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Immunoglobulin G4-related thoracic disease: Clinical and radiological findings of a Turkish cohort

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Abstract. *Background and Aim:* Thoracic involvement of Immunoglobulin G4-related disease (IgG4-RD) is relatively rare and may be disregarded at the time of initial diagnosis due to its asymptomatic nature. This study aimed to ascertain the prevalence and patterns of thoracic involvement in a retrospective cohort of Turkish patients with IgG4-RD. *Methods:* A total of 90 patients (47 males and 43 females, with a mean age of 57.7±15.5 years) diagnosed with IgG4-RD were reviewed retrospectively. All computed tomography (CT) scans were re-evaluated by two thoracic radiologists and IgG4-related thoracic disease was assessed on four compartments: The mediastinum, pulmonary parenchyma, airways, and pleura. IgG4-related thoracic disease was categorized as: definite, highly probable, probable or possible. *Results:* There were 64 patients who had undergone at least one thorax CT examination, and 18 (28%) were diagnosed with IgG4-related thoracic disease. The rate of IgG4-related thoracic disease increased by 20% and reached a ratio of 48.4% (n=31) after a thorough reevaluation of registry data specifically to thoracic findings. The mediastinum was the most frequently involved compartment, affecting 16 (51.6%) patients, followed by pulmonary parenchyma in 14 (45.2%) patients, and airways and pleura in 10 (32.3%) patients each. Other organ involvements were more prevalent and IgG4 levels were higher in patients with thoracic involvement. Eosinophils were significantly elevated in patients with thoracic involvement (p=0.023). *Conclusions:* IgG4-related thoracic disease is heterogeneous and likely to be more prevalent than currently recognized. The mediastinum is the most frequently involved compartment. It is important to assess IgG4-related thoracic disease at the time of initial diagnosis. Elevated levels of serum IgG4 and eosinophils, as well as a greater number of organ involvements may serve as indicators of thoracic involvement.

Key words: IgG4-related disease, lung, thorax, airway, pleura, mediastinum

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Introduction

Immunoglobulin G4-related disease (IgG4-RD) is an increasingly recognized systemic fibroinflammatory disease characterized by tumefactive lesions, dense lymphoplasmacytic infiltrates rich in IgG4-positive plasma cells, variable degrees of storiform fibrosis, and elevated serum IgG4 levels in majority of the patients (1,2). The exact prevalence of IgG4-RD is unknown. It was reported to be approximately 0.28-1.08 per 100,000 in Japan (3). However, with the growing recognition of the disease, this figure seems to become an underestimate of the true disease prevalence.

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 (4). Thoracic involvement in IgG4-RD is a relatively rare condition that can occur in isolation or in association with other organ involvements. It has been reported in 10 to 50% of the patients with IgG4-RD, and more than half of these patients are asymptomatic at the time of diagnosis. The clinical symptoms are nonspecific and may include cough, dyspnea, or chest pain (5, 6). Intrathoracic manifestations of IgG4-RD are numerous and can mimic several common and better-known clinical entities such as sarcoidosis and malignancies. The dominant radiological patterns are lung nodules, masses, interstitial involvement, airway involvement, pleural and mediastinal pathologies (7).

Intrathoracic manifestations of IgG4-RD can be easily overlooked at the time of initial diagnosis due to its asymptomatic nature, rare, and nonspecific involvement patterns. The aim of this study was to ascertain the prevalence and patterns of thoracic involvement in a retrospective cohort of Turkish patients with IgG4-RD who were registered at Hacettepe University Vasculitis Center (HUVAC).

Material and methods

Patients

The study included 90 patients registered in HUVAC's database (established in 2014) and were evaluated for thoracic involvement. Among these, 64 patients had undergone at least one thorax CT scan. Demographic information, clinical records, radiological images and laboratory results were reviewed retrospectively, and analyses were conducted based on the accessible data. The study was approved by the institutional ethics committee of Hacettepe University approved the study (17.03.2020/ GO 20/244).

The diagnosis of IgG4-RD and IgG4-related thoracic disease

The diagnosis of IgG4-RD was established according to the "Comprehensive diagnostic criteria for IgG4-related disease" published by *Umehara et al*. in 2011 (8), which is independent of the predominant organ involvement. The three diagnostic criteria are as follows: (1) Clinical examination showing characteristic diffuse/localized swelling or masses in single or multiple organs, (2) Hematological examination indicating elevated serum IgG4 concentrations (≥135 mg/dl), and (3) Histopathological examination revealing (i) marked lymphocyte and plasmocyte infiltration and fibrosis, (ii) infiltration of IgG4+ plasma cells with ratio of IgG4/IgG+ plasma cells >40% and a total of >10 IgG4+ cells per high powered field of biopsy sample. When all three criteria are satisfied, the diagnostic sensitivity reaches 100%, thereby confirming a "definite" diagnosis. In cases where the first and second criteria, or the first and third criteria are met together, a "probable" diagnosis is established. Furthermore, the pathological review adhered to the "Consensus statement on the pathology of IgG4-RD" published by *Deshpande et al* in 2012 (9). The three major histopathological features were defined as: (1) Dense lymphoplasmocytic infiltrate, (2) Fibrosis, arranged at least focally in a storyform pattern, and (3) Obliterative phlebitis.

The diagnosis of IgG4-related thoracic disease was categorized into four groups based on the criteria outlined by *Corcoran et al* (10). Patients with biopsy-proven thoracic involvement, a consistent clinical presentation, and a typical radiology were classified as having *"definite"* thoracic IgG4-RD. Patients with typical radiological findings but no alternative explanation for abnormalities, and clinical features, alongside proven extra-thoracic disease or good response to treatment, were classified as having *"highly probable"* thoracic IgG4-RD. Patients with typical radiological findings but no alternative explanation were considered as having *"probable"* thoracic IgG4-RD. Patients with radiological findings

potentially consistent with IgG4-related thoracic disease but with either atypical features and/or plausible alternative causes identified for radiological changes were considered as having *"possible"* thoracic IgG4-RD.

Thoracic imaging

Thoracic CT scans were performed between years 2009-2021, utilizing two different CT machines (SOMATOM Sensation 16, Siemens, Erlangen, Germany or SOMATOM Definition, Erlangen, Germany). Patients received iodinated contrast agent and a saline chaser bolus at a rate of 4.0 ml/s via antecubital intravenous catheter, administered by a dual-chamber power injector. CT scans were obtained in a supine position, arms raised, and in maximal inspiration. The scanning parameters included a tube voltage of 100-120 kV, detector collimation of 0.75 or 1.5 mm, effective mAs ranging from 70 to 130, slice thickness of 1 or 1.3 mm, and a gantry rotation time of 0.5 sec. Pre-treatment chest CT scans of patients admitted from other centers were transferred to PACS (Picture archiving and communication systems). CT scans of all patients included in the study consisted of thin sections and appropriate reconstruction filters. All CT scans were re-evaluated by two thoracic radiologists, blinded to clinical data, and decisions were reached by consensus. Abnormalities were described according to the Fleischner glossary, including bronchiolitis (tree in bud or alveolar nodules), bronchiectasis, solid nodules, masses, ground-glass opacities (GGO), areas of consolidation, pleural effusion or thickening, peribronchovascular thickening, mediastinal lymph nodes, mucoid impactions, septal thickening, honeycombing, reticulations, architectural distortion, and retroperitoneal fibrosis (paravertebral soft tissue band) (11). Lymph nodes were interpreted as enlarged when exceeding 1 cm in the short axis.

IgG4-related thoracic disease was evaluated on four compartments: Mediastinum, pulmonary parenchyma, airways, and pleura (5). Mediastinal lymphadenopathies/masses and fibrosis were considered as mediastinal involvement. Solid nodules/ masses or GGOs, consolidations, alveolar interstitial pattern, and thickening of bronchovasculary bundles were considered as pulmonary parenchymal involvement. Thickening of bronchial walls and/or stenosis of central airways were considered as airway disease. Pleural thickening, pleural effusions and pleural nodules/ masses were considered as pleural involvement.

Statistical analysis

Statistical analyses were performed using the SPSS Statistics Version 23.0. Data were presented as frequencies or mean ± standard deviation (SD). Mann-Whitney U or the χ^2 test were used for comparing two groups. A p-value <0.05 was considered statistically significant.

Results

The study included 90 patients (male/female: 47/43) with a mean age of 57.7±15.5 years at the time of initial diagnosis. Median follow-up time was 26 months (min-max: 1-192 months). The characteristics of study patients are presented in Table 1. IgG4-RD involvement was observed at 11 anatomic sites, including the thorax. The median number of organs affected was 2 (min-max: 1-5). Single organ involvement was noted in 35 (38.9%) patients. The most common site of involvement was the retroperitoneum/aorta in 44 (48.8%) patients. Respiratory symptoms were reported in 28 (31%) patients, with cough being the predominant symptom (n=11, 35.4%), followed by dyspnea (n=9, 29%), and sputum (n=5, 16.1%). Elevated IgG4 levels were present in 32 (35.6%) patients, and 17 (54.8%) of these had thoracic involvement. Median serum IgG4 levels were higher in patients with thoracic involvement (108.8 mg/dl vs. 88.5 mg/dl), however this finding did not demonstrate statistical significance. Thoracic involvement was also more prevalent in patients with other organ involvements.

Among these 90 patients with IgG4-RD, 64 were evaluated with thorax CT and 18 (28%) were recorded to have IgG4-related thoracic disease. However, upon reevaluating all thorax CT scans retrospectively, IgG4-related thoracic disease was detected in 31 (48%) patients. While 23 (74%) of them were at initial diagnosis, 8 (26%) were identified later in the disease course. The rate of IgG4-related thoracic disease increased by 20% (n=13 patients) after reevaluating registry data specifically for thoracic IgG4-RD. The characteristics of these 13 patients are shown in Table 2. All patients were in the *possible* thoracic disease category. Thorax CT findings compatible with IgG4-related thoracic disease

Table 1. The characteristics of 90 patients with IgG4-RD.

Characteristics	**Patients (N=90)**
Gender	Male, 47 (52.2%) Female, 43 (47.8%)
Mean age at initial diagnosis ±SD	57.7±15.5 years (range: 19-87)
History of tuberculosis	1 (1.1%)
History of asthma	8 (8.8%)
History of atopy	11 (12.2%)
Smoking history Active-smoker Ex-smoker Never-smoked Missing data	 10 20 41 19
Occupational/ environmental exposure	1 (1.1%) (asbestos)
Respiratory symptoms	28 (31%)
Elevated serum IgG4 (>135 mg/dl)	In whole patients: 32 (35.6%) In patients with thoracic disease: 17 (54.8%)
Follow-up time, median (25-75%) months	26 (6-57)
Organ/system involvements of IgG4-RD	
Median number of organs affected	2 (1-5)
Single organ involvement	35 (38.9%)
Thorax	31 (34.4%)
Retroperitoneum/Aorta	44 (48.8%)
Extrathoracic lymph nodes	25 (27.7%)
Orbits	21 (23.3%)
Major salivary glands	18 (20%)
Pancreas	18 (20%)
Lacrimal gland	16 (17.8%)
Bile ducts/biliary tract	8 (8.8%)
Thyroid gland	7 (7.8%)
Kidneys	6 (6.7%)
Pachymeninges	5 (5.5%)

were small parenchymal nodules in 7 patients, mediastinal LAP/mass in 5 patients, pleural effusion in 4 patients, airway thickening in 3 patients, and ground glass opacity in 1 patient. Some examples of IgG4-related thoracic disease involvement are demonstrated on thoracic CT sections in Figure 1.

IgG4-related thoracic disease evaluation and the diagnostic classification of the study subjects are shown in Table 3. There were 2 patients with a definite diagnosis. The biopsies were taken from mediastinal mass and pulmonary parenchyma. Most of the patients (87%) with thoracic disease had other organ involvements. Isolated thoracic disease was present in 4 (12.9%) patients.

The thorax CT findings of 31 patients with IgG4-related thoracic disease are presented in Table 4. The most frequently involved compartment was the mediastinum in 16 (51.6%) patients, followed by pulmonary parenchyma in 14 (45.2%) patients, airways and pleura in 10 (32.3%) patients each. Additionally thoracic paravertebral lesions were found in 4 (12.9%) and periaortitis in 16 (51.6%) patients. Thoracic involvement localizations are shown by a Venn diagram in Figure 2. The distribution of thorax CT findings among IgG4-related thoracic disease diagnostic classification is given as a Table S1.

The comparison of certain demographic and laboratory parameters in IgG4-RD patients with and without thoracic involvement is presented in Table 5. The patients with and without IgG4-related thoracic involvement were not significantly different in terms of age, gender, and median follow-up time. However, eosinophils were significantly elevated in patients with thoracic involvement (p=0.023).

Discussion

We investigated IgG4-related thoracic disease in a Turkish cohort with similar clinical features to European cohorts (12). Among 90 patients with IgG4-RD, 64 had undergone thorax CT and 18 (28%) had been recorded to have IgG4-related thoracic disease. After reevaluation of all thoracic CT scans and related clinical data dedicatedly for thoracic involvement, the rate of IgG4-related thoracic disease increased by 20% (n=13) and reached a ratio of 48.4% (n=31). Respiratory symptoms were reported in one-third of the patients, with cough being the predominant symptom. The mediastinum was the most frequently involved compartment in 16 (51.6%) patients. Serum IgG4 levels and eosinophils were higher in patients with thoracic involvement.

Thoracic involvement in IgG4-RD can occur either in isolation or in association with other organ involvements. Isolated thoracic involvement is extremely rare (13). In the present study, there were 4 (12.9%) patients with isolated IgG4-related thoracic disease, all of whom were in the definite or highly probable disease category. The exact incidence of thoracic involvement is not known, but it

Table 2. The characteristics of 13 patients who were diagnosed with IgG4-related thoracic disease after reevaluating registry data specifically to thoracic findings.

Patient Number	Age, gender	Symptom	Diagnostic class	Mediastinal LAP/mass	Airway thickening	Paranchymal small nodule	GGOs	Pleural effusion
1	28,M	Chest pain	Possible	+	-	-	-	-
2	63, F	-	Possible	-	+	-	-	-
3	19, F	-	Possible	+	+	+	-	-
4	36, F	-	Possible	-	-	+	-	-
5	30, F	-	Possible	-	-	-	-	+
6	64, M	-	Possible	+	-	-	-	-
7	47, M	-	Possible	-	-	+	-	+
8	42, F	-	Possible	-	-	+	-	-
9	39, F	Chest pain	Possible	+	-	+	-	+
10	60, F	-	Possible	-	-	-	-	+
11	60, M	Cough	Possible	-	-	+	+	-
12	50, M	-	Possible	-	-	+	-	-
13	34, M	-	Possible	+	+	-	-	-

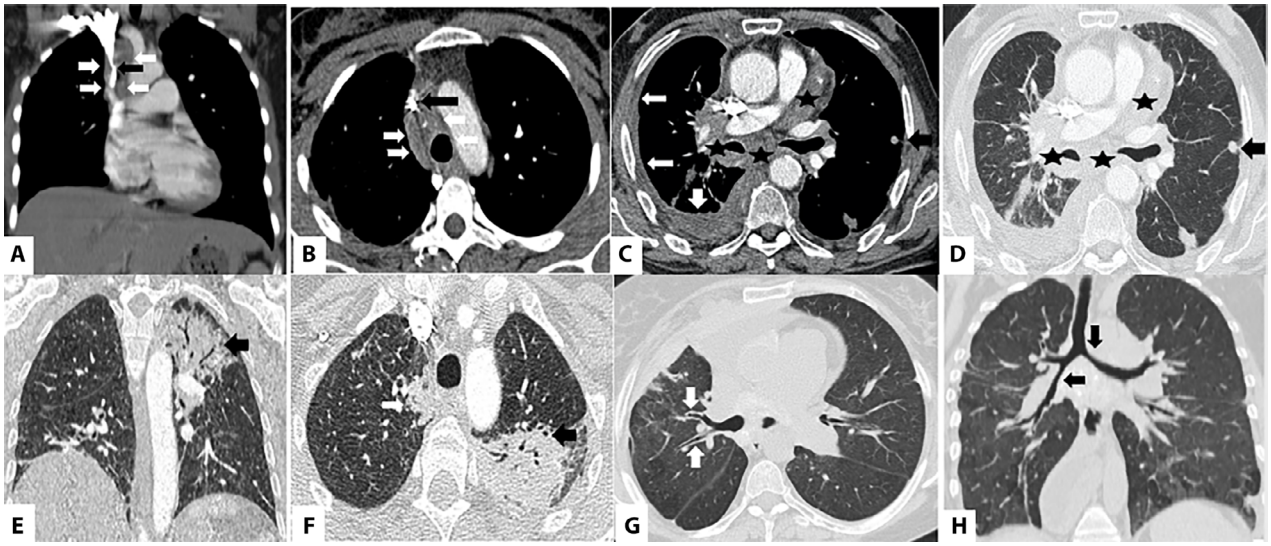

Figure 1. Coronal (A) and axial (B) contrast-enhanced CT images show right paratracheal mass (white arrows) causing narrowing of the superior vena cava (black arrows) and demonstrating the meadiastinal involvement. Right pleural effusion and thickening (white arrows) are seen on axial contrast-enhanced images in the mediastinal (C) and parenchymal (D) windows, demonstrating the pleural involvement. Additionally, a parenchymal nodule in the left upper lobe (black arrows) and mediastinal soft tissue surrounding the right main bronchus and left coronary artery are observed (stars). Coronal (E) and axial (F) CT images showing a pathologically proven IgG4 consolidation containing air bronchograms in the left lobe (black arrows), demonstrating the parenchymal involvement. Consolidation in the right upper lobe (white arrow) and small ground-glass opacities can also be seen within bilateral lung lobes. Axial (G) chest CT image shows thickening of the bronchial wall (white arrows), demonstrating airway involvement. On coronal reformatted CT image (H) stenosis of central airways (black arrows) is also depicted due to mediastinal masses.

Table 3. IgG4-related thoracic disease evaluation and the diagnostic classification of the study subjects.

IgG4-related thoracic disease evaluation		Number (%) of patients
Number of patients evaluated for thoracic disease		64
No thoracic involvement		33 (51.6%)
IgG4-related thoracic disease		31 (48.4%)
Diagnostic classification	Definite	2 (6.5%)
	Highly probable	6 (19.3%)
	Probable	2 (6.5%)
	Possible	21 (67.7%)
Isolated thoracic disease		4 (12.9%)
Two organs involved*		6 (19.4%)
Three organs involved*		10 (32.3%)
Four organs involved*		8 (25.8%)
Five organs involved*		3 (9.7%)

*Numbers are given including thoracic involvement.

Table 4. Thorax CT findings of 31 patients with IgG4-related thoracic disease.

Involved thoracic compartment	N (%)
Mediastinum	**16 (51.6%)**
LAP/ mass	11 (35.5%)
Fibrosis	7 (22.6%)
Pulmonary parenchyma	**14 (45.2%)**
Small nodules	9 (29%)
Large nodules	-
GGO	5 (16.1%)
Consolidation	1 (3.2%)
Alveolar interstitial	3 (9.7%)
Thickening of bronchovascular bundles	1 (3.2%)
Airways	**10 (32.3%)**
Thickening of bronchial wall	8 (25.8%)
Central airway stenosis	4 (12.9%)
Pleura	**10 (32.3%)**
Effusion	8 (25.8%)
Thickening	3 (9.7%)
Nodules	-

is usually reported to be 10-50% based on imaging studies (5). A thoracic CT scan is the most widely performed imaging modality for evaluating IgG4-related thoracic disease. Ideally, patients should be evaluated with dedicated thoracic imaging, and then

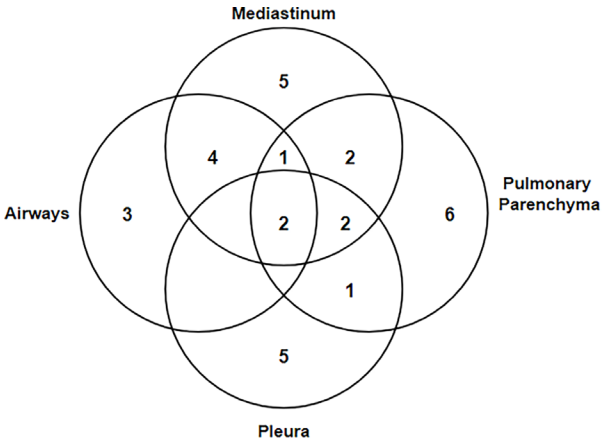

Figure 2. Thoracic involvement localizations of 31 patients with IgG4-related thoracic disease.

analyzed by radiologists specialized in thoracic imaging and familiar with the disease. A specialized review in tertiary center can significantly improve the diagnosis of abnormalities related to IgG4-RD (14). In this study, almost one-third of the patients had not undergone a thoracic CT examination. It is highly probable that the patients with pulmonary symptoms or cardiopulmonary comorbidities had received thoracic CT examination. Furthermore, a lack of awareness regarding thoracic involvement in the earlier years and asymptomatic nature of the disease hinders further investigation with thoracic imaging.

In the present study, the rate of IgG4-related thoracic disease was found to be 48.4% (n=31). This high ratio might be attributed to the inclusion of the *possible* diagnostic category in the diagnosis. The diagnostic categories were definite in 2 (6.5%), highly probable in 6 (19.3%), probable in 2 (6.5%), and possible in 21 (67.7%) patients. All of the patients in the possible category had associated IgG4-related other system involvements. Notably, all of the 13 patients who were realized to have IgG4-related thoracic disease were in *possible* diagnostic category. This finding supports the notion that as knowledge and awareness of IgG4-RD increase, the incidence and spectrum of intrathoracic manifestations will likely to increase. We attribute the identification of 13 "new" cases of IgG4-related thoracic disease to a more targeted examination approach conducted by two focused thoracic radiologists. The clinical significance of these new cases lies in two aspects. Firstly, they contribute to determining the extent of a chronic inflammatory disease. Secondly, some play a role in

Table 5. The comparison of certain demographic and laboratory parameters in IgG4-RD patients with and without thoracic involvement.

Parameter	Patients with thoracic disease (N=31)	Patients without thoracic disease (N=33)	p
Mean age (years)	54.8±17.7	56±15	0.77
Gender (female, %)	15 (48.4%)	14 (42.4%)	0.63
Median follow-up time (months)	26 (1-180)	25 (1-84)	0.17
IgG4 (mg/dl), median (min-max)	108.8 (12.3-3800)	88.5 (18.5–699)	0.51
IgE (IU/ml), median (min-max)	50.6 (1-327)	84.3 (3.1-1919)	0.59
CRP (mg/dl), median (min-max)	0.95 (0.13–39.3)	0.72 (0.12-36.2)	0.71
ESR (mm/hr), median (min-max)	31.5 (2-116)	24 (2-109)	0.42
LDH (U/L), median (min-max)	204 (129-349)	186 (123-462)	0.99
Eosinophils/µl, median (min-max)	200 (0-1200)	100 (0-400)	**0.023***

preventing unnecessary tests and medications. For example, we have noticed that two of these patients with airway involvement were misdiagnosed as having asthma and consequently received inappropriate medications. Moreover, some patients underwent additional examinations for various pulmonary or cardiac conditions and did not receive a definitive diagnosis. In the follow-up period, out of 21 possible cases, 10 were lost to follow-up. Eleven patients had attended appointments in the rheumatology clinic, where they reported no pulmonary symptoms and did not undergo a thoracic CT scan. The majority of the 10 patients in "definite", "highly probable", and "probable" groups remained stable in terms of thoracic involvement throughout the disease course. Only one patient in the "highly probable" group with numerous pulmonary nodules in bilateral lungs, has shown progression with newly onset nodules.

IgG-4 related thoracic disease can manifest in pulmonary parenchyma (as nodules, masses, interstitial lung disease), airways (as thickening of bronchovascular bundles, tracheobronchial stenosis), mediastinum (as lymphadenopathy, fibrosing mediastinitis), and pleura (as pleural thickening, nodules, effusion) (5,15,16). Among these manifestations, mediastinal and/or hilar LAPs are the most common intrathoracic manifestations in IgG4-RD, reported to be present in 40-90% of the patients with IgG4-RD (17,18). In this study, in accordance with the literature, mediastinum was the most frequently involved compartment in 16 (51.6%) patients. Pulmonary parenchymal involvement was present in 14 (45.2%) patients, while airway and pleura involvement were present in 10 (32.3%) patients each. Although pleural involvement is a less common feature compared to other intrathoracic patterns, pleuritis with fibrinous exudates and reactive changes have been relatively common histological findings on surgical lung biopsies of patients with IgG4-related thoracic disease (19). In the present study, none of the pleural involvements were confirmed with histology, but other common causes of pleural abnormalities were excluded based on clinical and laboratory data.

Elevated serum concentrations of IgG4 (≥135 mg/dl) are found in 60-70% of the patients with IgG4-RD (20). Some patients exhibit normal serum IgG4 levels, despite the presence of the typical histopathological findings in the biopsies, categorizing them as "probable" diagnosis of IgG4-RD (8). In our cohort, we believe that the reason IgG4 levels were not as high as expected is that some patients had IgG4 levels measured after treatment. Furthermore, the common phenotype in our cohort was retroperitoneum/aorta involvement, which is a fibrotic subgroup with lower IgG4 levels, as defined in literature (21). In a previous study of 125 biopsy proven IgG4-RD patients, 51% of the patients were found to have elevated serum IgG4 concentrations (2). In our cohort, only 35.6% (n=32) of the patients were found to have elevated serum IgG4 (>135 mg/dl) concentrations. However, elevated serum IgG4 concentrations were more common in patients with thoracic disease, accounting for 54.8% (n=17). When comparing median serum IgG4 levels in patients with and without thoracic involvement, median serum IgG4 levels were higher in patients with thoracic involvement (108.8 mg/dl vs. 88.5 mg/dl), but this finding was not statistically significant. Thoracic involvement was also more prevalent in patients with other organ involvements. In the literature, thoracic

involvement was reported with a higher frequency in patients with elevated serum IgG4 levels and systemic involvements, indicating -greater disease activity and spread (10, 22). As a result, the evaluation of IgG4-related thoracic disease is important in patients with high serum IgG4 levels and other organ involvements.

The thoracic manifestations of IgG4-RD are numerous and can mimic several common and better-known neoplastic and non-neoplastic conditions such as tuberculosis or sarcoidosis (23). The lesions might exhibit varying degrees of 18-F-fluorodeoxy glucose avidity on positron emission tomography (24). In our patient group, there were 4 patients who had been misdiagnosed as having tuberculosis and were initially prescribed anti-tuberculosis therapy. Additionally, there was a patient who had undergone liver biopsy, diagnosed with granulomatous hepatitis, and was treated with anti-tuberculosis therapy.

Allergic features such as atopy, eczema, asthma and eosinophilia are more prevalent in patients with IgG4-RD (25). In our cohort, 8 patients (8.8%) had a history of asthma and 11 patients (12.2%) had allergies. Eosinophils were significantly elevated in patients with pulmonary involvement compared to those without pulmonary involvement (p=0.023).

The strength of this study is comprising a relatively high number of patients with IgG4-RD. The registry data is updated continuously as patients come for follow-up. While the patients in the registry underwent retrospective evaluation, it is noteworthy that all CT scans were re-evaluated by two experienced thoracic radiologists for the detection of IgG4-related thoracic disease. The weakness of this study is its retrospective design. Additionally, some patients were unable to be evaluated for thoracic involvement because they had not undergone a thorax CT examination previously. There were 64 patients who had received thorax CT evaluation. The number of patients with a definite category diagnosis for IgG4-related thoracic disease is extremely low, since thorax is not typically the primary choice for a diagnostic biopsy.

In conclusion, IgG4-related thoracic disease is heterogeneous and likely to be more prevalent than currently recognized. Increased awareness of the disease and a focused approach by specialized thoracic radiologists would enhance the diagnosis of IgG4-related thoracic disease. This mainly contributes to determining the severity of a chronic inflammatory disease that has the potential to affect multiple organs. The mediastinum is the most frequently involved compartment, followed by pulmonary parenchyma, airways, and pleura. Evaluation for IgG4 related thoracic disease should be considered in all patients at the initial diagnosis. Elevated levels of serum IgG4 and eosinophils, as well as a greater number of organ involvements may serve as indicators of thoracic involvement.

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Appendix

Supplementary files

Table S1. The distribution of thorax CT findings among IgG4-related thoracic disease diagnostic classification.

	Definite N=2	**Highly probable N=6**	**Probable N=2**	**Possible N=21**
Mediastinum	**2 (6.5%)**	**5 (16.1%)**	**2 (6.5%)**	**7 (22.6%)**
LAP/mass	-	2	2	7
Fibrosis	2	5	-	-
Pulmonary parenchyma	**1 (3.2%)**	**3 (9.7%)**	**2 (6.5%)**	**8 (25.8%)**
Small nodules	-	2	-	7
Large nodules	-	-	-	-
GGO	1	2	-	2
Consolidation	-	-	-	1
Alveolar interstitial	-	1	2	-
Thickening of bronchovascular bundles	-	-	1	-
Airways	**1 (3.2%)**	**4 (12.9%)**	**-**	**5 (16.1%)**
Thickening of bronchial wall	1	2	-	5
Central airway stenosis	-	3	-	1
Pleura	**1 (3.2%)**	**2 (6.5%)**	**-**	**7 (22.6%)**
Pleural effusion	1	2	-	5
Pleural thickening	-	1	-	2
Pleural nodules	-	-	-	-