Case Report

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Immunoglobulin G4-Related Disease in the Diaphragm: A Case Report

횡격막에 발생한 면역글로불린 G4 연관 질환: 증례 보고

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Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated condition characterized by mass-forming inflammation with a sclerosing pattern that can affect nearly any organ. However, involvement of the diaphragm in IgG4-RD is exceptionally rare. We present the case of a 62-year-old male patient with chest radiographic abnormalities. Further investigation with CT revealed an infiltrative mass in the right hemidiaphragm. This mass, composed of engorged feeding vessels, an atypical manifestation of IgG4-RD, was also associated with lymphadenopathy. Surgical excision confirmed the presence of IgG4-positive cell infiltration, solidifying the diagnosis of IgG4-RD. Notably, the patient remained asymptomatic and did not require any treatment postoperatively. This case highlights the uncommon presentation of IgG4-RD as an infiltrative diaphragmatic mass.

Index terms Case Report; Immunoglobulin G4-Related Disease; Diaphragm; Computed Tomography

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated condition characterized by elevated serum IgG4 levels and histopathological features including lymphocyte and IgG4-positive plasma cell infiltration, storiform fibrosis, and obliterative phlebitis (1).

IgG4-RD can affect various organs, posing a diagnostic challenge due to its ability

to mimic malignancy, infections, or other inflammatory conditions. While virtually any organ can be involved, certain organs such as major salivary glands, orbits and lacrimal glands, the pancreas and biliary tree, lungs, kidneys, aorta and retroperitoneum, meninges, and the thyroid gland are more frequently affected. Additionally, thoracic manifestations encompassing the heart, vessels, lungs, pleurae, lymph nodes, mediastinum, and bones have been documented (2). However, involvement of the diaphragm in IgG4-RD is exceptionally rare, with only one reported case to date (3).

This report presents a unique case of IgG4-RD presenting as an infiltrative mass in the right hemi-diaphragm.

CASE REPORT

A 62-year-old male, with no significant past medical history or current medications, presented with an incidental chest radiograph abnormality identified during a routine health check-up. The initial chest radiograph revealed a 7 cm lobulated mass in the right lower lung zone, obscuring the right hemidiaphragm margin and cardiac border (Fig. 1A).

Initial laboratory workup showed mild eosinophilia (660/uL, normal: 0–500) and an elevated erythrocyte sedimentation rate (ESR) of 46 mm/hr. Blood chemistry results were unremarkable except for elevated eosinophilic cationic protein (32.1 ug/L, normal: <15.0) and IgE (604 IU/mL, normal: ≤87). Bronchial washings and sputum cultures for acid-fast bacilli, bacteria, and fungus all yielded negative results.

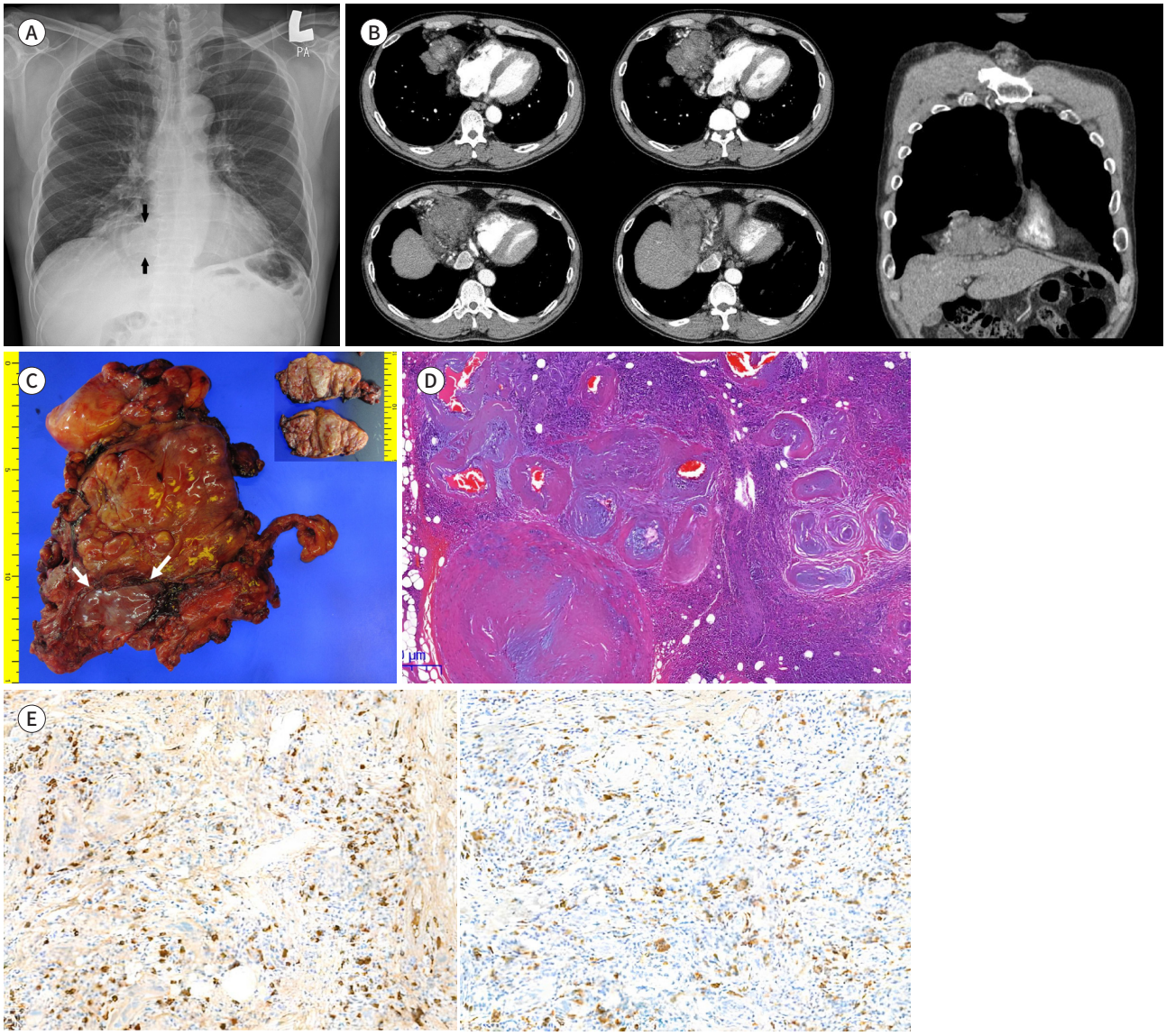
Further evaluation with contrast-enhanced chest CT, revealed a multi-lobulated mass measuring 7.8 × 4.8 × 4.6 cm with homogeneous enhancement in the right anterosuperior diaphragmatic space (Fig. 1B). The mass obscured the margins of the right hemidiaphragm and pericardium, raising concern for pericardial involvement. Notably, the adjacent lung parenchyma showed no abnormalities except for mild compressive atelectasis. Based on the location and vascular supply from the right inferior phrenic artery, the mass was suspected to originate from the diaphragm with possible pericardial invasion. Additionally, enlarged lymph nodes were observed in the paraesophageal and supradiaphragmatic regions. Imaging differentials included malignant neoplasms arising from the diaphragm, such as malignant solitary fibrous tumors, fibrosarcoma, or rhabdomyosarcoma.

Given the presence of enlarged and tortuous tumor vessels around the diaphragmatic mass, and to avoid potential biopsy complications, surgery was performed immediately without a percutaneous needle biopsy. A thoracotomy approach was used to excise the mass, which originated from the diaphragm. Due to the inseparable attachment between the mass and a portion of the diaphragm, the involved diaphragm tissue was resected and reconstructed.

Gross pathological examination revealed a lobulated, whitish-yellow, solid tumor measuring approximately 5.4 × 2.9 cm (Fig. 1C). Microscopic examination showed significant lymphoplasmacytic infiltration, a moderate number of eosinophils, and obliterative phlebitis within the mass and resected diaphragm (Fig. 1D). Immunohistochemistry demonstrated infiltration by plasma cells with an IgG4-to-IgG positive cell ratio >60% (Fig. 1E), consistent with a diagnosis of IgG4-RD. Notably, the diaphragmatic lymph node removed with the mass did not show any abnormalities.

Further laboratory tests were performed to confirm the diagnosis of IgG4-RD. Serum IgG4 levels were significantly elevated at 473.0 mg/dL (normal range: 3.9–86.4), while other IgG subclass levels remained within normal limits. Additional tests to evaluate for associated sys-

Fig. 1. Radiologic and histopathologic findings of a 62-year-old male with IgG4-related disease.
A. Chest radiograph shows a 7 cm-sized lobulated mass in the right lower lung zone. Positive silhouette signs are noted at the right hemidiaphragmatic margin and right cardiac border (arrows).
B. Serial axial and coronal chest CT images reveal a 7.8 × 4.8 × 4.6 cm sized multilobulated mass arising from the anterior and superior aspect of the right hemidiaphragm and obscuring the border of the right hemidiaphragm and pericardium. The mass features engorged and tortuous feeding vessels supplied from the right inferior phrenic artery. Multiple lymphadenopathies are observed in the paraesophageal and supradiaphragmatic areas.
C. A gross examination of the resected specimen shows a lobulated, whitish-yellow, solid tumor measuring approximately 5.4 × 2.9 cm, with the mass attached to the diaphragm (arrows). Inset; cut the surface of the tumor.
D. Lymphoplasmacytic infiltration and obliterative phlebitis are observed on a hematoxylin and eosin-stained tissue section (×40).
E. Immunohistochemistry assessments demonstrate IgG (left)- and IgG4 (right)-positive plasma cells. The IgG4/IgG-positive plasma cell ratio is >60% (×100).
IgG = immunoglobulin G



temic conditions, including autoimmune antibody panels, amylase, lipase levels, abdominal CT scan, and ^{18}F fluorodeoxyglucose PET-CT scan, all yielded normal results.

Based on these findings, fulfilling the comprehensive diagnostic criteria, a definitive diagnosis of IgG4-RD was established. This diagnosis was supported by the presence of a mass in a single organ (diaphragm), elevated serum IgG4 levels (>135 mg/dL), and characteristic histopathological features (4).

During follow-up, the patient's serum IgG4 levels remained elevated. An increase in the size of a soft tissue lesion involving the pericardium was observed, suggestive of residual IgG4-RD manifestation. However, the patient remained asymptomatic and was managed conservatively with regular follow-up visits without the need for medical treatment.

This case report was determined to be exempt from formal ethical approval by our Institutional Review Board. The study was conducted following the ethical principles outlined in the Declaration of Helsinki (2013).

DISCUSSION

IgG4-RD is characterized by mass-forming inflammation with a sclerosing pattern and infiltration by abundant IgG4-positive plasma cells. Distinctive histopathological features include lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis (1).

The radiographic presentation of IgG4-RD varies depending on the affected organ and the degree of fibrosis and cellular infiltration. It can often mimic malignant neoplasms or other inflammatory conditions (5). In the thorax, the most common findings are enlarged mediastinal lymph nodes (50%–80%) and peribronchovascular interstitial thickening in the lungs (60%) (2). Pleural involvement (8%–15%) can manifest as pleural effusion or thickening, with involvement of airways or blood vessels that can cause wall thickening or stenosis, although these are less frequent (2).

This case report describes a patient with a unique presentation of IgG4-RD. Imaging revealed a relatively homogeneous, infiltrative mass originating from the diaphragm with prominent vascular structures and associated with multiple enlarged lymph nodes. To our knowledge, only one other documented case of diaphragmatic IgG4-RD exists (3). Unlike the previous case where autoimmune pancreatitis was the primary presenting feature, our patient's diaphragm was the sole site of IgG4-RD involvement.

Furthermore, the CT scan in the previously reported case (3) showed a diaphragmatic mass with slight initial enhancement followed by delayed and prolonged enhancement. These features align with prior studies describing the typical imaging characteristics of IgG4-RD in various regions, including the thorax (6) and abdomen (5). Mass lesions associated with IgG4-RD typically appear on CT scans as well-defined soft tissue masses with uniform attenuation or on MR images with homogenous signal intensity. They also demonstrate uniform and progressive enhancement (5, 6). Internal calcifications or cystic components are usually absent (6).

While most reported cases describe well-defined margins, Zhang et al. (6) documented a few cases with irregular borders similar to our patient's presentation. Their study focused on IgG4-RD involving the thoracic paravertebral area and categorized the lesions into three types: simple or multiple saddle-like masses, multiple nodules, and invasively irregular masses.

The prominent vascular structures observed in our case are a noteworthy finding. A single prior case report described a uterine mass with similarly conspicuous feeding vessels, leading to diagnostic challenges in differentiating it from sarcoma and malignant lymphoma (7).

While some studies mention the presence of intra-lesional vessels within IgG4-RD lesions (6), these appeared to be normal vasculature encased within the lesion, rather than the neovascularized engorged feeding vessels.

The atypical presentation, with diaphragmatic location and prominent vascularity, led to a differential diagnosis focused on malignant neoplasms like malignant solitary fibrous tumors, fibrosarcoma, or rhabdomyosarcoma.

This case highlights the importance of considering IgG4-RD in the differential diagnosis, even for lesions in uncommon locations and with atypical features like prominent vascularity. In such cases, particularly when soft tissue masses with homogeneous enhancement are identified in the diaphragm or paravertebral region, additional workup are crucial.

The presence of elevated ESR, peripheral blood eosinophilia, or elevated serum IgE on blood tests can further support the need for investigating IgG4-RD. Serum IgG4 level measurement or even a percutaneous needle biopsy, if feasible and safe, should be considered before surgery to improve diagnostic accuracy and potentially avoid unnecessary surgical intervention.

Immunosuppressive medications like glucocorticoids, rituximab, and azathioprine are the mainstay treatment for symptomatic patients with IgG4-RD (2). Response to glucocorticoids can be particularly helpful in confirming the diagnosis, especially for unusual presentations of IgG4-RD (1). In some cases, surgical resection may be indicated for localized disease, as in this case.

However, our patient remained asymptomatic throughout follow-up, eliminating the need for specific treatment and precluding the evaluation of glucocorticoid response.

This case report presented a rare instance of IgG4-RD involving the diaphragm and characterized by prominent vascularity. It emphasized the potential for IgG4-RD to affect any organ and exhibit atypical imaging features. The presence of a hypervascular mass in an uncommon location, such as the diaphragm, should prompt consideration of IgG4-RD in the differential diagnosis. This can help ensure accurate diagnosis and appropriate management.

Author Contributions

Conceptualization, J.Y.J., K.Y.S.; data curation, K.J.W., J.Y.J., K.Y.S.; funding acquisition, K.Y.S.; investigation, K.J.W., K.T., J.Y.J., S.D.H., K.Y.S.; methodology, K.J.W., J.Y.J., K.D., S.D.H.; supervision, J.Y.J., K.K.; writing—original draft, K.J.W., J.Y.J.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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횡격막에 발생한 면역글로불린 G4 연관 질환: 증례 보고

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면역글로불린(immunoglobulin; 이하 Ig) G4 연관 질환은 경화성 패턴의 종괴를 형성하는 염증 질환으로 거의 모든 장기에 영향을 미칠 수 있는 면역 매개 질환이다. 그러나 횡격막을 침범하는 경우는 매우 드물다. 우리는 흉부 X선 검사에서 이상 소견이 발견된 62세 남성 환자의 증례를 보고한다. 추가로 시행한 흉부 전산화단층촬영에서 비대화된 혈관과 림프절염을 동반하는 침윤성 종괴가 우측 횡격막에 발견되었다. 수술적 절제로 IgG4 양성 세포의 침윤을 확인하여 IgG4 연관 질환으로 진단하였다. 환자는 증상이 없어 수술 후에 특별한 치료는 하지 않았다. 이 증례는 IgG4 연관 질환이 드물게는 횡격막의 침윤성 종괴로 나타날 수 있음을 강조한다.

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