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Asymptomatic pleural thickening with effusion as the only manifestation of IgG4-related disease

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Abstract

Immunoglobulin G4 (IgG4)-related disease is a systemic fibroinflammatory disorder that can affect almost any tissue. Isolated IgG4 pleural disease is a rare manifestation and, when present, is usually described in patients presenting with dyspnoea. We present a case of asymptomatic isolated IgG4 pleural effusion and highlight that IgG4-related disease should be remembered as a differential diagnosis in patients with pleural effusion and pleural thickening, even if asymptomatic and without any other organ involvement.

Introduction

Immunoglobulin G4 (IgG4)-related disease is a systemic fibroinflammatory disorder that can lead to severe and irreversible organ damage [1] and has been reported to affect almost any tissue [2]. Isolated IgG4 pleural disease is a rare manifestation usually described in patients presenting with dyspnoea [3]. We present an asymptomatic case of isolated IgG4-related pleural effusion.

Case Report

A 65-year-old man, non-smoker with no exposure to asbestos, presented with few days of non-specific malaise, dizziness, and no respiratory symptoms to his general practitioner. His symptoms resolved spontaneously, but as chest X-ray showed a right-sided pleural effusion, he was referred to our department for work-up. Diagnostic ultrasound-guided aspiration of 30 mL of clear serous pleural fluid revealed an exudative, culture- and cytology-negative effusion. Contrast-enhanced computed tomography (CT) of the thorax and abdomen confirmed a right-sided pleural effusion and pleural thickening, normal lung parenchyma, and no other lesions (Fig. 1A). No abnormalities were found in the abdomen. A positron emission tomography-CT (PET-CT) showed increased metabolic activity in the thickened pleura and in morphologically normal mediastinal and hilar lymph nodes (Fig. 1B). Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsies from normal size and appearance lymph nodes at stations 7, 4R, 11R, and 12R showed lymphatic tissue without granulomas or malignant cells. Bronchoscopy was normal. Serum antinuclear antibodies and rheumatoid factor were absent. Peptidyldipeptidase A and serum(s)-interleukin 6 (IL6) was in the normal range, whereas s-IgG4 was 7.15 (0.03–2.01 g/L). A right-sided video-assisted thoracic surgery (VATS) with pleural biopsies revealed fibrin coatings

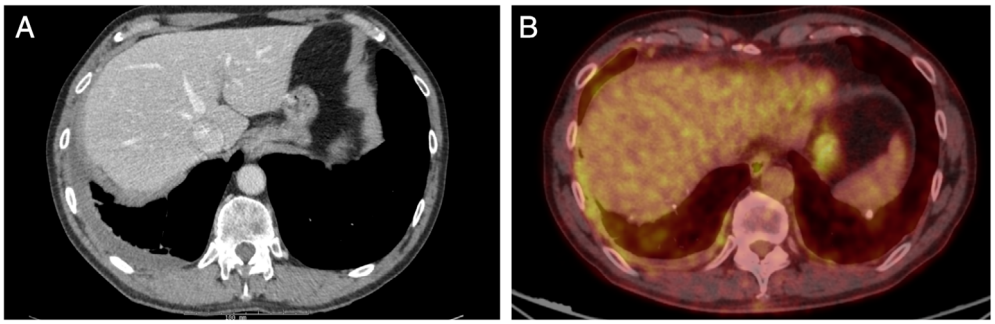

Figure 1. (A) Contrast-enhanced computed tomography (CT) showing a minimal amount of pleural fluid and pleural thickening but no other lesions. (B) Positron emission tomography-CT showing increased metabolic activity in the thickened pleura.

and pronounced underlying lymphoplasmacytic infiltration rich in IgG4-positive plasma cells (absolute number of IgG4-positive cells per high-power field was 80 (>10) and IgG4/IgG was 27% (>40%)) without signs of monoclonality, malignancy, mesothelioma, or granulomas (Fig. 2). Biopsy culture for *Mycobacterium tuberculosis* was negative. A diagnosis of IgG4-related disease was made according to guidelines. Treatment was not indicated but follow-up with six-monthly chest CT and blood tests is planned.

Discussion

The epidemiology of IgG4-related disease is poorly described due to the relative rarity but also of likely under-recognition. The diagnosis is difficult, as up to 5% of healthy subjects demonstrate an elevated level of s-IgG4, and s-IgG4 levels may be normal in patients with IgG4-related disease [1]. In our patient, the s-IgG4 level was elevated. The diagnosis of IgG4-related disease cannot be based on biopsy alone as differential diagnoses must be excluded such as infection, tuberculosis, sarcoidosis, connective tissue disease, multicentric Castleman's disease (MCD), lymphoma, and solid malignancy [4]. In our case, neither blood tests, imaging nor tissue samples showed signs of any of these diseases. This was supported by the absence of symptoms of any kind. The incidence of asymptomatic IgG4-related pleural effusion is unknown. Long-term follow-up is important, as IgG4-related pleural effusion is an exclusion of diagnosis and there is a risk of complicating malignancy.

We did not treat our patient with corticosteroids, as this is only recommended in case of vital organ involvement (e.g. aorta, heart, pancreas, or kidneys) to avoid irreversible organ damage [5]. In conclusion, asymptomatic pleural effusion and pleural thickening without any other organ involvement may be caused by IgG4-related disease. This finding

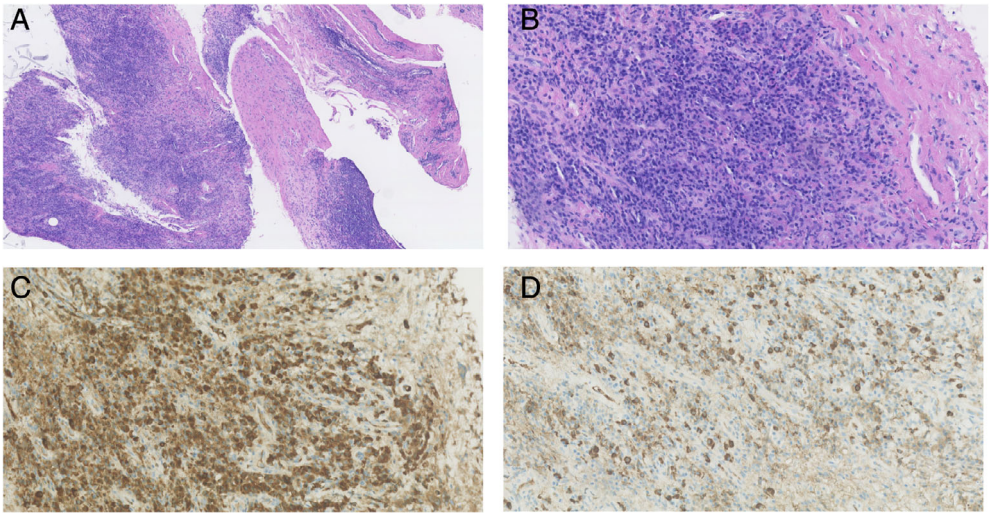

Figure 2. Pleural biopsy with massive lymphoplasmacytic inflammation. (A) Overview (100×). (B) Inflammation dominated by plasma cells (400×). (C) Immunohistochemical reaction for immunoglobulin G (IgG) (400×). (D) Immunohistochemical reaction for IgG4 (400×).

may represent a transient condition or the early manifestation of clinically significant IgG4-related disease. We recommend long-term surveillance for complicating malignancy.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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