Case Report

Aphthous stomatitis and laryngitis, another form of presentation of an IgG4-related disease?

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ABSTRACT

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RESUMEN

La enfermedad relacionada con IgG4 (ER-IgG4) se caracteriza por un infiltrado linfoplasmocítico rico en células plasmáticas IgG4 positivas, fibrosis estoriforme y flebitis obliteratoriva. Se puede presentar como seudotumor orbitario, parotidomegalia, nefritis túbulo intersticial, fibrosis retroperitoneal o pancreatitis, aunque prácticamente cualquier órgano puede verse afectado. Presentamos el caso de una mujer de 37 años, que presenta un cuadro de disfonía severa y aftosis oral dolorosa recurrente, con unos hallazgos histopatológicos a nivel laríngeo que muesran infiltrado linfoplasmocítico y positividad para IgG4, así como amplios estudios descartando otras etiologías, por lo que se confirma una laringitis por ER-IgG4, cuya descripción en la literatura es excepcional.

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A 27-year-old woman who presented with severe dysphonia of 3 year onset, and painful oral aphthous ulcers which spontaneously receded after around 2 weeks, with several outbreaks per year. She did not report dry syndrome, uveitis, arthritis, acne, thrombosis, diarrhoeas, abdominal pain or episodes of chondritis. She had received treatment with omeprazol, as well as aciclovir and low doses of oral corticoids due to the aphthosis, with no improvement.

General and ophthalmological examination was normal, except for the dysphonia and a fibroscopy confirmed intense laryngitis. Complete blood count, general biochemistry, ESR and C-reactive protein tested normal. Determination of HLA-B5, ANA, ANCA, anti-transgluaminase IgA antibodies and HIV serology tested negative. Computerized tomography of the neck and chest only showed contrast enhanced uptake at laryngeal level and small non-specific laterocervical adenopathies. A laryngeal biopsy showed an inflammatory infiltrate with positive immunohistochemistry for IgG4, and IgG4/IgG-related disease of nearly 40% (Fig. 1). No plasmablasts were observed (lymphocytes with CD19+CD24−CD38+ phenotype) in peripheral blood. Serum IgG4: 1.40 U (N: .05–1.25), A 18F-FDG PET/CT scan showed laryngeal level uptake, but not at blood vessel or other cartilaginous structure level (Fig. 2).

On diagnosis of IgG4-related disease with laryngeal involvement, treatment was initiated with 3 boluses of 125 mg of methylprednisolone, followed by oral prednison (4 mg/kg/day) with gradual tapering, adding azathioprine as a steroid replacement, with improvement of dysphonia and with no further outbreaks of aphthosis.

IgG4-related disease is a fibro-inflammatory disease, which was first described in 2003 and the clinical spectrum of which has extended. An IgG4-related disease is considered possible when it affects a typical organ and there is elevated serum IgG4, probable IgG4-related disease due to the presence of typical histological findings and IgG4/IgG >40%. It is considered a definitive IgG4-related disease when there is a combination of involvement of a typical organ, elevated serum IgG4 levels and compatible histopathology. In our patient, diagnosis of IgG4-related disease could be considered probable. Involvement of IgG4-related disease to ENT level is exceptional, and as far as we know has only been described in one case of pseudo tumour at tracheal level.

Furthermore, the patient reported recurrent oral aphthosis for which the differential diagnosis with a Behçet disease (BD) was suggested, ruling out the most common diseases involving oral ulcers. A case has recently been reported of a laryngeal and oral aphthosis IgG4-related disease, similar to that of our patient, which was focused as a overlapping BD syndrome. Overlapping between systemic diseases is well known, including that of BD and polychondritis (MAGIC syndrome) or that of positive ANCA vasculitis and IgG4-related disease. In these cases treatment was based on the severity of the disease and the affected organs. In IgG4-related diseases glucocorticoids are the treatment of choice, whilst steroid replacements used are azathioprine or mycophenolate and rituximab for refractory or severe cases.

Finally, we believe that laryngitis should be included in the clinical spectrum of IgG4-related diseases. As with other presentations of the disease which may mimic other diseases, in this case it was a BD, which could be a new overlapping syndrome.

![Fig. 1. Biopsy of the larynx. Haematoxylin–eosin: (A) Chronic inflammatory infiltrate (×100). (B) lymphoplasmocytic type infiltrate (×200). (C) Using immunohistochemical techniques, plasmatic cells CD138+ (×100). (D) Specific staining for IgG4 (×100).](image-url)
**Conflict of interests**

The authors have no conflict of interests to declare.

**References**


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Fig. 2. Laryngeal uptake (arrow) in the 18F-FDG PET/CT scan.