

## Immunoglobulin G4-related disease presenting as a mass in the lung

Sevda Akyol<sup>1</sup>, Seçil Hasdemir<sup>2</sup>, Elif Ülker Akyıldız<sup>3</sup>

<sup>1</sup>Department of Pathology, Yüksekova State Hospital, Hakkari, Turkey

<sup>2</sup>Department of Pathology, Midyat State Hospital, Mardin, Turkey

<sup>3</sup>Department of Pathology, Uludağ University Medicine Faculty, Bursa, Turkey

Immunoglobulin G4-related disease (IgG4-RD) is a fibroinflammatory disease which can involve any organ in the body<sup>1</sup> Lung involvement of IgG4-RD is not uncommon.

A 25-year-old female patient was admitted to our hospital for the tests requested during the job application. She had no complaints and no known systemic disease. Computed tomography revealed a localized subpleural mass in the left lung upper lobe (Figure 1). Positron emission tomography was performed to assess the spread, as malignancy was suspected clinically. The mass was 1.5 cm in diameter and increased 18F-fluorodeoxyglucose uptake with a maximum standardized uptake value of 3. Lung wedge resection was performed for diagnostic purposes. A gray-yellow colored, relatively well-circumscribed lesion was observed on the lung wedge resection material (Figure 2). Microscopic examination revealed a nodular lesion in the lung parenchyma characterized by intense lymphoplasmacytic infiltration, lymphoid follicles, and fibrosis. In immunohistochemical studies, approximately 150 to 200 plasma cells showed positive staining with the IgG4 antibody in a high-power field (HPF) (Figure 3). The ratio of IgG4/immunoglobulin G (IgG)-positive plasma

cells was over 50%. When the patient's serum immunoglobulin levels were analyzed after the operation, the level of serum IgG4 was found to be 141 mg/dL (range, 0 to 125 mg/dL). As a result of clinical, laboratory, morphological, and immunohistochemical staining, the patient was found to be compatible with IgG4-RD. The patient was followed postoperatively and no additional treatment was given.



**Figure 1.** T1-weighted axial magnetic resonance images of the lung showing a localized subpleural mass in the left lung upper lobe.

**Received:** December 30, 2020 **Accepted:** March 17, 2021 **Published online:** June 24, 2021

**Correspondence:** Sevda Akyol, MD. Yüksekova Devlet Hastanesi Patoloji Kliniği, 30300 Yüksekova, Hakkari, Türkiye.  
Tel: +90 544 - 224 65 63 e-mail: sevdaakyol1@gmail.com

### Citation:

Akyol S, Hasdemir S, Ülker Akyıldız E. Immunoglobulin G4-related disease presenting as a mass in the lung. Arch Rheumatol 2021;36(x):i-iii.

©2021 Turkish League Against Rheumatism. All rights reserved.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes (<http://creativecommons.org/licenses/by-nc/4.0/>).



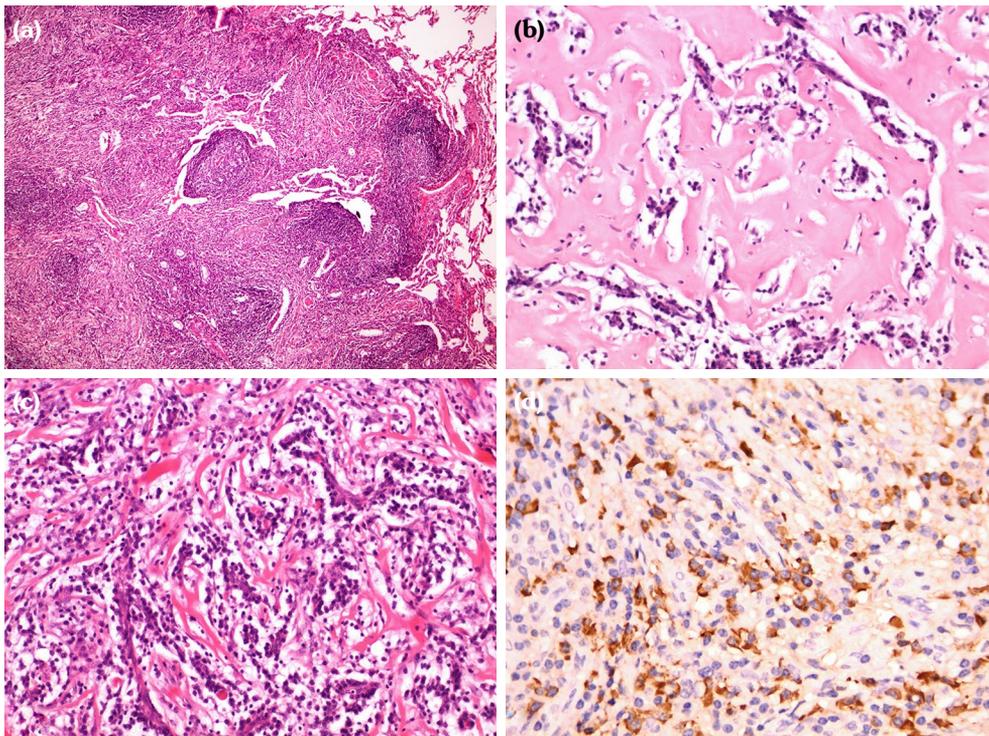
**Figure 2.** A macroscopic view of lesion on cross-sectional surface of lung wedge resection material.

Immunoglobulin G4-related disease may present with symptoms resulting from damage of the affected organ, as well as with the

incidental radiological findings without any clinical symptoms. The first pulmonary involvement cases were reported in 2004 and they were found to be associated with autoimmune pancreatitis.<sup>2,3</sup> Our patient had no complaints and no known systemic diseases. She had asymptomatic IgG4-RD detected by incidental radiological findings.

Furthermore, IgG4-RD may occur radiologically as hilar or mediastinal lymphadenopathy, bronchovascular bundle thickening, nodules, pleural involvement, ground-glass opacity, and alveolar interstitial involvement.<sup>4</sup> It is most commonly seen as lymphadenopathy and solitary nodule, respectively. When encountered as a nodule, lung cancer should be considered in the differential diagnosis.<sup>1</sup> In our case, the lesion was radiologically in the form of a solid nodule which suggested a suspicion of malignancy.

The diagnosis of IgG4-RD is based on three criteria: clinical, laboratory, and histopathological features. If these three criteria exist, the diagnosis



**Figure 3.** (a) Lymphoplasmacytic inflammatory cell infiltration accompanied by pronounced lymphoid follicles (H-E,  $\times 100$ ). (b) Fibrosis (H-E,  $\times 100$ ). (c) Accumulation of plasma cells in perivascular areas of lesion (H-E,  $\times 100$ ). (d) Immunoglobulin G4-positive plasma cells ranging from 150 to 200 in a HPF (IHC,  $\times 400$ ).

H-E: Hematoxylin-eosin; HPF: High-power field; IHC: Immunohistochemistry.

of IgG4-RD is definitive. If only one of the laboratory or histopathological criteria is present in the patient along with clinical findings, the patient is likely to have IgG4-RD.<sup>5</sup> In our case, all these three criteria were present.

The serum IgG4 level in IgG4-RD is expected to be above 135 mg/dL; however, only 50% of those who have IgG4-RD have high serum levels of IgG4.<sup>6</sup> On the other hand, serum IgG4 levels can be high in other diseases, such as pancreatic cancer, atopic diseases, and infections.

Immunoglobulin G4-related disease is characterized by histopathologically storiform fibrosis, lymphoplasmacytic infiltration, and obliterative phlebitis.<sup>7</sup> Inflammatory infiltration is rich in IgG4-positive plasma cells and may be accompanied by eosinophils.<sup>8</sup> In immunohistochemical studies, more than 50 IgG4-positive plasma cells are present in the HPF. The ratio of IgG4-positive cells/IgG-positive cells should be more than 40%.<sup>7</sup>

The differential diagnosis of IgG4-RD includes multiple myeloma, lymphoproliferative diseases, inflammatory myofibroblastic tumor, nodular lymphoid hyperplasia, multicentric Castleman disease. Accurate diagnosis is of utmost importance in patient management, as IgG4-RD responds well to prednisone treatment. If histopathologically compatible findings are present, IgG4-RD should be considered in the differential diagnosis.

In conclusion, we presented a case of immunoglobulin G4-related disease presenting as a mass. In this disease, it may be possible to prevent organ damage with early diagnosis and treatment. Clinical, laboratory and histopathological findings

should be evaluated together for an early and accurate diagnosis.

#### **Declaration of conflicting interests**

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

#### **Funding**

The authors received no financial support for the research and/or authorship of this article.

## **REFERENCES**

1. Ryu JH, Sekiguchi H, Yi ES. Pulmonary manifestations of immunoglobulin G4-related sclerosing disease. *Eur Respir J* 2012;39:180-6.
2. Taniguchi T, Ko M, Seko S, Nishida O, Inoue F, Kobayashi H, et al. Interstitial pneumonia associated with autoimmune pancreatitis. *Gut* 2004;53:770.
3. Duvic C, Desrame J, Lévêque C, Nedelec G. Retroperitoneal fibrosis, sclerosing pancreatitis and bronchiolitis obliterans with organizing pneumonia. *Nephrol Dial Transplant* 2004;19:2397-9.
4. Inoue D, Zen Y, Abo H, Gabata T, Demachi H, Kobayashi T, et al. Immunoglobulin G4-related lung disease: CT findings with pathologic correlations. *Radiology* 2009;251:260-70.
5. 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;22:21-30.
6. 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.
7. Stone JH, Zen Y, Deshpande V. IgG4-related disease. *N Engl J Med* 2012;366:539-51.
8. Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, et al. Consensus statement on the pathology of IgG4-related disease. *Mod Pathol* 2012;25:1181-92.