0.75 mg/kg body weight a day and a follow-up CT scan after three months showed near complete resolution of the consolidation [Figure 4] and the IgG4 level decreased to 1190 mg/l. The pathological features proposed for the diagnosis of IgG4 disease include, the presence of marked lymphocyte plasma cell infiltration and fibrosis, with IgG4-positive plasma cell infiltrates, that is, aIgG4/IgG ratio of >40%, and the occurrence of 10 IgG4-positive cells per HPF.[1] The characteristic CT features of IgG4 -related pulmonary lesions include, (a) solitary nodular opacities, (b) Round, ground glass–like opacities with relatively discrete margins, (c) honeycomb lung opacities, and (d)bronchovascular type.

Other organs that are commonly involved include, the pancreas, bile ducts, lacrimal glands, salivary glands, central nervous system, thyroid, lungs, gastrointestinal tract, kidneys, prostate, retroperitoneum, aorta, lymph nodes, skin, and mammary glands.[3] The present case showed collapse and consolidation in the right upper lobe with adjacent areas of branching opacities. In addition, the immunohistochemical findings of the biopsy specimens were similar to those observed in earlier studies.

Castleman disease is characterized by lymph node enlargement because of hyperplasia of the abnormal lymphoid follicles and paracortical lymphocytic hyaline vascular stroma or plasmacytosis.[4] IgG4 diseases respond well to glucocoticosteriods within several weeks, especially

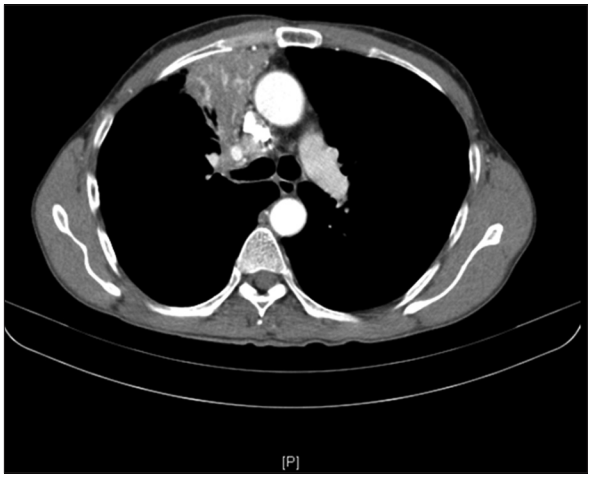

Figure 1: CT showed collapse and consolidation in the right upper lobe with adjacent areas of branching opacities

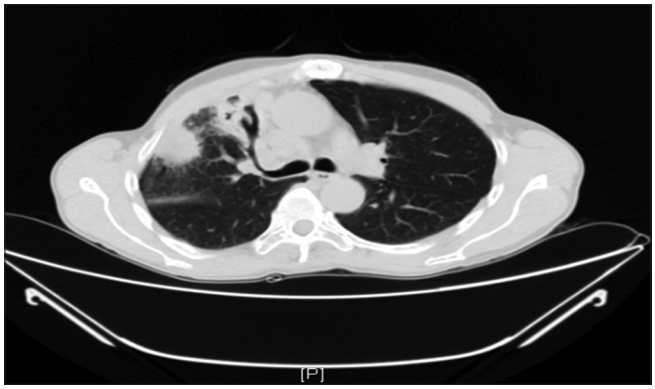

Figure 3: CT of the chest shows there was recurrence of the lesion

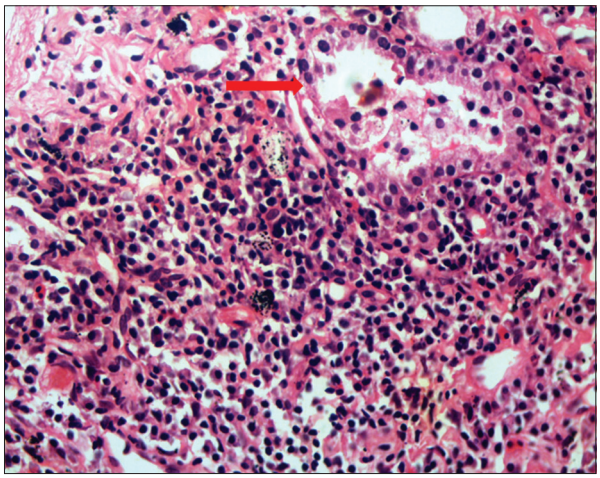

Figure 2: The histology photographed revealed a dense lymphoplasmacytic infiltrate with entrapped bronchial glands (arrow). The IgG immunostain showed dense infiltrates of plasma cells. The IgG4 immunostain showed positive cytoplasmic staining in most of the plasma cells

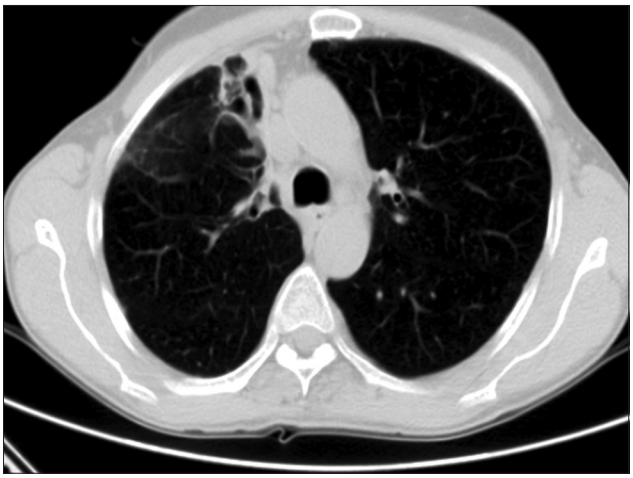

Figure 4: CT scan shows the resolved lesion

with symptomatic improvement, reduction in the size of the masses, and often a decrease in the serum levels of IgG4. However, some require a few months to respond and there are some patients who have a relapse. Our patient initially responded well to corticosteroids, but later relapsed, when the dosage of steroids was reduced. Those who do not respond very well generally have advanced fibrotic changes; we recommend starting with 0.75 mg/kg body weight of prednisolone and follow-up after a few months. Generally, the disease responds well within a few months. Once a significant response is clinically evident in the affected organ system, the dose of glucocorticoids can be gradually tapered by 5 mg every month.

Patients who are resistant to glucocorticoids or who are unable to maintain the remission phase, may need alternate options. The choices are azathioprine (2 mg/kg/day), mycophenolate mofetil (up to 2.5 g/day as tolerated) and B-cell depletion therapy with rituximab.[5]

The IgG4 diseases are not well-defined. Some patients improve spontaneously without treatment, but many relapse.

The solitary manifestation of an IgG4-related pulmonary lesion may show findings similar to those of sarcoidosis and Castleman disease. Therefore, differentiation between these conditions, correlation with serum IgG4 levels, and the histopathology of lung biopsy specimens is necessary.

In conclusion, IgG4 disease has a myriad of pulmonary manifestations. It should be considered in cases of non-resolving pneumonia and atypical parenchymal opacities, as described earlier. Histopathology with IgG4 imunostaining and measuring serum levels of IgG4 help in clinching the diagnosis. The correlation of clinicoradiological and pathological features is of extreme importance for the diagnosis of IgG4-related lung disease. This disease is steroid-responsive and these have to given for an adequate duration, of at least one year, with appropriate gradual tapering.

Ranjit Kumar Singh, Thomas Jesudason Barney Isaac, Balamugesh Thangakunam,[1] Nittin Mathews[1], Anila Korula[1]

Departments of Pulmonary Medicine and [1]Pathology, Christian Medical College, Vellore, Tamil Nadu, India
E-mail: ranjitcmc. 2011@gmail.com

REFERENCES

1. Khosroshahi A, Stone JH.A clinical overview of IgG4-related systemic disease. Curr Opin Rheumatol 2011; 23:57-66.
2. Ryu JH, Sekiguchi H, Yi ES. Pulmonary manifestations of immunoglobulin G4 related sclerosing disease. Eur Respir J 2012;39:180-6.
3. Kitada M, Matuda Y, Hayashi S, Ishibashi K, Oikawa K, Miyokawa N, *et al*. IgG4-related lung disease showing high standardized uptake values on FDG-PET: Report of two cases. J Cardiothorac Surg 2013;8:160.
4. Menke DM, Tiemann M, Camoriano JK, Chang SF, MadanA, Chow M, *et al*. Diagnosis of castleman's disease by identification of an immunophenotypically aberrant population of mantle zone B lymphocytes in paraffin-embedded lymph node biopsies. Am J Clin Pathol 1996;105:268-76.
5. Khosroshahi A, Bloch DB, Deshpande V, Stone JH. Rituximab therapy leads to rapid decline of serum IgG4 levels and prompt clinical improvement in IgG4-related systemic disease. Arthritis Rheum 2010;62:1755-62.

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/0970-2113.168110