The Primary Brain Eosinophilic Angiocentric Fibrosis, A Rare Case Report

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Received November 26, 2021; Accepted April 11, 2022.

Key words: Eosinophilic angiocentric fibrosis – Suprasellar mass – Surgical resection – Glucocorticosteroid

Abstract: Eosinophilic angiocentric fibrosis (EAF) is a rare progressive fibrosing lesion involving the nasal cavity, paranasal sinuses, and the upper respiratory tract. There are few reports that it rarely involves the orbit; however, there is no report of intracranial involvement. Here, we report and share our experience with a rare case of primary intracranial EAF. A 33-year-old woman with a history of a suprasellar mass and unsuccessful surgical and medical treatment referred to us. Physical examination demonstrated right-sided blindness and ptosis, left-sided decreased visual acuity, and visual field defect. The brain imaging revealed an extra-axial intradural well-defined large suprasellar mass with parasellar (more on the right side) and retrosellar extension. Via pterional craniotomy and subfrontal approach, a very firm creamy-brownish well-defined fibrotic mass was encountered. The tumour texture was too firm to be totally resected. The microscope exited the surgical field off, and the tumour was incompletely resected using a rongeur. The histopathology finding favoured EAF. Further histopathology evaluation failed to show histologic features of IgG4-related disease. Although the preoperative diagnosis of EAF is impossible, in the setting of an indolent slow-growing lesion demonstrating hypointensity on the T2 image sequence of MRI (magnetic resonance imaging), EAF should be considered a differential diagnosis. In the setting of this diagnosis, the systemic and other organ involvement for a diagnosis of IgG4-RD should be evaluated. However, more cases are needed to illustrate the relation between these two entities.

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https://doi.org/10.14712/23362936.2022.12

Introduction

Eosinophilic angiocentric fibrosis (EAF) is a rare progressive fibrosing lesion involving the nasal cavity, paranasal sinuses, and the upper respiratory tract (Ahn and Flanagan, 2018). There are few reports that it rarely involves the orbit; however, there is no report of intracranial involvement (Radhakrishnan et al., 2015; Ahn and Flanagan, 2018). Here, we report and share our experience with a rare case of primary intracranial EAF.

Case report

A 33-year-old woman referred to us due to progressive visual loss. Her medical history demonstrated previous craniotomy and biopsy, glucocorticosteroid prescription, and radiation therapy for a suprasellar mass. However, all treatments failed to be effective. The physical examination demonstrated right-sided blindness and ptosis, left-sided decreased visual acuity, and visual field defect, which was confirmed on perimetry. The brain imaging revealed a large intradural but extra-axial well-defined suprasellar mass with parasellar (more on the right side) and retrosellar extension. The lesion was hyperdense on a CT (computed tomography) scan (Figure 1). On MRI (magnetic resonance imaging), the lesion was isointense on T1, and hypointense on T2, and it showed inhomogeneous moderate enhancement on T1 with Gd injection (Figure 2). The laboratory data and hypophysial laboratory profiles were normal except for secondary hypothyroidism. Considering the progressive symptoms, surgical intervention was scheduled. Regarding the history of craniotomy, failure of all therapeutic modalities, and radiologic features of the lesion, we anticipated an unusual pathology and decided to carry out craniotomy again to achieve total resection. Via pterional craniotomy and subfrontal approach, a very firm creamy-brownish well-defined fibrotic mass was encountered. The tumour texture was too firm to be totally resected. The microscope exited the surgical field off, and the tumour was incompletely resected using a rongeur (Figure 3). The histopathology report was as follows: concentric proliferation of small vessels with obliteration of their luminal, which were confluent with extensive hyaline fibrosis and foci of fibrinoid necrosis. The involved area was surrounded by

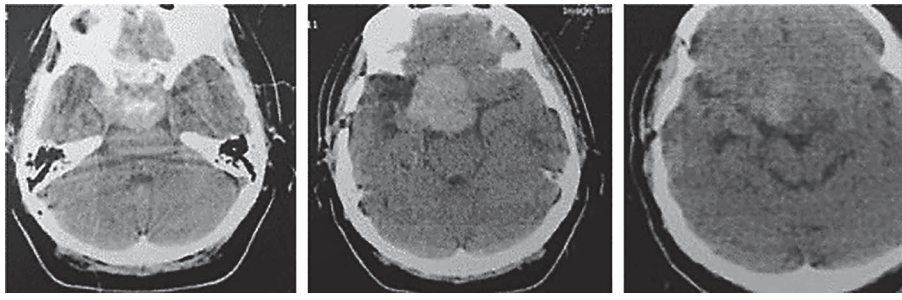

Figure 1 – The patient's brain computed tomography scan.

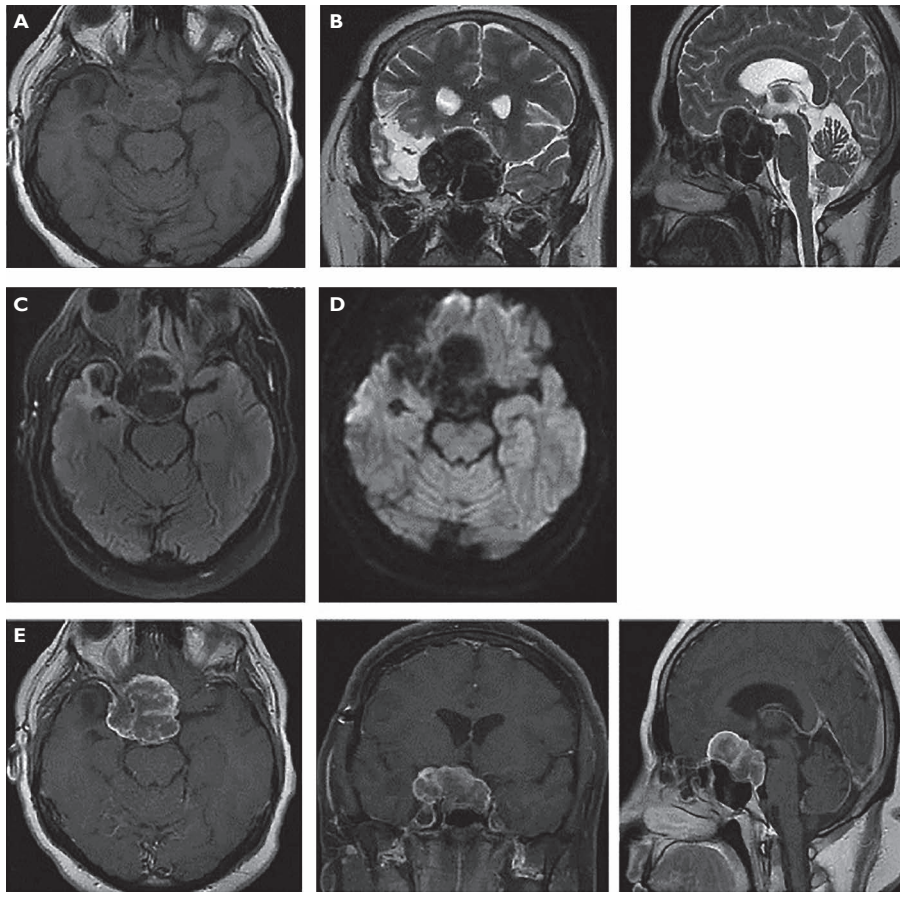

Figure 2 – The brain magnetic resonance imaging demonstrated a well-defined lobulated suprasellar mass with parasellar and retrosellar extension. The lesion is isointense on T1 (A), hyperintense on T2 (B) and FLAIR (C), and hypointense on DWI (no restriction effusion) (D), and exhibits inhomogeneous moderate enhancement on T1 with Gd injection images sequences (E).

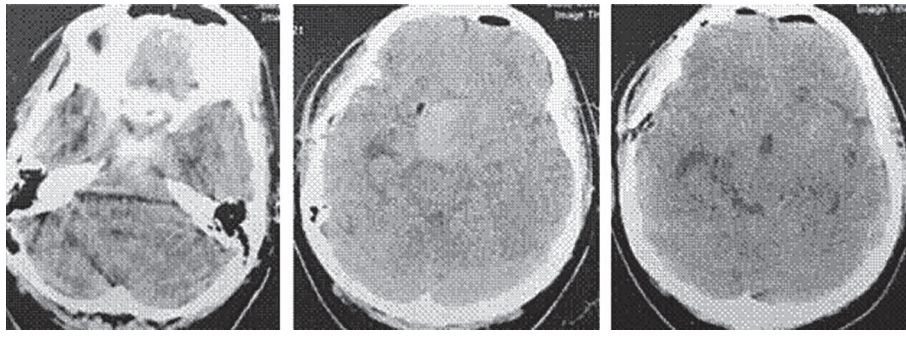

Figure 3 – The postoperative brain computed tomography scan demonstrated incomplete resection.

some lymphoplasmacell infiltration and considerable eosinophils. This finding was in favour of EAF. Further histopathology evaluation revealed that IgG4 was positive in less than 20% of IgG4 plasma cells, and immunostaining for IgG and IgG4 failed to exhibit histologic features of IgG4-related disease (IgG4-RD). Another expert and skilled neuropathologist reviewed the pathology specimen to avoid misdiagnosis.

Considering the course of the lesion (incomplete resection, no response to the medical therapy including corticosteroid and radiotherapy), the patient was referred to a radiation oncologist for monoclonal antibody therapy (Rituximab).

Discussion

EAF is a rare, benign, slow-growing but progressive lesion with an unknown etiology. It involves the nasal cavity, paranasal sinuses, and the upper respiratory tract. It has an indolent course, and patients present commonly with a prolonged history of nasal obstruction, nasal deformity, and epistaxis. Men are more involved than women are, and the mean age of involvement is 48 years old with a range of 16–79 years old (Karligkiotis et al., 2014; Ahn and Flanagan, 2018).

Tumour grossly is a tan to white fleshy, firmly submucosal lesion with varying size and extension. Orbital involvement occurs rarely and can result in epiphora, proptosis, and diplopia (Lloyd et al., 2015; Ahn and Flanagan, 2018).

The etiology of the disease is unknown. Some researchers showed its association with allergic and atopic disorders, and recently, some others have noted that it is an IgG4-RD. In addition, there are reports of its association with the granuloma faciale and granulomatosis with polyangiitis (GPA) (previously Wegener's granulomatosis). Furthermore, some maintain that it is a progressive fibrotic reaction rather than a true separate disease (Lloyd et al., 2015; Radhakrishnan et al., 2015; Ahn and Flanagan, 2018).

CT scan and MRI may be non-specific. On CT scan, the lesion is usually homogenous in a dense mass. Calcification is a rare finding. The lesion is isointense on T1 and hypointense on T2 images sequences and exhibits moderate inhomogeneous enhancement on T1 with Gd injection (Jin et al., 2016).

The histologic finding in the early stage includes patchy eosinophilic vasculitis in submucosa small vessels, eosinophils aggregation, migration through the vessel wall and evidence of degranulation, and a variable number of plasma cells and lymphocytes. At the mature stage, the histology demonstrated the foci of early fibrosis, spindle-shape fibroblasts resulting in the pseudo granulomatosis appearance, and reactive lymphoid follicles. True granulomatosis reaction and cytologic atypia are absent. The histologic features of the late-stage are as follows: dense fibrosis thickening in the subepithelial stroma, plasma cells, lymphocytes progressive loss, prominence of the eosinophils, concentric lamellar collagen deposition giving the onionskin fibrosis appearance (a characteristic feature of EAF), and no necrosis, mitotic activity, and true granuloma (Ahn and Flanagan, 2018).

After histologic confirmation of EAF, the immunohistochemistry for IgG and IgG4 should be performed. The diagnostic histologic features for IgG-RD include morphologic appearance, storiform type fibrosis, increased number of IgG4 plasma cells (more than 50 cells in each high-power field), and a ratio of plasma-cells IgG4/IgG more than 40%. In this situation, other pathologies associated with increased IgG should be evaluated and rolled out, such as primary sclerosing cholangitis, rheumatoid arthritis, and lymphoma (Radhakrishnan et al., 2015; Ahn and Flanagan, 2018).

The broad spectrum of the disease accounted for the differential diagnosis of EAF. These include reactive conditions (Wegener's granulomatosis, sarcoidosis, Sjogren's disease, Kimura's disease, erythema elevatum diutinum, granuloma faciale, granulomatosis with polyangiitis, Churg-Strauss syndrome, and angio lymphoid hyperplasia with eosinophilia), neoplastic lesions, such as neurogenic tumours (schwannoma), vascular tumours (angiofibroma, hemangiomas), and mesenchymal tumours (fibroma, fibrosarcoma, nodular fasciitis, and fibromatosis). Many of these diseases can be ruled out by using history and physical examination, autoimmune serology and other laboratory data, as well as the absence of granuloma on histology (Radhakrishnan et al., 2015; Ahn and Flanagan, 2018).

Considering the treatment of EAF, there are some challenges. First, there is no definite treatment. Second, the recurrence rate is high, being up to approximately 70% recurrence rate, despite the total resection. Third, multiple surgical resections are needed due to the high recurrence rate. Fourth, both surgical and medical treatment may fail to treat the disease. The treatment options include surgery, systemic corticosteroid, intralesional corticosteroid, monoclonal antibody (Rituximab), and their combination. Furthermore, the laser has been used with limited long-term success (Karligkiotis et al., 2014; Jin et al., 2016; Ahn and Flanagan, 2018).

The treatment of choice is surgery, and the goal of surgery should be gross total resection. Corticosteroid is used for growth control, but it does not affect disease progression. Steroid-free agents are also used with inconclusive results and include mycophenolate mofetil, azathioprine, azathioprine, hydroxychloroquine, dapsone, anti-fibrotic agents like tamoxifen, and antihistamines. The role of radiotherapy is not obvious. Considering the side effects profile of radiotherapy and its potential for the malignant transformation, it does not appear to be a suitable treatment for this benign lesion, but it should be considered in a special situation (Jin et al., 2016).

Although the lesion demonstrates a benign, indolent, slow-growing natural history, and there is some evidence that the lesion may stabilize over time, most researchers report the high recurrence rate despite the optimal treatment. The prognosis is the most favourable in cases with complete surgical resection, despite the need for multiple surgical resections. There are no reports of fatality, but a high recurrence rate results in significant morbidity (Karligkiotis et al., 2014; Jin et al., 2016; Ahn and Flanagan, 2018).

It should be noted that if EAF is considered a separate entity, the present case is interesting and unique, since the suprasellar and intradural involvement were not reported previously. A review of the literature demonstrated only orbital and extradural involvement other than the sinonasal cavity and the upper respiratory tract. Moreover, in the present case, some points can be explained by the pathology of EAF. First, the patient suffers from an indolent, slow-growing tumour. Second, two sessions of surgical interventions fail to achieve complete resection due to the extremely firm texture of the tumour. Third, the lesion did not respond to corticosteroids and radiation therapy.

Recently, some authors considered the relation between EAF and IgG-RD, and some explained that EAF might be a type of IgG-related disease (Deshpande et al., 2011; Gallo et al., 2017; Ahn and Flanagan, 2018). Diagnostic criteria for IgG4-RD include histologic finding (as noted earlier), presence of a tumefactive lesion, multiple classic organ involvement, subacute onset, elevated serum IgG4, and plasma cells, and rapid response to immunosuppressive treatment (Radhakrishnan et al., 2015; Ahn and Flanagan, 2018).

Therefore, if this case is considered IgG4-RD (IgG4 related hypophysitis), some issues are encountered. First, although the level of IgG4 was elevated in our case, the ratio of IgG4 was less than 20% (although the elevated IgG4 is a criterion for the diagnosis of IgG4-RD, it is not pathognomonic and can be elevated in other conditions). Second, systemic evaluation could not show any evidence of systemic disease or other organ involvement. Third, there are many reports of IgG4-related hypophysitis presented radiologically as a macroadenoma. Radiologically, they usually demonstrate enlargement of the hypophysis or a macroadenoma with or without somewhat suprasellar extension, and occasional enlargement of the pituitary stalk. However, in the present case, the MRI finding does not support the diagnosis of a macroadenoma with suprasellar extension and appears to be primarily an extra-axial, intradural suprasellar mass. Fourth, a good diagnostic criterion for IgG4-RD is a favourable response to glucocorticoid therapy; however, the present case did not respond. Fifth, almost all cases of IgG4-related hypophysitis were treated by surgery or glucocorticosteroid; however, both treatments failed in our case.

Conclusion

Although the preoperative diagnosis of EAF is impossible, in the setting of an indolent slow-growing lesion demonstrating hypointensity on the T2 image sequence of MRI, EAF should be considered a differential diagnosis. In the setting of this diagnosis, the systemic and other organ involvement for the diagnosis of IgG4-RD should be evaluated. However, more cases are needed to illustrate the relation between the two entities.

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