



## Case Report

# Immunoglobulin G4-related disease presenting as an intracranial mass extended from the infratemporal fossa

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## ABSTRACT

**Background:** Neurological manifestations in immunoglobulin G4-related diseases (IgG4-RD) are rare and documented in <2% of cases. It commonly involves pachymeninges forming hypertrophic pachymeningitis and rarely forms tumor-like masses.

**Case Description:** We present our experience with a biopsy-proven case of IgG4-RD presenting with an intracranial extradural tumor-like mass infiltrating the temporal lobe. The patient was treated with high doses of corticosteroids followed by slow tapering. The neurological manifestations gradually improved and resolved after 2 months with a cerebral MRI showing a significant reduction in the tumoral size.

**Conclusion:** When it comes to intracranial mass, IgG4-RD neuropathy is one of the rarest differential diagnoses for the central nervous system tumors. Early recognition of IgG4-RD and appropriate establishment of its long-term treatment may avoid unnecessary investigations and morbidity.

**Keywords:** Corticosteroids, Extra-axial neoplasm, Immunoglobulin G4-related disease, Neurological manifestations, Pseudo-tumors

## INTRODUCTION

IgG4-related disease (IgG4-RD) is a recently recognized chronic inflammatory condition and characterized by tissue infiltration with lymphocytes and IgG4-secreting plasma cells, which can involve any organ or system.<sup>[1,17]</sup>

It is a relapsing-remitting disease associated with a tendency to form tissue-destructive lesions. It can damage several sites especially the pancreas, bile ducts, lacrimal, and salivary glands. Head and brain involvement is rare.<sup>[1,17]</sup> Principal neurological manifestations result from pachymeningitis, pituitary gland, and stalk involvement.<sup>[8]</sup>

In this article, we present one of the rarest cases of an intracranial tumor-like mass in IgG4-RD.

The purpose of this report is to supply further information helpful in distinguishing this disease from other extra-axial tumors.

## CASE PRESENTATION

We report the case of a 37-year-old man with a 6-month history of headaches and blurred vision. Our patient had been followed by an otorhinolaryngologist for 2 years for cervical lymphadenopathy and a right submandibular swelling. The cervical lymphadenopathy biopsy was non-diagnostic twice, showing a non-specific inflammatory disease. He had no other medical background and no personal or familiar history of an autoimmune disease.

On examination, he had significant swelling of the right hemi face and the neck with trismus and a decrease in the visual acuity of the right eye. The dilated fundus examination showed a right papillary paleness.

Peripheral blood markers of inflammation were elevated. Screening for immunodeficiency and mycobacterial infections was negative.

Cerebral MRI showed a pseudotumoral lesion developing in the right pterygoid-palatine fossa spreading to the orbital and the intracranial cavity through the superior orbital fissure. The intracranial portion forms a temporal extra-axial mass mimicking a meningioma that infiltrates the lateral wall of the cavernous sinus. The lesion was strongly enhanced after the injection of gadolinium [Figure 1]. CT scans of the chest, abdomen, and pelvis were normal.

The patient was operated through a pterional approach. Our first strategy was a gross total resection of the intracranial portion of the tumor. Regarding its very firm consistency, we opted for a large biopsy of the extra-axial lesion. The tumor was solid, well-delineated, and strongly adherent to the temporal lobe.

Histological examination showed dense lymphoid-plasmacytic infiltrate with storiform fibrosis [Figures 2 and 3]. Immunohistochemical staining revealed an increased number of IgG4-positive plasma cells [Figure 4]. The inflammation is often focal, predominantly in a perivascular location.

Our patient received high doses of corticosteroids (0.6 mg/kg/day) followed by progressive tapering. His neurological manifestations gradually improved and resolved after 2 months. A cerebral MRI was done 1 month after a well-conducted treatment and showed a reduction of the tumor's size [Figure 5].

## DISCUSSION

In 2001, Hamano *et al.* were the first to identify IgG4-RD after finding elevated serum levels of IgG4 in patients having autoimmune pancreatitis compared to patients with other causes of chronic pancreatitis.<sup>[3]</sup> Nowadays, IgG4-RD is known as a systemic and chronic inflammatory process with

poorly understood origin despite some theories suggesting an autoimmune or allergic mechanism. It is characterized by increasing IgG4-positive plasma cells and lymphocytes that infiltrate one or multiple organs such as the lacrimal gland, salivary gland, pancreas, bile duct, liver, kidney, and retroperitoneum.<sup>[10,15,17]</sup> It occurs predominantly in men and is more common in the fifth to the sixth decade.<sup>[2]</sup>

The neurological manifestations in IgG4-RD were only documented in <2% of cases and it commonly involves pachymeninges forming hypertrophic pachymeningitis. In a rare instance, it may form inflammatory pseudotumoral masses resembling meningiomas. To the best of our knowledge, only two cases of intracranial spread of IgG4-RD through skull base foramina have been reported in the literature.<sup>[2]</sup>

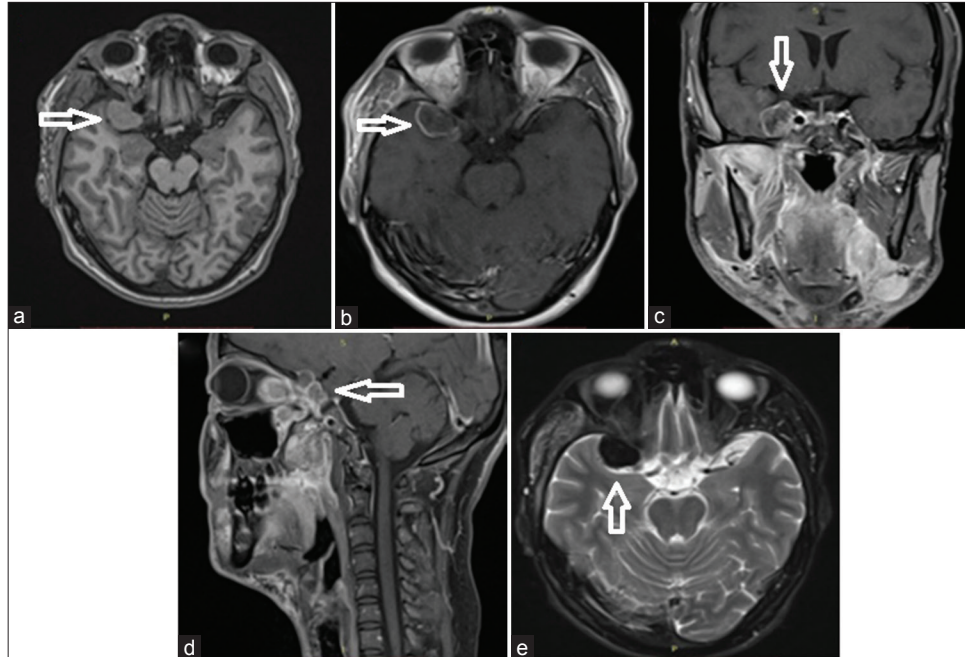
The clinical presentations of IgG4 neuropathy are various. Chronic headache is the most frequent symptom. Patients with IgG4-RD usually have increased serum IgG4 levels. However, this elevation is not constant which makes it a nonspecific index of this pathology.<sup>[1,9,10]</sup>

Imaging studies in IgG4-RD are useful both for diagnostic and monitoring purposes of these intracranial masses. On computed tomography (CT) scans, lesions are hypodense and demonstrate strong contrast enhancement. On T2-weighted-MRI images, lesions are typically hypointense. T1-weighted images usually demonstrate homogeneous and gradual gadolinium enhancement.<sup>[1,6,7,16]</sup>

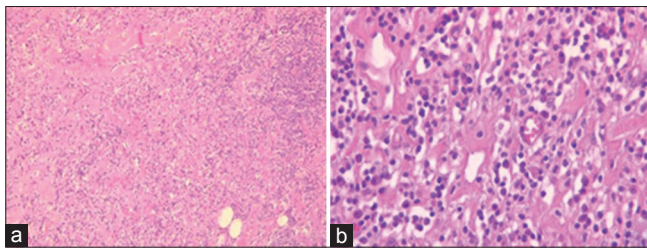
Despite the increasing frequency of IgG4-related neuropathy, there are no consensus guidelines on its treatment. Commonly, glucocorticoids, usually methylprednisolone or prednisolone, are the first-line treatment with an excellent response.<sup>[5,11]</sup> A dose of 0.6 mg/kg/day is given for at least 2–4 weeks for a response, followed by a tapering schedule over 3–6 months down to a maintenance dose of 2.5–5 mg/day maintained for up to 3 years.<sup>[15]</sup> In the case of steroid resistance, other immunosuppressants, such as cyclophosphamide and methotrexate, were used with success in refractory cases.<sup>[4,12–14]</sup>

When it comes to intracranial pseudotumors, it is still unclear whether a biopsy or partial/subtotal resection is better. Surgical decompression may be required only in the presence of compressive symptoms.<sup>[12,18]</sup>

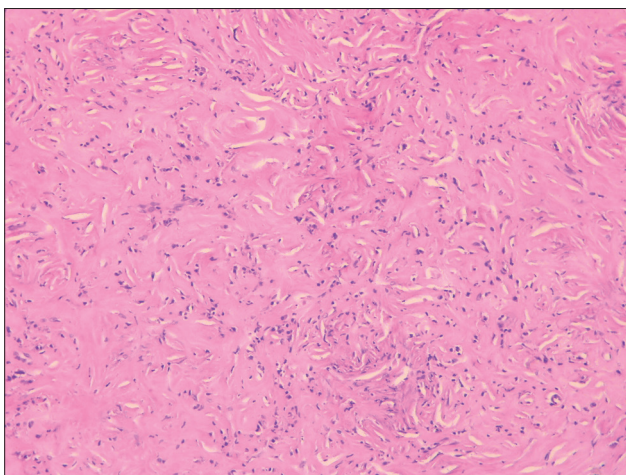
Finally, the present case suggests that IgG4-RD can form intracranial pseudotumoral masses, meaning that serologic and histologic examinations for IgG4-positive plasma cells must be performed to diagnose the etiology of unusual intracranial masses. However, at present, reports of patients with IgG4-related pseudotumors are still rare. Further reports will be useful to establish this disease concept and guidelines on its treatment.



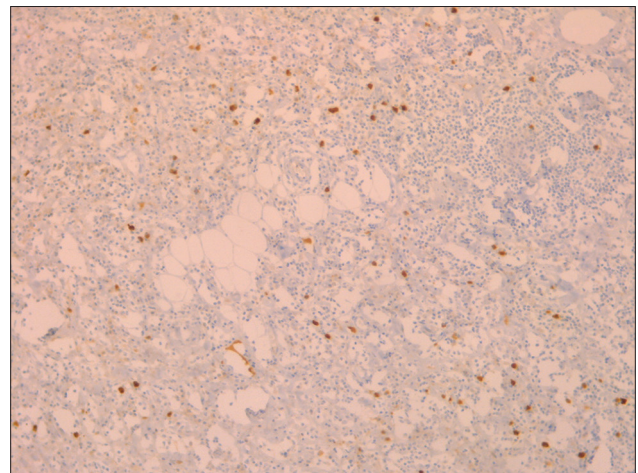
**Figure 1:** Preoperative MRI demonstrating a sharply margined extra-axial temporal mass with relatively homogeneous contrast-enhancement and extends to the sella turcica and the sub-temporal fossa (a) T1-weighted image (arrow), (b-d) T1-weighted image with gadolinium contrast on transverse, coronal, and sagittal section, and (e) T2-weighted image (arrow).



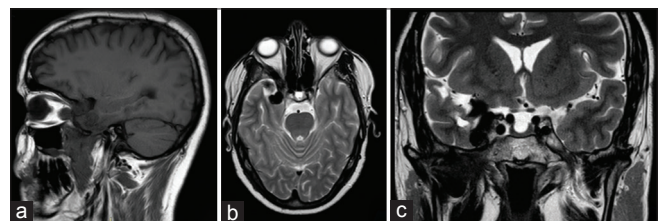
**Figure 2:** Dense lymphoplasmocytic infiltrate (a: Hematoxylin and Eosin  $\times 100$ ; b: Hematoxylin and Eosin  $\times 400$ ).



**Figure 3:** Storiform fibrosis (Hematoxylin and Eosin  $\times 100$ ).



**Figure 4:** Immunostaining of many plasma cells with the IgG4 antibody ( $\times 100$ ).



**Figure 5:** Postoperative MRI (a) T1-weighted image in sagittal section and (b and c) T2-weighted image in axial and coronal section.

## CONCLUSION

The IgG4-RD is one of the rare differential diagnoses of the central nervous system tumors. Early recognition of IgG4-RD and appropriate establishment of its long-term treatment may avoid unnecessary investigations and morbidity.

## Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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## Conflicts of interest

There are no conflicts of interest.

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