ACTA RADIOLÓGICA PORTUGUESA
January-April 2028 | Vol 40 nº 1 | e45763 https://doi.org/10.25748/arp.45763

Images of Interest / Imagens de Interesse

Pulmonary Nodule as a Manifestation of IgG4-Related Disease

Nódulo Pulmonar como Manifestação de Doença Relacionada à IgG4

Lourenço Resende[1], Beatriz Cabaço Santos[2], Francisco Carvalho[1], Diogo Castelo[1], Célia Sousa[1]

[1]Serviço de Imagiologia, Unidade Local de Saúde Gaia e Espinho, Vila Nova de Gaia, Portugal
[2]Serviço de Pneumologia, Unidade Local de Saúde da Região de Leiria, Leiria, Portugal

Address

Lourenço Resende
Serviço de Imagiologia
Unidade Local de Saúde Gaia e Espinho
R. Conceição Fernandes,
4434-502 Vila Nova de Gaia
e-mail: lourenco.martins@ulsge.min-saude.pt

Received: 02/03/2026
Accepted: 15/04/2026
Published: 03/07/2026

Abstract

IgG4-related disease is a systemic fibroinflammatory condition that can affect virtually all organs and systems of the human body, most frequently involving the pancreas. We describe the case of a 76-year-old man under follow-up for idiopathic pulmonary fibrosis who, during routine follow-up examinations, was found to have a growing nodule in the apical segment of the right upper lobe. He underwent a transthoracic biopsy in order to exclude pulmonary neoplasia. Histopathological analysis revealed areas of fibrosis and inflammatory infiltrate composed of lymphocytes and IgG4-positive plasma cells, with an IgG4/IgG ratio greater than 40%, findings consistent with IgG4-related lung disease.

Keywords

Immunoglobulin G4-related disease; Lung; Fibrosis; Biopsy.

Resumo

A doença relacionada com IgG4 é uma patologia fibroinflamatória sistémica que pode manifestar-se virtualmente em qualquer órgão ou sistema, sendo o pâncreas o mais frequentemente afetado. Descrevemos o caso de um homem de 76 anos, em seguimento por fibrose pulmonar idiopática que, em exames de follow-up, apresentou um nódulo em crescimento no segmento apical do lobo superior direito, o qual foi submetido a uma biópsia trans-torácica, com o objectivo de excluir neoplasia pulmonar. A análise histo-patológica revelou áreas de fibrose e infiltrado inflamatório com linfócitos e plasmócitos IgG4+, com um ratio IgG4/IgG superior a 40%, achados compatíveis com envolvimento pulmonar por doença relacionada com IgG4.

Palavras-chave

Doença relacionada com imunoglobulina G4; Pulmão; Fibrose; Biópsia.

Case Report

A 76-year-old patient undergoing routine computed tomography (CT) surveillance for idiopathic pulmonary fibrosis (IPF) (Figure 1), was found to have an irregular nodular area with 25 mm in the apical segment of the right lung that demonstrated a 10 mm growth after one year (Figure 2). PET-CT with 18F-FDG showed uptake within the lesion with a maximum SUV of 4.2 (Figure 3), raising suspicion for malignancy and leading to image guided biopsy (Figure 4). Histopathological analysis showed fibrosis with inflammatory infiltrate with lymphocytes and plasma cells IgG4+, with a IgG4/IgG ratio superior to 40%. Given this diagnosis, additional manifestations of IgG4-related disease were investigated. Abdominal CT revealed diffuse pancreatic enlargement consistent with a "sausage-shaped" pancreas (Figure 5), as well as diffuse thickening of the common bile duct wall (Figure 6). Ultrasound examination demonstrated marked heterogeneity of the submandibular salivary glands (Figure 7).

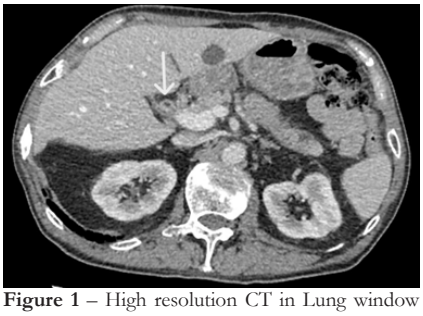

Figure 1 – High resolution CT in Lung window showing pulmonary fibrosis with UIP pattern in the lung bases, with honeycombing, irregular interlobular septal thickening and traction bronchiectasis.

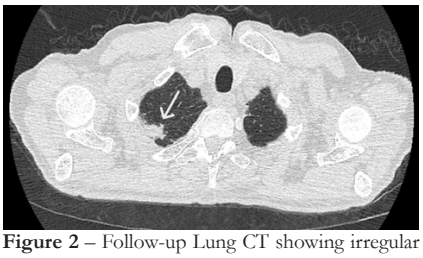

Figure 2 – Follow-up Lung CT showing irregular nodule with 25 mm in the right pulmonary apex (arrow).

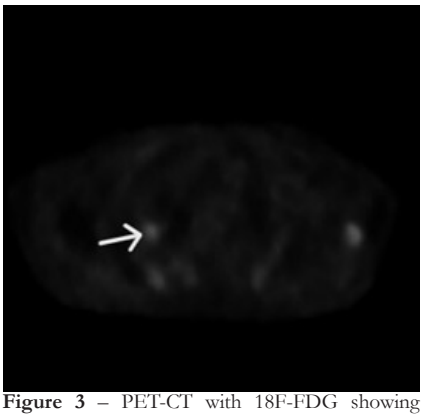

Figure 3 – PET-CT with 18F-FDG showing intense uptake in the area of interest (arrow).

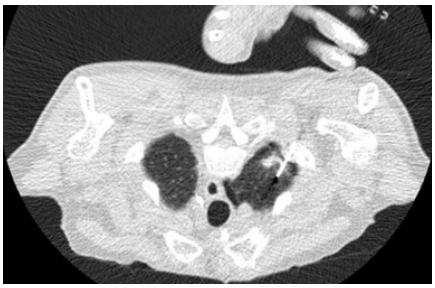

Figure 4 – CT-guided biopsy performed to exclude a neoplastic process.

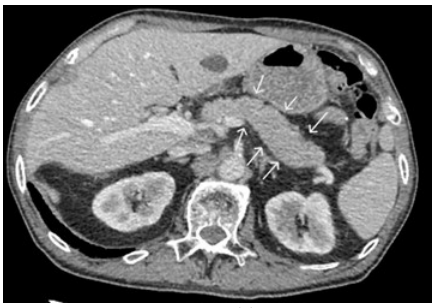

Figure 5 – Abdominal CT performed to look for other signs of IgG4-RD, showing diffuse enlargement of the pancreatic gland (arrows) – sausage shaped pancreas – which is usually seen in the context of autoimmune pancreatitis.

Discussion

IgG4-related disease (IgG4-RD) is a systemic immune-mediated fibroinflammatory disorder that can affect virtually any organ system, most commonly the pancreas. Due to its systemic nature, comprehensive imaging evaluation is recommended to assess for multiorgan involvement. Clinically, IgG4-RD often presents with subacute mass-forming lesions that may closely mimic neoplastic processes. The disease is frequently associated with elevated serum IgG4 levels (>135 mg/dL) and is histopathologically characterized by storiform fibrosis, obliterative phlebitis, and lymphoplasmacytic infiltration, with a ratio of IgG4+/IgG+ cells superior to 40%.[1,2,4,5]

There is growing literature that describes a broad spectrum of pulmonary manifestations of IgG4-RD, that can occur with or without concurrent extrapulmonary disease. Pulmonary IgG4-RD may be asymptomatic or may present with nonspecific respiratory symptoms such as cough, dyspnea, hemoptysis, chest pain, or, in severe cases, respiratory failure.[3] The most frequent intrathoracic manifestation of IgG4-RD is mediastinal and/or hilar lymphadenopathy.[6] Lung parenchymal involvement most commonly manifests as rounded opacities, mass-like lesions, and interstitial lung disease (ILD). Pulmonary nodules may demonstrate solid or ground-glass attenuation, can be solitary or multiple and vary in size, mimicking primary lung malignancy, as in the present case. The radiological appearance of ILD in IgG4-RD is heterogeneous and may include patchy ground-glass opacities, consolidation, reticular changes, thickening of the bronchovascular bundles and interlobular septa, as well as honeycombing. These overlapping imaging features pose a diagnostic challenge, as they resemble other pulmonary conditions such as IPF, as observed in our patient. Airway involvement may also occur, leading to bronchiectasis, which is thought to be secondary to parenchymal fibrosis in the peripheral lung zones - traction bronchiectasis. Additionally, pleural involvement may manifest as pleural effusions or pleural nodules.[1,2,6]

Pulmonary involvement typically demonstrates a favorable response to corticosteroid therapy, associated with clinical and radiological improvement.[3]

IgG4-related disease is a relatively recently recognized systemic condition characterized by fibroinflammatory tissue infiltration that can mimic inflammatory, infectious, or neoplastic diseases.

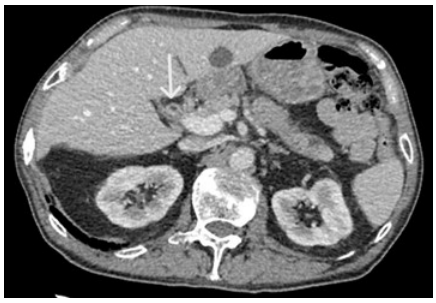

Figure 6 – Abdominal CT also revealed diffuse wall thickening of the common bile duct (arrow), raising suspicion for IgG4-related Sclerosing Cholangitis.

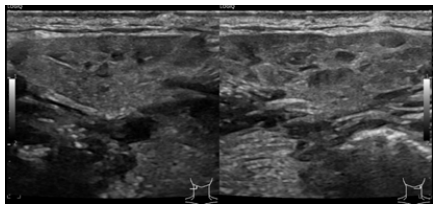

Figure 7 – Ultrasound of the submandibular salivary glands showing enlargement and marked parenchymal heterogeneity, which can be due to salivary and lacrimal gland involvement in IgG4-RD.

Conclusion

While pancreatic involvement is most common in IgG4-RD, the range of recognized extra-pancreatic manifestations continues to expand. Radiologists should be familiar with the imaging features of IgG4-RD as early recognition is crucial, given the marked responsiveness to corticosteroid therapy and the potential to avoid unnecessary invasive diagnostic procedures.

Ethical Disclosures / Divulgações Éticas

Conflicts of interest: The authors have no conflicts of interest to declare.

Conflitos de interesse: Os autores declaram não possuir conflitos de interesse.

Financing Support: This work has not received any contribution, grant or scholarship.

Suporte financeiro: O presente trabalho não foi suportado por nenhum subsídio ou bolsa.

Confidentiality of data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Confidencialidade dos dados: Os autores declaram ter seguido os protocolos do seu centro de trabalho acerca da publicação dos dados de doentes.

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Protecção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

References

1. Martínez-de-Alegría A, Baleato-González S, García-Figueiras R, Bermúdez-Naveira A, Abdulkader-Nallib I, Díaz-Peromingo JA, Villalba-Martín C. IgG4-related disease from head to toe. Radiographics. 2015 Nov-Dec;35:2007-25.

2. Muller R, Habert P, Ebbo M, Graveleau J, Groh M, Launay D, Audia S, Pugnet G, Cohen F, Perlat A, Benyamine A, Bienvenu B, Gaigne L, Chanez P, Gaubert JY, Schleinitz N. Thoracic involvement and imaging patterns in IgG4-related disease. Eur Respir Rev. 2021 Oct 5;30:210078.

3. Morales AT, Cignarella AG, Jabeen IS, Barkin JS, Mirsaeidi M. An update on IgG4-related lung disease. Eur J Intern Med. 2019 Aug;66:18-24.

4. Corcoran JP, Culver EL, Anstey RM, Talwar A, Manganis CD, Cargill TN, Hallifax RJ, Psallidas I, Rahman NM, Barnes E. Thoracic involvement in IgG4-related disease in a UK-based patient cohort. Respir Med. 2017 Nov;132:117-21.

5. Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, Klöppel G, Heathcote JG, Khosroshahi A, Ferry JA, Aalberse RC, Bloch DB, Brugge WR, Bateman AC, Carruthers MN, Chari ST, Cheuk W, Cornell LD, Fernandez-Del Castillo C, Forcione DG, Hamilos DL, Kamisawa T, Kasashima S, Kawa S, Kawano M, Lauwers GY, Masaki Y, Nakanuma Y, Notohara K, Okazaki K, Ryu JK, Saeki T, Sahani DV, Smyrk TC, Stone JR, Takahira M, Webster GJ, Yamamoto M, Zamboni G, Umehara H, Stone JH. Consensus statement on the pathology of IgG4-related disease. Mod Pathol. 2012 Sep;25:1181-92.

6. Ryu JH, Sekiguchi H, Yi ES. Pulmonary manifestations of immunoglobulin G4-related sclerosing disease. Eur Respir J. 2012 Jan;39:180-6.