Review Article

Access this article online

Quick Response Code:

Website: www.eurasianjpulmonol.com

DOI: 10.4103/ejop.ejop_112_20

Intrathoracic manifestations of immunoglobulin G4-related disease: A pictorial review

Umran Ozden Sertcelik[1,2], Asli Oncel[2], Deniz Koksal[2]

ORCID:
Umran Ozden Sertcelik: https://orcid.org/0000-0001-8394-6544
Asli Oncel: https://orcid.org/0000-0001-7708-1732
Deniz Koksal: https://orcid.org/0000-0001-8374-3691

Abstract:

Immunoglobulin G4-related disease (IgG4-RD) is an increasingly recognized systemic fibro-inflammatory disease associated with elevated serum IgG4 levels. It affects virtually any organ system including the gastrointestinal system, salivary glands, periorbital tissues, kidneys, lungs, lymph nodes, central nervous system, large vessels, thyroid, and skin. Although the involved organ systems vary between studies and are influenced by the medical center and specialty, the most frequent manifestation of IgG4-RD is regarded to be type 1 autoimmune pancreatitis. The incidence of intrathoracic involvement is not known exactly, but it is thought to be relatively rare. Intrathoracic manifestations of IgG4-RD can be observed in airways (tracheobronchial stenosis, thickening of bronchovascular bundles), pulmonary parenchyma (nodules, masses, interstitial lung disease), pleura (pleural thickening, nodules, effusion), and mediastinum (lymphadenopathy, fibrosing mediastinitis). This review aimed to briefly describe the pathogenesis, histopathology, clinical features, diagnosis, and treatment of IgG4-RD; and make a pictorial review of its intrathoracic manifestations.

Keywords:

Airway disease, immunoglobulin G4, immunoglobulin G4-related disease, lung, mediastinum, pleura, pulmonary, thoracic

Introduction

Immunoglobulin G4-related disease (IgG4-RD) is an increasingly recognized systemic fibro-inflammatory disease associated with elevated serum IgG4 levels.[1,2] It was first described as an autoimmune-mediated and steroid-responsive form of pancreatitis in 1995.[3] Subsequently, in 2001, this type of autoimmune pancreatitis had been linked to elevated levels of serum IgG4.[4] IgG4-RD can affect virtually any organ system including the gastrointestinal system, salivary glands, periorbital tissues, kidneys, lungs, lymph nodes, central nervous system, large vessels, thyroid, and skin.[2,5] Single or multiple organ systems can be involved as tumefactive lesions which may occur simultaneously or consecutively. The exact prevalence of IgG4-RD is unknown. In Japan, the prevalence has been reported to be approximately 0.28–1.08/100,000 of the population.[6] However, as recognition of this clinical entity increases, this estimate seems to an underestimate of the true disease prevalence. IgG4-RD is mainly described in adults, more often in males (70%–80%), with a median age of 40–65 years (range = 17–80 years).[7]

Although the involved organ systems vary between studies and are influenced

[1]Department of Chest Diseases, Ankara City Hospital, [2]Department of Chest Diseases, Hacettepe University School of Medicine, Ankara, Turkey

Address for correspondence:
Dr. Umran Ozden Sertcelik, Department of Chest Diseases, Ankara City Hospital, Ankara, Turkey.
E-mail: umranozdensertcelik@yahoo.com

Received: 31-10-2020
Accepted: 01-01-2021
Published: 12-08-2021

How to cite this article: Sertcelik UO, Oncel A, Koksal D. Intrathoracic manifestations of immunoglobulin G4-related disease: A pictorial review. Eurasian J Pulmonol 2021;23:83-8.

by the medical center and specialty, the most frequent manifestation of IgG4-RD is regarded to be type 1 autoimmune pancreatitis.[1] Intrathoracic involvement is relatively rare and observed in airways, pulmonary parenchyma, pleura, and mediastinum.[7] This review aimed to briefly describe the pathogenesis, histopathology, clinical features, and diagnosis of IgG4-RD; and make a pictorial review of its intrathoracic manifestations.

Pathogenesis

The pathogenesis of IgG4-RD is not fully understood. However, there is growing evidence that it has an autoimmune basis, with important roles of both B- and T-cells, especially CD4+ and T-follicular helper cells (Tfh). Tfh cells, which reside mainly within and around lymph node germinal centers, have been found to be increased in the peripheral blood, and the affected tissues of patients with IgG4-RD.[8] Several candidate autoantigens such as galectin-3, laminin 111, and annexin A11 have been reported, but all require confirmatory studies and it is likely that more than one autoantigen can trigger this condition.[9-11] The immune complex deposition has been reported in affected tissues such as the pancreas.[12] Certain genetic factors of the host have been identified for IgG4-RD, including human leukocyte antigen (HLA) haplotypes and non-HLA genes.[13-15]

IgG4 antibodies do not seem to be pathogenic themselves, but rather represent an epiphenomenon, possibly having an anti-inflammatory role during the pathogenesis of the disease. They are produced in response to cytokines such as interleukin-4 as a part of the immune response.[16] The decline of IgG4 concentrations following the achievement of disease control supports the concept that IgG4 itself does not drive the disease.

Histopathology

The hallmarks of histopathology in IgG4-RD are dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells in the affected tissue, usually accompanied by a variable degree of fibrosis and often by obliterative phlebitis and an increased number of eosinophils. The fibrosis associated with IgG4-RD usually has a characteristic "storiform" pattern, typified by a cartwheel appearance of the arranged fibroblasts and inflammatory cells.[17]

IgG4 immunostaining is an essential test for the pathologic diagnosis of IgG4-RD. This applies particularly to cases without elevated levels of serum IgG4. The presence of >10 IgG4+ plasma cells in each area at high power magnification has been proposed as a component of a comprehensive diagnostic panel.[18] However, the appropriate cut-off point may vary from organ to organ based on the predominance of fibrosis at the time of initial diagnosis.[17] IgG4+/IgG+ cell ratio is a more powerful tool for establishing the diagnosis of IgG4-RD. As noted some inflammatory lesions that are not related to IgG4-RD are associated with high numbers of IgG4+ plasma cells simply because of the abundance of plasma cells. Therefore, the ratio of IgG4+/IgG+ cells in the tissue is over 40% is suggested for the proper diagnosis.[17,19]

Diagnosis

The diagnosis of IgG4-RD is based on the combination of clinical, serological, histopathological, and radiological findings, but clinical suspicion is essential. The disease has a wide spectrum of clinical manifestations. The symptomatology mostly depends on the affected organ system. Some patients can be asymptomatic or some have systemic symptoms such as fever or weight loss.[20]

Tumor-like swellings of the involved organs is a common feature of this multisystemic disorder. A diagnostic biopsy is strongly recommended for the exclusion of malignancies or other diseases that can mimic IgG4-RD. The histopathological findings are characteristic for dense lymphoplasmacytic infiltrate, variable degree of storiform fibrosis, and obliterative phlebitis. The presence of these findings together with mild tissue eosinophilia is strongly suggestive for the diagnosis if accompanied by the increased numbers of IgG4+ plasma cells in the affected tissue.[17,18]

Elevated serum concentrations of IgG4 (≥135 mg/dL) are found in 60%–70% of the patients.[21] A minority of patients have normal serum IgG4 levels, despite the presence of the typical histopathological findings in the biopsies. A good initial therapeutic response to steroid therapy is typical, particularly if tissue fibrosis is not abundant.[22]

The diagnostic classification of IgG4-RD can be made by the presence of parameters such as symptoms, serology, and histopathology. A definite diagnosis can be made by the presence of all three parameters. A probable diagnosis can be made by the presence of symptoms and histopathology. A possible diagnosis can be made by the presence of symptoms and serology.[23]

Intrathoracic Manifestations of Immunoglobulin G4-Related Disease

IgG4-RD has several patterns of intrathoracic involvement. It may involve the airways, pulmonary parenchyma, pleura, mediastinum, or a combination of these [Table 1]. The first two cases of IgG4-RD

involving pulmonary parenchyma were reported in 2004. Histopathological diagnosis was confirmed by transbronchial biopsy in the first and surgical biopsy in the second case.[24,25] Airway, pleura, and mediastinal involvements were reported subsequently. Radiological and pathological findings demonstrated that the intrathoracic lesions mainly contain lymphatic routes associated with vascular involvements.[26] The incidence of intrathoracic involvement is not known exactly. However, as awareness of IgG4-RD increases, the incidence and the spectrum of intrathoracic manifestations will increase. IgG4-related pulmonary involvement was reported in 13% of 30 patients with autoimmune pancreatitis.[27] Pulmonary involvement was present in 12% (n = 75) of the patients in a series of 620 patients with systemic IgG4-RD.[28]

The clinical symptoms are generally mild and mainly depend on the location of the lesions.[26] Sometimes, they are nonspecific and may include cough, dyspnea, chest pain, hemoptysis, and fever. Some patients are asymptomatic and intrathoracic involvement was noted during the workup of extrathoracic IgG4-RD.[29] Intrathoracic manifestations and imaging features can be easily confused with malignancy or sarcoidosis, thus a biopsy is required for accurate diagnosis.[30] The lesions might have varying degrees of 18-F-fluorodeoxy glucose avidity on positron-emission tomography.[31]

Airway disease

Tracheobronchial stenosis due to airway involvement and external compression of central airways secondary to parenchymal involvement or fibrosing mediastinitis can be seen in IgG4-RD.[7] Bronchiectasis seen in this context appears to be associated with parenchymal fibrosis in the peripheral zones of the lung.[32]

Ito *et al*. first reported a 63-year-old patient with autoimmune pancreatitis who was admitted with the cough. The bronchoscopic examination revealed irregular tracheobronchial stenosis accompanied by edematous and hypervascular mucosa resembling the appearance seen in sarcoidosis.[33] We have previously reported another patient who had been diagnosed with of IgG4-RD and referred for the evaluation of bronchial wall thickenings seen incidentally on her thorax computed tomography (CT). Fiberoptic bronchoscopic examination revealed irregular bronchial stenosis accompanied by mucosal edema and increased vascularity.[34] Sekiguchi *et al*. reported a 44-year-old male patient with clinical features of asthma, pulmonary function testing with borderline airflow obstruction, and a positive bronchial challenge. Bronchoscopy revealed inflammatory changes, and immunostaining of biopsies showed an increased number of IgG4+ plasma cells.[35]

The CT of the thorax from two different patients with IgG4-related airway disease demonstrates markedly thickened lobar and segmental bronchial walls in Figure 1a and narrowed intermediate bronchus due to external compression in Figure 1b.

Pulmonary parenchymal disease

Solid or subsolid nodular opacities, masses or interstitial pneumonia (ground-glass opacities, reticular shadows, consolidation, fibrosis, honeycombing, bronchiectasis) can be seen in patients with IgG4-RD.[7,32] While nodules or masses are thought to correspond to inflammatory pseudotumors, interstitial lung disease has mainly been defined as lymphoproliferative lesions involving the peribronchial interstitium and interlobular septum. Rounded opacities commonly raise suspicion of malignancy, particularly when associated with speculated margins.[30,32] Thus, some patients with these types of lung lesions have undergone wedge resection or lobectomy for suspected malignancy.

Radiological features associated with interstitial lung disease presentations vary on CT of the thorax. These features may resemble those found in idiopathic interstitial pneumonia such as usual interstitial pneumonia, nonspecific interstitial pneumonia, and cryptogenic organizing pneumonia.[7,26,32] Pulmonary function testing reveals a reduced diffusing capacity and restrictive impairment, particularly in the presence of extensive parenchymal involvement.

Table 1: Intrathoracic manifestations of immunoglobulin G4-related disease

Airway	Tracheobronchial stenosis
	Thickening of bronchovascular bundles
Pulmonary parenchyma	Nodules <3 cm (solid or ground glass)
	Masses ≥3 cm
	Interstitial lung disease (usual interstitial pneumonia, nonspecific interstitial pneumonia, cryptogenic organizing pneumonia)
Pleura	Pleural thickening
	Pleural nodules
	Pleural effusion
Mediastinum	Lymphadenopathy (mediastinal and/or hilar)
	Fibrosing mediastinitis

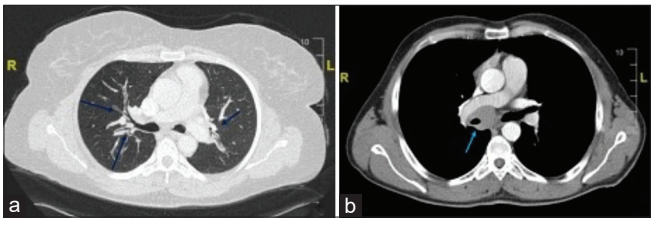

Figure 1: Computed tomography of thorax demonstrating markedly thickened lobar and segmental bronchial walls (a) and narrowed intermediate bronchus due to external compression (b)

Bilateral apical consolidations [Figure 2a] and interstitial lung disease [Figure 2b] are seen in thoracic CT of two different patients with IgG4-RD.

Pleural disease

IgG4-RD may present with visceral and parietal pleural thickening, pleural nodules, and pleural effusion. Although the involvement rate of pleura is uncertain, it is less common compared to other intrathoracic patterns. In a study including 21 patients with IgG4 related pulmonary disease, 5 (24%) of them had the pleural lesions described as pleural nodules.[36] Pleural effusion is an uncommon feature in patients with IgG4 related pulmonary disease. However, pleuritis with fibrinous exudates and reactive changes have been relatively common histological findings on surgical lung biopsies of patients with intrathoracic IgG4-RD.[37]

Right pleural effusion is demonstrated in CT of the thorax of a patient with IgG4-RD [Figure 3].

Mediastinal disease

Mediastinal and/or hilar lymphadenopathies are the most common intrathoracic manifestations of IgG4-RD. They have been reported to be present in 40%–90% of the patients with IgG4-RD.[4,38,39] In a retrospective study including 18 patients with IgG4-RD, all patients had hilar and mediastinal lymphadenopathies.[26]

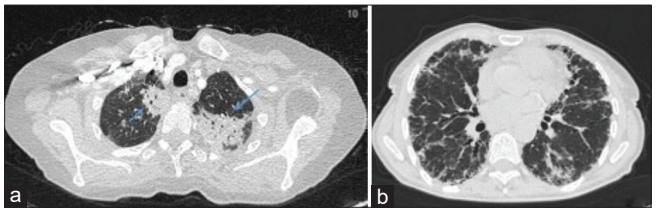

Figure 2: Computed tomography of thorax demonstrating bilateral apical consolidations (a) and interstitial lung disease (b) in two different patients with immunoglobulin G4-related disease

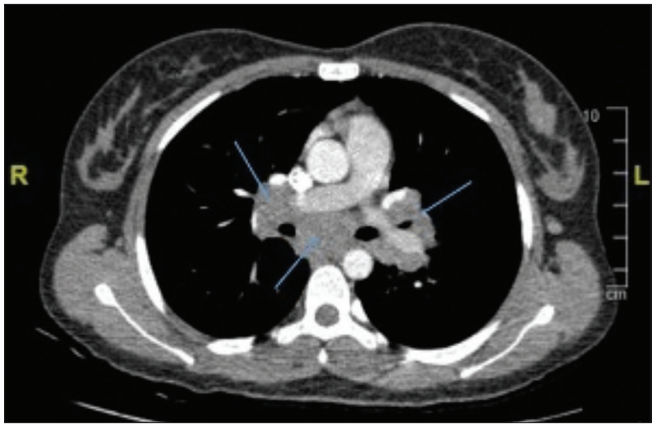

Figure 4: Computed tomography of thorax demonstrating bilateral hilar and mediastinal lymphadenopathies in a patient with immunoglobulin G4-related disease

Bilateral hilar and mediastinal lymphadenopathies are demonstrated in CT of the thorax of a patient with IgG4-RD [Figure 4].

Fibrosing mediastinitis is a rare manifestation of IgG4-RD. Inoue *et al*. reported the first case of fibrosing mediastinitis with increased levels of IgG4 and IgG4+ plasma cell infiltration. This patient improved with steroid therapy and the authors suggested that elevated IgG4 levels might indicate steroid responsiveness in patients with fibrosing mediastinitis, a disease generally considered to be a condition refractory to pharmacological therapy.[40]

IgG4-RD may also present with multiple patterns of intrathoracic involvement [Figure 5]. Mediastinal lymphadenopathies, thickening of bronchovascular bundles, parenchymal nodular opacities, and interlobular septal thickenings are seen in a patient with IgG4-RD [Figure 5a]. Another patient presenting with mediastinal lymphadenopathies, bronchial stenosis, pleural thickening, and pleural effusion is shown in Figure 5b.

Treatment

The optimal treatment for IgG4-RD has not been established. There are not any randomized trials

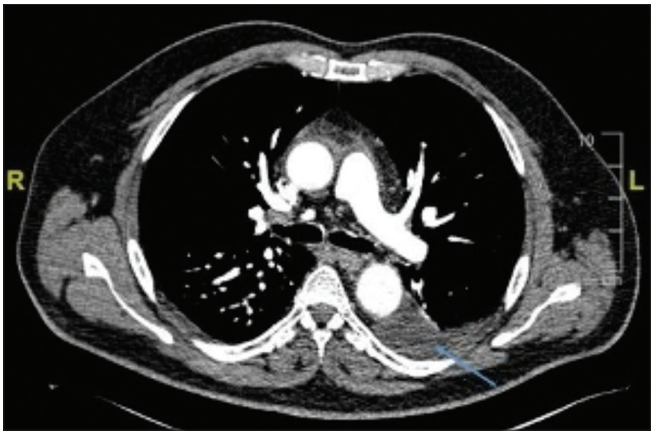

Figure 3: Computed tomography of thorax demonstrating right pleural effusion in a patient with immunoglobulin G4-related disease

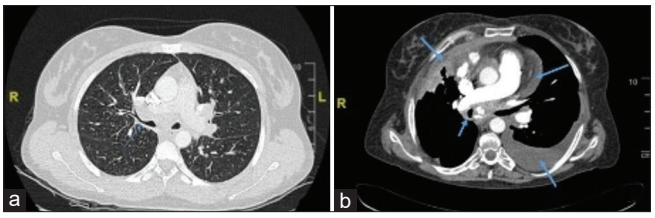

Figure 5: Computed tomography of thorax demonstrating mediastinal lymphadenopathies, thickening of bronchovascular bundles, parenchymal nodular opacities, and interlobular septal thickenings in a patient with immunoglobulin G4-related disease (a); mediastinal lymphadenopathies, bronchial stenosis, pleural thickening, and pleural effusion in another patient with immunoglobulin G4-related disease (b)

that have been performed to compare different approaches to the treatment of IgG4-RD overall or for any organ-specific disease subset. Corticosteroids are the mainstay of therapy in IgG4-RD.[41] Intrathoracic lesions usually respond well to steroid treatment like extrathoracic lesions. Prednisone monotherapy is usually initiated at a dose of 0,6 mg/kg (30–40 mg/day) once daily. Nearly all patients respond to prednisone 40 mg daily within 2–4 weeks or even earlier. Once a significant response is clinically evident, the prednisone dose is gradually tapered, with a planned reduction over 2 months, as tolerated, with the goal of discontinuing the therapy entirely. The disease recurrence rates after discontinuation are 32%, 52%, and 92% within 6 months, 1 and 3 years, respectively.[7] Immunosuppressive drugs such as rituximab, cyclosporine, azathioprine, and mycophenolate mofetil are used for steroid-refractory disease, for patients unable to reduce steroid dose sufficiently or those who have contraindications to steroid therapy.[42-44] There are very limited data regarding how to treat patients who are refractory to rituximab and other immunosuppressives.

Conclusion

IgG4-RD is an increasingly recognized systemic fibro-inflammatory disease associated with elevated serum IgG4 levels. Although IgG4-RD is a rare condition, it is likely that with growing awareness and recent advances in research, the number of patients diagnosed with IgG4-RD will increase in future. The disease can affect virtually any organ system simultaneously or consecutively. The most frequent manifestation of IgG4-RD is regarded to be type 1 autoimmune pancreatitis. Intrathoracic manifestations are relatively rare. Intrathoracic manifestations of IgG4-RD can be observed in pulmonary parenchyma (nodules, masses, interstitial lung disease), airways (tracheobronchial stenosis, thickening of bronchovascular bundles), pleura (pleural thickening, nodules, effusion), and mediastinum (lymphadenopathy, fibrosing mediastinitis). The diagnosis of IgG4-RD is based on the combination of clinical, serological, histopathological, and radiological findings. Intrathoracic manifestations and imaging features can be easily confused with malignancy or sarcoidosis, so a biopsy is required for an accurate diagnosis. Corticosteroids are the mainstay of therapy. Immunosuppressive drugs such as rituximab, cyclosporine, azathioprine, and mycophenolate mofetil are used for steroid-refractory disease, for patients unable to reduce steroid dose sufficiently or those who have contraindications to steroid therapy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. **Stone** JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012;366:539-51.
2. Ramponi S, Gnetti L, Marvisi M, Bertorelli G, Chetta A. Lung manifestations of IgG4-related disease. A multifaceted disorder. Presentation of two cases and short review of the literature. Sarcoidosis Vasc Diffuse Lung Dis 2018;35:74-80.
3. Yoshida K, Toki F, Takeuchi T, Watanabe S, Shiratori K, Hayashi N. Chronic pancreatitis caused by an autoimmune abnormality. Proposal of the concept of autoimmune pancreatitis. Dig Dis Sci 1995;40:1561-8.
4. Hamano H, Kawa S, Horiuchi A, Unno H, Furuya N, Akamatsu T, *et al*. High serum IgG4 concentrations in patients with sclerosing pancreatitis. N Engl J Med 2001;344:732-8.
5. Saeki T, Saito A, Hiura T, Yamazaki H, Emura I, Ueno M, *et al*. Lymphoplasmacytic infiltration of multiple organs with immunoreactivity for IgG4: IgG4-related systemic disease. Intern Med 2006;45:163-7.
6. Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, *et al*. A novel clinical entity, IgG4-related disease (IgG4RD): General concept and details. Mod Rheumatol 2012;22:1-4.
7. Ryu JH, Sekiguchi H, Yi ES. Pulmonary manifestations of immunoglobulin G4-related sclerosing disease. Eur Respir J 2012;39:180-6.
8. Chen Y, Lin W, Yang H, Wang M, Zhang P, Feng R, *et al*. Aberrant expansion and function of follicular helper t cell subsets in IgG4-related disease. Arthritis Rheumatol 2018;70:1853-65.
9. Perugino CA, AlSalem SB, Mattoo H, Della-Torre E, Mahajan V, Ganesh G, *et al*. Identification of galectin-3 as an autoantigen in patients with IgG4-related disease. J Allergy Clin Immunol 2019;143:736-45.
10. Shiokawa M, Kodama Y, Sekiguchi K, Kuwada T, Tomono T, Kuriyama K, *et al*. Laminin 511 is a target antigen in autoimmune pancreatitis. Sci Transl Med 2018;10:eaaq0997.
11. Hubers LM, Vos H, Schuurman AR, Erken R, Oude Elferink RP, Burgering B, *et al*. Annexin A11 is targeted by IgG4 and IgG1 autoantibodies in IgG4-related disease. Gut 2018;67:728-35.
12. Deshpande V, Chicano S, Finkelberg D, Selig MK, Mino-Kenudson M, Brugge WR, *et al*. Autoimmune pancreatitis: A systemic immune complex mediated disease. Am J Surg Pathol 2006;30:1537-45.
13. Umemura T, Ota M, Hamano H, Katsuyama Y, Kiyosawa K, Kawa S. Genetic association of Fc receptor-like 3 polymorphisms with autoimmune pancreatitis in Japanese patients. Gut 2006;55:1367-8.
14. Kawa S, Ota M, Yoshizawa K, Horiuchi A, Hamano H, Ochi Y, *et al*. HLA DRB10405-DQB10401 haplotype is associated with autoimmune pancreatitis in the Japanese population. Gastroenterology 2002;122:1264-9.
15. Chang MC, Chang YT, Tien YW, Liang PC, Jan IS, Wei SC, *et al*. T-cell regulatory gene CTLA-4 polymorphism/haplotype association with autoimmune pancreatitis. Clin Chem 2007;53:1700-5.
16. Mahajan VS, Mattoo H, Deshpande V, Pillai SS, Stone JH. IgG4-related disease. Annu Rev Pathol 2014;9:315-47.
17. 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.
18. Chari ST. Diagnosis of autoimmune pancreatitis using its five cardinal features: Introducing the Mayo Clinic's HISORt criteria. J Gastroenterol 2007;42 Suppl 18:39-41.
19. Cheuk W, Chan JK. IgG4-related sclerosing disease: A critical appraisal of an evolving clinicopathologic entity. Adv Anat Pathol 2010;17:303-32.

20. Kamisawa T, Okamoto A. IgG4-related sclerosing disease. World J Gastroenterol 2008;14:3948-55.
21. Carruthers MN, Khosroshahi A, Augustin T, Deshpande V, Stone JH. The diagnostic utility of serum IgG4 concentrations in IgG4-related disease. Ann Rheum Dis 2015;74:14-8.
22. Okazaki K, Chiba T. Autoimmune related pancreatitis. Gut 2002;51:1-4.
23. 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.
24. Taniguchi T, Ko M, Seko S, Nishida O, Inoue F, Kobayashi H, *et al*. Interstitial pneumonia associated with autoimmune pancreatitis. Gut 2004;53:770.
25. 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.
26. Matsui S, Hebisawa A, Sakai F, Yamamoto H, Terasaki Y, Kurihara Y, *et al*. Immunoglobulin G4-related lung disease: Clinicoradiological and pathological features. Respirology 2013;18:480-7.
27. Hirano K, Kawabe T, Komatsu Y, Matsubara S, Togawa O, Arizumi T, *et al*. High-rate pulmonary involvement in autoimmune pancreatitis. Intern Med J 2006;36:58-61.
28. Brito-Zerón P, Ramos-Casals M, Bosch X, Stone JH. The clinical spectrum of IgG4-related disease. Autoimmun Rev 2014;13:1203-10.
29. Campbell SN, Rubio E, Loschner AL. Clinical review of pulmonary manifestations of IgG4-related disease. Ann Am Thorac Soc 2014;11:1466-75.
30. Lang D, Zwerina J, Pieringer H. IgG4-related disease: Current challenges and future prospects. Ther Clin Risk Manag 2016;12:189-99.
31. Nakajo M, Jinnouchi S, Fukukura Y, Tanabe H, Tateno R, Nakajo M. The efficacy of whole-body FDG-PET or PET/CT for autoimmune pancreatitis and associated extrapancreatic autoimmune lesions. Eur J Nucl Med Mol Imaging 2007;34:2088-95.
32. 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.
33. Ito M, Yasuo M, Yamamoto H, Tsushima K, Tanabe T, Yokoyama T, *et al*. Central airway stenosis in a patient with autoimmune pancreatitis. Eur Respir J 2009;33:680-3.
34. Oncel A, Ozden Sertcelik U, Susesi K, Saglam Ayhan A, Koksal D. Bronchoscopic Evaluation of central airway involvement in IgG4-related disease. J Bronchol Interv Pulmonol 2020;27:e22-4.
35. Sekiguchi H, Horie R, Aksamit TR, Yi ES, Ryu JH. Immunoglobulin G4-related disease mimicking asthma. Can Respir J 2013;20:87-9.
36. Zen Y, Inoue D, Kitao A, Onodera M, Abo H, Miyayama S, *et al*. IgG4-related lung and pleural disease: A clinicopathologic study of 21 cases. Am J Surg Pathol 2009;33:1886-93.
37. Shrestha B, Sekiguchi H, Colby TV, Graziano P, Aubry MC, Smyrk TC, *et al*. Distinctive pulmonary histopathology with increased IgG4-positive plasma cells in patients with autoimmune pancreatitis: Report of 6 and 12 cases with similar histopathology. Am J Surg Pathol 2009;33:1450-62.
38. Fujinaga Y, Kadoya M, Kawa S, Hamano H, Ueda K, Momose M, *et al*. Characteristic findings in images of extra-pancreatic lesions associated with autoimmune pancreatitis. Eur J Radiol 2010;76:228-38.
39. Cheuk W, Yuen HK, Chu SY, Chiu EK, Lam LK, Chan JK. Lymphadenopathy of IgG4-related sclerosing disease. Am J Surg Pathol 2008;32:671-81.
40. Inoue M, Nose N, Nishikawa H, Takahashi M, Zen Y, Kawaguchi M. Successful treatment of sclerosing mediastinitis with a high serum IgG4 level. Gen Thorac Cardiovasc Surg 2007;55:431-3.
41. Khosroshahi A, Wallace ZS, Crowe JL, Akamizu T, Azumi A, Carruthers MN, *et al*. International consensus guidance statement on the management and treatment of IgG4-related disease. Arthritis Rheumatol 2015;67:1688-99.
42. Hart PA, Topazian MD, Witzig TE, Clain JE, Gleeson FC, Klebig RR, *et al*. Treatment of relapsing autoimmune pancreatitis with immunomodulators and rituximab: The mayo clinic experience. Gut 2013;62:1607-15.
43. Huggett MT, Culver EL, Kumar M, Hurst JM, Rodriguez-Justo M, Chapman MH, *et al*. Type 1 autoimmune pancreatitis and IgG4-related sclerosing cholangitis is associated with extrapancreatic organ failure, malignancy, and mortality in a prospective UK cohort. Am J Gastroenterol 2014;109:1675-83.
44. Sekiguchi H, Horie R, Kanai M, Suzuki R, Yi ES, Ryu JH. IgG4-related disease: Retrospective analysis of one hundred sixty-six patients. Arthritis Rheumatol 2016;68:2290-9.