

Sclerosing mediastinitis and periaortitis in a patient with IgG4 disease. A case report

Mediastinitis esclerosante y periaortitis en un paciente con enfermedad por IgG4. Presentación de caso

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Summary

Caudal regression syndrome, also known as caudal dysplasia sequence, is a rare severe congenital IgG4-related disease is a systemic inflammatory condition, where IgG4-positive plasma cell complexes play a fundamental role, which infiltrate various organs and systems and manifest with elevated serum IgG4 levels. The diagnosis of this disease is complex and the clinical findings are not pathognomonic, however, it should be considered among the differential diagnoses of inflammatory diseases with multiple organ involvement. The most affected organs are the salivary glands, biliary tract, pancreas, retroperitoneum, lungs, trachea and skin; however, recently, the presence of sclerosing mediastinitis has been described as a form of IgG4 disease, whose early recognition and diagnosis are essential, since a delay in the initiation of adequate treatment leads to progressive fibrosis with irreversible damage and poor prognosis for the patient. The following is the case of a patient with imaging findings of sclerosing mediastinitis, with infradiaphragmatic adenopathies and periaortitis as main manifestations and in whom, together with blood tests and clinical history, the diagnosis of IgG4 disease was made. Special emphasis is made on the imaging findings and their importance for the radiologist when suspecting and/or diagnosing this disease.

Resumen

La enfermedad relacionada con IgG4 es una patología inflamatoria sistémica en la que juegan un papel fundamental los complejos formados por células plasmáticas IgG4 positivas, los cuales infiltran diversos órganos y sistemas; se manifiesta con niveles elevados de IgG4 en el suero. El diagnóstico de esta enfermedad es complejo y los hallazgos clínicos no son patognomónicos; sin embargo, se debe considerar entre los diagnósticos diferenciales de enfermedades inflamatorias con afectación de múltiples órganos. Los órganos más afectados son las glándulas salivares, la vía biliar, el páncreas, el retroperitoneo, los pulmones, la tráquea y la piel. Recientemente, la mediastinitis esclerosante se ha descrito como una forma de enfermedad por IgG4 cuyo reconocimiento y diagnóstico tempranos son esenciales, dado que un retraso en el inicio del tratamiento adecuado conduce a una fibrosis progresiva con daño irreversible y mal pronóstico para el paciente. Se presenta el caso de un paciente con hallazgos por imágenes de mediastinitis esclerosante, con adenopatías infradiafragmáticas y periaortitis como principales manifestaciones, a quien, junto con los exámenes de sangre e historia clínica, se le diagnosticó enfermedad por IgG4. Se enfatiza en la importancia que tienen para el radiólogo los hallazgos por imagen a la hora de sospechar y/o diagnosticar esta enfermedad.

Introduction

Immunoglobulin G4 (IgG4)-related disease is an inflammatory condition that can affect any organ and is associated with high levels of circulating IgG4, infiltration of IgG4-producing plasma cell complexes, and fibrosis of the affected organs (1). Currently, it is not well established whether IgG4 antibodies play a direct pathogenic role, but what is known is that their levels rise as a result of B-cell activation, which also acts as antigen presentation, thereby stimulating the proliferation of cytotoxic CD4+ T cells. These cells induce the production of cytokines such as gamma interferon gamma, transforming growth factor-beta (TGF), and interleukin (IL)-1 beta, which drive fibroblast activity, leading to the fibrosis characteristic of this condition. Furthermore, IL-4 and IL-10 induce increased production of IgG4 in plasma cells (2). This systemic fibroinflammatory condition, which affects virtually any organ and generally manifests as "mass-like" lesions, encompasses a broad spectrum of intrathoracic involvement, including parenchymal lung diseases, pleural lesions, and airway, vascular, lymph node, and mediastinal lesions (3).

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Case report

A 52-year-old male patient with no significant past medical history. He presented with a four-month history of dysphonia and vocal cord paralysis. Imaging studies revealed a partially calcified mediastinal lymph node cluster in the pre-vascular region (Figure 1). Staging studies were performed using 18F-FDG PET-CT, which documented signs of periaortitis (Figure 2) and lymphadenopathy in the right common iliac chain with increased metabolism (Figure 3). A mediastinal biopsy was performed via thoracoscopy, with the pathology report stating: "dense fibrous and adipose tissue with no conclusive findings for oncological disease or lymphoproliferative syndrome." Multiple tests were performed to rule out other causes: normal C3 and C4 levels, elevated acute-phase reactants (CRP and ESR), serum immunoglobulins: normal IgG 1, 2, and 3, and elevated IgG4 at 1.208 (normal range 0.039–0.864), normal total IgE. Based on the biopsy findings and the elevated IgG4 levels, a diagnosis of sclerosing mediastinitis secondary to IgG4-related disease was made.

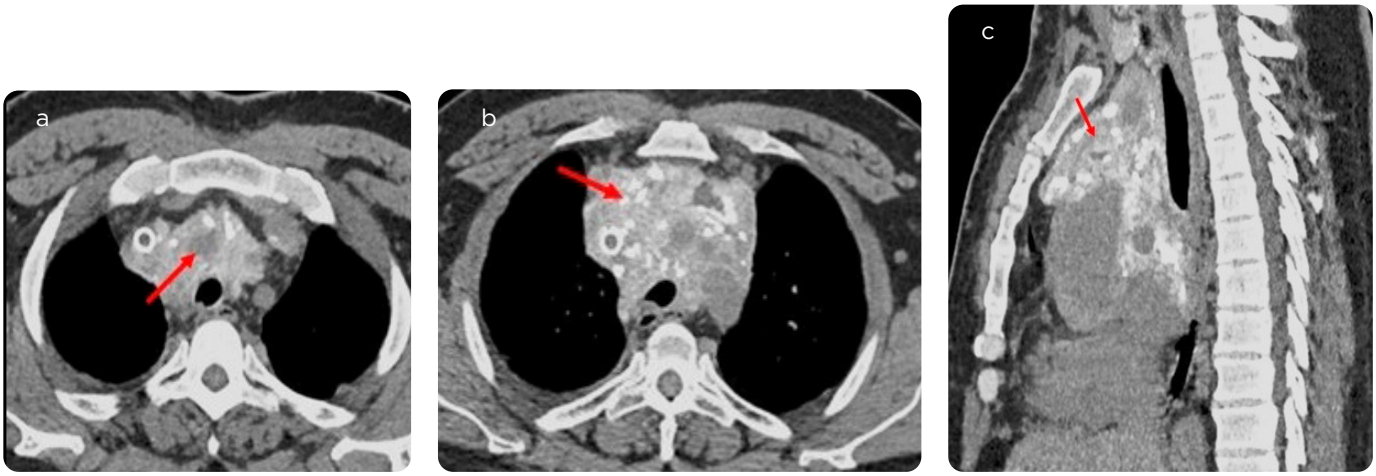


Figure 1. Uncontrasted chest CT in axial (a and b) and sagittal (c) sections, showing a mediastinal mass/lymph node cluster in the pre-vascular region, partially calcified (red arrows), surrounding the aortic arch, the origin of the supra-aortic vessels, the pulmonary artery, the superior vena cava, and the innominate vein. The lesion also comes into close contact with the anterior margin of the trachea. Subsequent mediastinal biopsy confirmed the diagnosis of sclerosing mediastinitis.

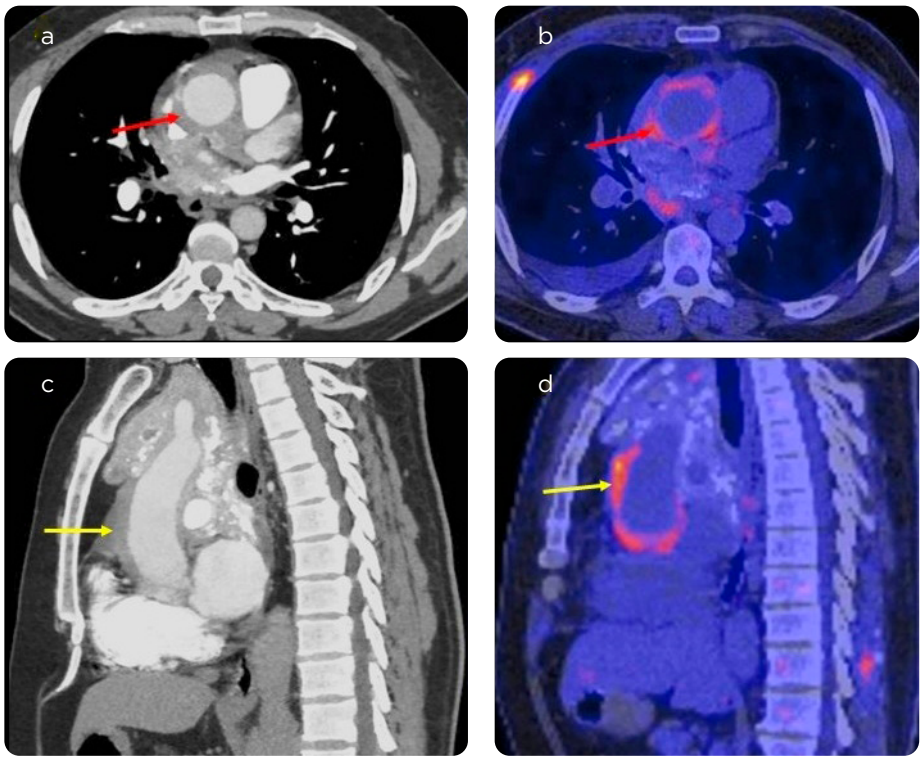


Figure 2. Contrast-enhanced chest CT, axial (a) and sagittal (c) reconstructions. 18F-FDG PET-CT, axial (b) and sagittal (d) reconstructions. Concentric thickening of the ascending aorta extending to the origin of the supra-aortic vessels (yellow arrows), with diffuse increased FDG uptake (red arrows), findings consistent with periaortitis.

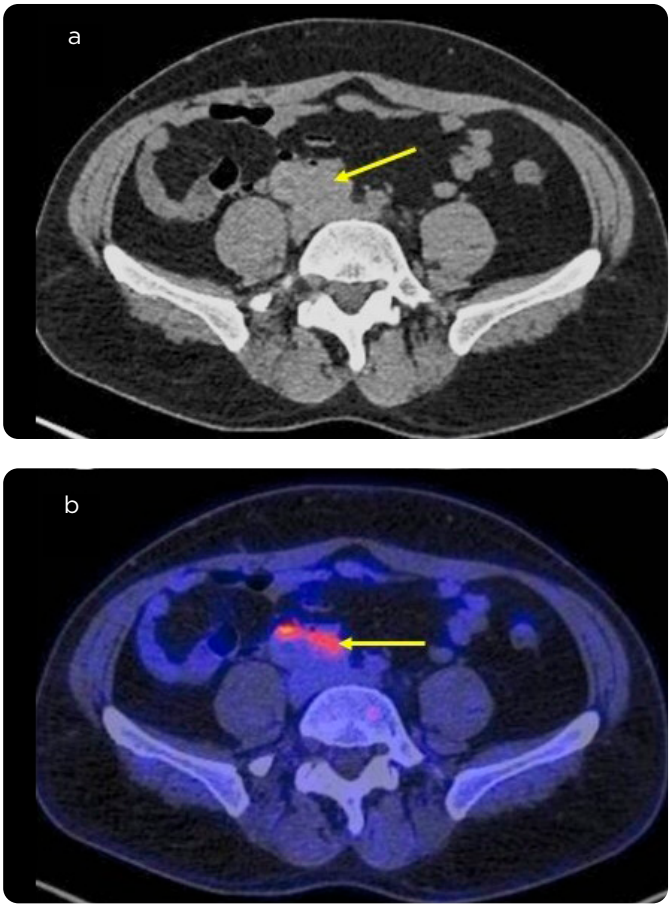


Figure 3. Axial sections of a) plain abdominal CT and b) 18F-FDG PET-CT. A lymph node cluster is observed in the right common iliac chain (yellow arrows) with increased FDG uptake.

Discussion

Given the heterogeneity of clinical manifestations, it is important for treating physicians to consider IgG4-related disease as a differential diagnosis for conditions involving isolated or systemic inflammation. This condition occurs in men and women at a 3:1 ratio and affects all age groups, although it is most common around age 60 (4). The main organs involved are the salivary glands, bile ducts, pancreas, retroperitoneum, lungs, trachea, and skin (5). Recently, fibrosing mediastinitis has been described as a rare form of IgG4-related disease, for which early recognition and diagnosis are critical, as a delay in diagnosis and initiation of appropriate treatment leads to irreversible damage, which can result in severe disability and a poor prognosis for the patient (6). Although severe fibrosis is one of the key features of IgG4-related fibrosing mediastinitis, the mechanism underlying fibrosis formation remains unclear. Some studies report that M2 macrophages contribute to the development of severe fibrosis (7), which can cause compression and dysfunction of vital mediastinal structures. Clinical symptoms are nonspecific and include pain, cough, dyspnea, or symptoms due to mass effect (8).

Fibrosing mediastinitis is also known as mediastinal fibrosis or sclerosing mediastinitis (6). The diagnosis of IgG4-related fibrosing mediastinitis is based on three pillars: clinical and radiological, serological, and histological. The radiological component is crucial, as it identifies edema or mass formation in one or more organs, making it an essential first clue for suspecting the disease. This component, together with clinical findings, allows for a probable diagnosis even without the other two criteria. The histological component is also fundamental, as it confirms the diagnosis when there is stellate fibrosis, lymphoplasmacytic infiltration, and a high number of IgG4-positive plasma cells. The combination of these findings allows for a definitive diagnosis when all three pillars are present, underscoring the importance of both radiological and histological analysis in the comprehensive management of IgG4-related disease. This is particularly relevant because up to 30% of cases may have normal IgG4 levels, which limits the reliability of the serological criterion (1).

Radiological findings are varied. Chest X-rays may reveal mediastinal widening, thickening of the bronchial and tracheal cartilage, compression of large vessels—including the pulmonary arteries with pulmonary hypertension—and esophageal narrowing (9). Based on findings on CT and magnetic resonance imaging (MRI), fibrosing mediastinitis can be classified into two forms: focal, in which a well-defined mass with punctate calcifications is usually seen, predominantly located paratracheally, subcarinally, or hilarly; and diffuse, represented as an infiltrating mass that is not usually calcified and tends to affect several mediastinal compartments as well as major bronchial collaterals (10).

In the patient in this case, lymph node and vascular involvement were the key manifestations leading to the respective diagnosis. In the literature, lymph node involvement has been described in association with the affected organ and in the form of polyadenopathy (11). Among the characteristics of lymph node involvement in IgG4-related disease, lymphadenopathy is the most common manifestation in thoracic disease; it is observed in 86.4% of patients with confirmed or probable thoracic involvement. These lymphadenopathies are typically large (≥1 cm in diameter on the short axis) and represent a key radiological finding, as they may be asymptomatic or associated with nonspecific systemic symptoms. The high frequency of this involvement highlights the importance of its detection through imaging studies such as CT scans, to facilitate differential diagnosis with other multisystemic diseases and contribute to appropriate disease management (12).

On the other hand, one of the most important features of vascular involvement in IgG4-related disease is aortitis, a manifestation observed in a significant percentage of patients with thoracic involvement; therefore, its identification is crucial due to associated risks, such as stenosis or aneurysm formation. Radiologically, these cases are characterized by thickening of the aortic wall and, occasionally, the formation of pseudoaneurysms, which underscores the importance of a detailed evaluation to prevent serious complications (13). Aortitis associated with IgG4-related disease was initially described as affecting the abdominal aorta, but involvement of the thoracic aorta, particularly the aortic arch, is now also recognized. Furthermore, it is sometimes associated with aneurysmal dilation, usually abdominal, and periaortic fibrosis. Aortic involvement in the context of IgG4-related mediastinitis can be very difficult to diagnose, especially when there is no involvement of other organs amenable to biopsy. It is important to note that, in this context, 33% of cases of thoracic aortitis have been reported to involve other organs—which is the situation in this patient—and 29% present as an abdominal aneurysm (14).

In this regard, it is worth noting that radiologists should pay special attention to the possible association between idiopathic sclerosing mediastinitis as an extrathoracic manifestation of the IgG4-related disease spectrum (15).

The objective of this case report is to describe the importance of imaging findings in diagnosing IgG4-related disease with sclerosing mediastinitis as an atypical clinical manifestation, since this is a rare and potentially serious condition due to compression of vital mediastinal structures, CT and MRI play a fundamental role in both diagnosis and in assessing severity and evaluating the therapeutic response in these patients. Thus, emphasis is placed on the common imaging signs that help guide the diagnosis, ensuring a correct correlation with laboratory and clinical findings, to facilitate the implementation of a comprehensive and timely approach. This prevents progression to severe fibrosis with negative outcomes for the patient, which may even result in death.

The patient described in this case report is currently under follow-up and treatment by the hematology department, with adequate symptom control and regular follow-up via imaging and laboratory tests.

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