Two interesting cases of intracranial IgG4-related disease and discussion of therapy options

Sirs,

IgG4-RD is an immune-mediated condition characterised by tumefactive fibrosis and dense lymphoplasmacytic infiltrates containing numerous IgG4-positive plasma cells. IgG4-RD can involve a wide range of tissues and organs; however, intracranial involvement is rare (1). Intracranial IgG4-RD, depending on the site, can result in neurologic dysfunction. Being a recently characterised disease entity, IgG4-RD treatment protocols are not extensively described. Here, we report two cases of intracranial IgG4-RD and present a brief review of the current therapeutic approaches.

Case 1. A 48-year-old woman presented with left eye visual field loss. Brain MRI showed a mass along the anterior clinoid process with compression of the left optic nerve (Fig. 1A-B), concerning for a meningioma. Biopsy showed fibrotic tissue with a predominance of IgG4 plasma cells, sufficient for a formal designation of IgG4-RD (Fig. 1E-F). The patient was treated with dexamethasone, which continued as prednisone 12.5 mg daily and then tapered over seven months. This patient also received two biweekly infusions of rituximab (1000 mg/infusion). This treatment was repeated six months later for evidence of relapsing disease. Although the patient's visual field deficit did not resolve, her symptoms remained stable on low-dose maintenance prednisone for 18 months after the last Rituxan infusion.

Case 2. A 60-year-old woman presented with one year of visual changes and hypopituitarism. Brain MRI showed a sellar lesion with optic chiasm compression, concerning for a pituitary adenoma (Fig. 1C-D). The biopsy showed characteristic fibrosis with a predominance of IgG4 plasma cells and was formally designated as IgG4-RD (Fig. 1G-H). There was improvement in her clinical symptoms, and the patient remained on treatment with low-dose prednisone for one year. One year later, the brain MRI showed increase in the size of the sellar lesion with suprasellar extension. She was treated with two biweekly infusions of Rituxan and has been stable for one year on low-dose prednisone.

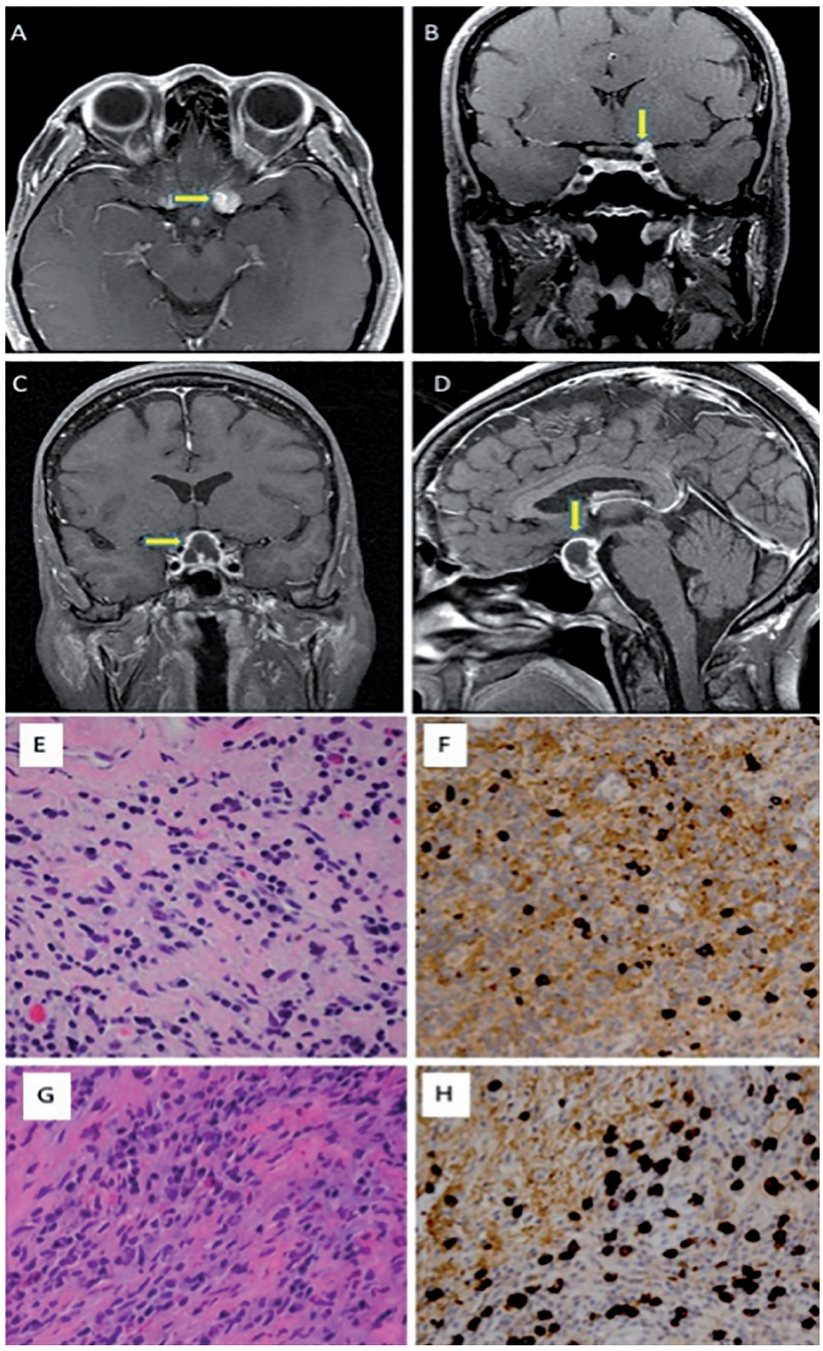

Fig. 1. Case 1: Axial and coronal MRI showing soft tissue mas abutting left optic nerve (**A-B**).
Case 2: Coronal and sagittal MRI images show intra/suprasellar mass (**C-D**).
Both cases, Case 1 (**E-F**) and Case 2 (**G-F**) contained tissue fibrosis and IgG4 rich lymphoplasmacytic infiltrates.

Previous reports demonstrate that IgG4-RD is responsive to glucocorticoids (2, 3). A retrospective study demonstrated efficacy of treatment with glucocorticoids in IgG4-related aortitis, periaortitis, and periarteritis (4). IgG4-RD is often a relapsing disease, and prolonged glucocorticoid treatment is commonly required. Methotrexate and azathioprine have been used as steroid-sparing agents (5, 6). Chen *et al*. reported successful treatment of orbital disease with a combination of rituximab and glucocorticoids (7).

In the SMART (Sapporo Medical University and Related Institutes Database for Investigation and Best Treatments of IgG4-related Disease) database of 122 patients with IgG4-related dacryoadenitis and/or sialadenitis, glucocorticoids were used to treat 92.1% of cases. The mean maintenance dose of prednisolone was 4.8 mg/day. Three cases required treatment with rituximab. Fifty percent of the cases relapsed within seven years of initial treatment, and the annual relapse rate was 11.5% (8). In a series of 10 patients who had failed glucocorticoid and other disease-modifying anti-rheumatic drugs (DMARDs), rituximab led to clinical improvement and tapering/discontinuation of glucocorticoids. Four out of ten patients, however, relapsed and required retreatment after the two initial biweekly infusions of rituximab (9). In a case of severe refractory IgG4-RD, fludarabine was used in combination with rituximab (10).

In summary, IgG4-RD is a recently described, relapsing disease which can involve nearly any tissue, usually at the expense of the organ's function. The diagnosis of this treatable entity requires not only histopatho-

logic confirmation of the disease, as well as exclusion of neoplastic and infectious processes. Although IgG4-RD is responsive to steroids, B-cell depleting antibodies and/or DMARDs have been used in isolated cases. Further studies are needed to direct therapy and interventions that will lead to improved patient outcomes.

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Competing interests: none declared.

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