

## Radiological Case Report / Caso Clínico

**IgG4-Related Disease Presenting as Mass-Like Sclerosing Mesenteritis***Doença Relacionada à IgG4 Apresentando-se como Massa de Mesenterite Esclerosante*Ana Luísa Proença<sup>1</sup>, João Lopes Dias<sup>2</sup><sup>1</sup>Serviço de Radiologia do Hospital Curry Cabral, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal<sup>2</sup>Serviço de Radiologia do Hospital de São José, Centro Hospitalar Universitário Lisboa Central, Lisboa, Portugal**Address**Ana Luísa Proença  
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e-mail: proenca.ana.luisa@gmail.com**Abstract**

IgG4 related disease (IgG4 RD) is a newly recognized entity that includes a group of immune-mediated fibro-inflammatory conditions. It can affect a wide range of organs, producing a broad spectrum of presentations. The selection of imaging modality is based on patient symptoms and the organs under evaluation. The diagnosis is based on a combination of radiological findings, serum IgG4 elevation levels, histopathological features, association with other IgG4-related diseases and response to steroids. We report a rare case of an IgG4-related sclerosing mesenteritis in a man who presented with an incidental right lower quadrant mesenteric mass and was unsuccessfully treated with corticoids. Isolated mesentery involvement is a rare presentation of IgG4-related disease and only few cases were reported in literature.

**Keywords**

IgG4-related disease; Sclerosing mesenteritis; Computed tomography.

**Resumo**

A Doença relacionada à IgG4 é uma entidade recentemente reconhecida que inclui um grupo de doenças fibroinflamatórias auto-imunes que apresentam características histológicas típicas. Pode afectar múltiplos órgãos, produzindo um amplo espectro de apresentações clínicas. A seleção dos métodos de imagem adequados é baseada nos sintomas do doente e no órgão em avaliação. O diagnóstico baseia-se na integração de achados radiológicos e histopatológicos, elevação da IgG4 sérica, associação com outras doenças IgG4 e resposta a corticoides. Descrevemos um caso raro de mesenterite esclerosante relacionada à IgG4 num homem que se apresentou com uma massa mesentérica incidental no quadrante inferior direito e que teve insucesso terapêutico com corticoides. O envolvimento isolado do mesentério é uma forma rara de apresentação da doença relacionada à IgG4, estando apenas poucos casos descritos na literatura.

**Palavras-chave**

Doença relacionada à IgG4; Mesenterite esclerosante; Tomografia computadorizada.

**Introduction**

IgG4-related disease (IgG4-RD) represents a heterogeneous group of immune-mediated fibro-inflammatory conditions that can affect multiple organs, leading to tumefactive, tissue-destructive lesions, and organ failure.<sup>1,2</sup> The epidemiology of this rare disease remains poorly described, but it seems to have a predilection for middle-aged to elderly males.<sup>3</sup>

The disease most commonly implicates the pancreas, but it can also involve the biliary tract, salivary glands, lacrimal glands, retroperitoneum or lymph nodes.<sup>4</sup> Clinical presentation is typically subacute with varied and unspecific manifestations, depending on the affected organs and the mass effect exerted by the lesions on the viscera and vessels.<sup>5</sup> Some cases remain asymptomatic and are detected incidentally.<sup>6</sup>

The selection of an imaging modality should be based on symptoms and the organs under evaluation.<sup>1</sup> Elevated serum IgG4 concentration is often, but not always present, so it is unreliable as diagnostic marker.<sup>3</sup> However, it remains important for patient assessment as it seems to correlate with the number of organs involved.<sup>1</sup> Tissue biopsy for diagnostic confirmation and exclusion of malignancies is strongly recommended and clinicopathologic correlation is essential.<sup>3</sup>

Multiple treatment approaches have been suggested, including “watchful waiting” in asymptomatic patients, use of systemic corticoids, and surgical debulking.<sup>1</sup> In refractory cases, “steroid-sparing” immunosuppressive drugs or biologic agents may be used.

**Case Report**

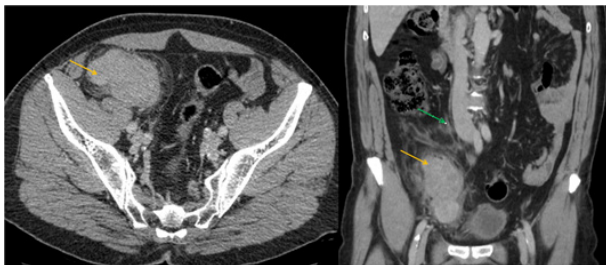
A 60-year-old man was admitted to our hospital to study an incidental right mesenteric mass found during a routine pelvic ultrasound. The patient was asymptomatic and had no relevant surgical or medical history. His physical examination and laboratory workup were normal. Computed tomography (CT) revealed a 8-cm, lobulated, well-circumscribed, soft tissue mass, located at the mesentery fat of the right lower quadrant, anterior to the right psoas muscle and external iliac vessels, with surrounding fatty straining. The mass pushed the right ureter without causing upstream dilatation. No lymphadenopathy, vascular encasement or signs of local invasiveness were present (Figure 1). Further magnetic resonance imaging (MRI) was performed. The lesion showed hypersignal in T2-weighted images (T2WI), hyposignal in T1-weighted images (T1WI),

and slight enhancement after gadolinium-based contrast administration (Figure 2).

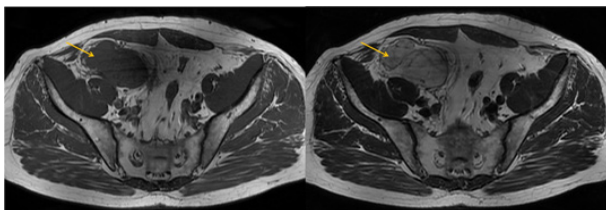
Percutaneous biopsy revealed a fibrosing lesion with storiform pattern, focal areas of lymphoplasmocitary infiltration and high number of IgG4-positive plasmacytes (more than 40% and more than 30 cells/HPF). Obliterative vasculitis lesions were also observed, with no evidence of neoplastic or granulomatous tissue. The histological findings were compatible with IgG4-RD.

Post-biopsy serum IgG4 levels were within the normal range, and the remaining laboratory research was unremarkable.

The final diagnosis was IgG4-related mass-like sclerosing mesenteritis. The patient was discharged with scheduled follow-up and underwent no treatment, as he was asymptomatic. A year later, the patient remained free of symptoms, but the mass showed continuous growth on follow-up CT, so 40mg/day prednisolone was started. The mass kept growing under steroid therapy and methotrexate 15mg/6months was introduced. Four years of follow-up documented clinical and radiological stability.



**Figure 1** – Axial and coronal contrast enhanced-CT showing the mass (yellow arrow). The green arrow shows the right ureter, without upstream dilatation.



**Figure 2** – MRI with axial T1-WI and T2-WI. Yellow arrows show the mass, which has isointensity to muscle in T1-WI and hypersignal in T2-WI.

## Discussion

Isolated mass-like sclerosing mesenteritis (SM) is a rare form of presentation of IgG4-RD, with only few cases described in literature. Most frequently, retroperitoneal or diffuse mesenteric root involvement are observed.<sup>7</sup>

Both IgG4-RD and SM show male predominance, in middle-aged to elderly man, and have unclear etiology, as in the case described.<sup>8,9,10</sup>

The course of IgG4-RD is uncertain. A few cases improve spontaneously, and most show subacute or chronic progression. The severity of symptoms depends on the disease activity and the pattern of organ involvement.<sup>11</sup> Constitutional symptoms and fever are unusual.<sup>2</sup> In the particular case of SM, chronic abdominal pain is the most common presentation, often associated with nausea, vomiting, cramping or diarrhea.<sup>6,9</sup> However, patients may be asymptomatic and diagnosed incidentally through radiologic findings, as in our case, or in pathological specimens.

Although the current gold standard for the diagnosis of IgG4-RD is histological assessment, it also depends on the combination of other features like radiological findings, elevated serum IgG4 levels, association with other IgG4-related diseases, and response to steroids (Table 1).<sup>3</sup> It remains a challenging diagnosis due to the broad spectrum of affected organs and lack of universal criteria including all patients with IgG4-RD.<sup>11,12</sup> Established diagnostic criteria were proposed for the most common involved organs (pancreas, biliary tree, kidney and salivary/lachrymal glands), but are not yet established for the remaining sites.<sup>11,12</sup> Appropriate histopathological findings are essential for diagnosis plus at least one additional criterion (serology, steroid responsiveness or other organ involvement).<sup>11</sup>

**Table 1** – Adapted from Current Topics in Microbiology and Immunology, 2016<sup>11</sup>

Diagnostic criteria for IgG4-RD, 2011
<b>1. Clinical examination showing characteristic diffuse/localized swelling or masses in single or multiple organs</b>
<b>2. Hematological examination shows elevated serum IgG4 concentrations (<math>\geq 135</math>mg/dL)</b>
<b>3. Histopathological examination shows:</b>
(3.1) Marked lymphocyte and plasmacyte infiltration and fibrosis
(3.2) Infiltration of IgG4+ plasma cells: ratio of IgG4+/IgG+ cells $>40\%$ and $>10$ IgG4+plasma cells/ high power field
<b>Definite: 1 +2 +3</b>
<b>Probable: 1 +3</b>
<b>Possible: 1 +2</b>

The major histological findings include abundant infiltration of IgG4-positive plasma cells and lymphocytes, storiform fibrosis, and obliterative phlebitis.<sup>11</sup> Persistent inflammation has been shown to lead to swelling and fibrosis, leading to organ dysfunction. The diagnosis may be difficult in chronic lesions that have become predominantly fibrotic.

A majority of patients with IgG4-RD have high serum IgG4 levels, but approximately 30% of patients have values within normal range, mostly patients with early or limited disease.<sup>3</sup> Elevated serum IgG4 levels may also be seen in autoimmune or allergic conditions, carcinomas and Castleman's disease.<sup>11</sup> Despite not being sensitive neither specific, the degree of serum IgG4 elevation correlates with the number of organs involved.<sup>1</sup>

IgG4-RD's imaging findings are nonspecific.<sup>2,5</sup> Contrast-enhanced-CT images may show diffuse or focal swelling of organs or soft tissue masses, usually with well-defined margins and homogeneous delayed phase enhancement. Isointensity to muscle on T1-weighted MRI and hypointensity on T2-weighted MRI reflect fibrosis, while high T2 signal may be seen in active phases of disease, representing inflammatory edema.<sup>10</sup> Fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET/CT) can be useful for assessing IgG4-RD involvement in other organs by highlighting hypermetabolic activity.<sup>11</sup>

Mesenteric involvement in IgG4-RD is more common in the small bowel mesentery.<sup>5</sup> However, in our patient, single involvement of the mesocolon was seen, which has been described in 20% of cases.<sup>9</sup> In general, it can present as diffuse thickening of the root of mesentery, or as single or multiple masses. Some signs were described, including the "fat-ring" sign (area of preserved fat around the mesenteric vessels) and a "tumoral pseudocapsule" (band

of soft tissue surrounding the inflamed mass).<sup>5,9</sup> Misty mesentery sign is a nonspecific feature and refers to diffuse increased attenuation in the mesentery often associated with small to borderline-sized nodes, representing chronic inflammation. Calcification and fat necrosis may also be seen.<sup>10</sup> With disease progression, fibrosis becomes prominent and retractile changes may encase vessels and compress abdominopelvic organs.<sup>10</sup>

Based only on imaging findings, our differential diagnoses had to include both neoplastic and inflammatory diseases, such as sarcoma, inflammatory malignant fibrous histiocytoma, lymphoma, desmoid tumor, inflammatory pseudotumor, and mass-like sclerosing mesenteritis, so percutaneous biopsy and consequent histological analysis were critical for the final diagnosis.<sup>6,7</sup>

No generalized consensus regarding the treatment of SM in IgG4-RD exists, so it is customized for each patient.<sup>6,8</sup> Asymptomatic patients may delay treatment and be kept in “watchful waiting”. However, fewer long-

term complications and higher rates of remission were reported on patients that received prompt treatment.<sup>1</sup> For symptomatic patients, prednisone is recommended to induce remission and continued for up to 3 years at reduced doses (2,5mg or 5mg/day).<sup>3</sup> Alternative treatments in refractory disease or steroid intolerance have been proposed, including immunomodulatory drugs (azathioprine, methotrexate) or rituximab.<sup>2,11</sup> IgG4-related disease generally responds well to glucocorticoids during its inflammatory stage, but in chronic, highly fibrotic lesions, recurrent or refractory cases are common.<sup>1,2</sup> Surgical resection or debulking may have a role in symptomatic relief, but does not prevent disease progression.<sup>6</sup>

In summary, we present a case of focal mass-like SM, representing a rare manifestation of an IgG4-RD. Due to its rarity, wide range of organs affected and confusing nomenclature in literature, more cases and studies are needed to characterize the IgG4-RD spectrum and raise awareness about this condition.

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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).  
Proteção 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.

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