

CASE REPORT

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A rare lumpy inflammatory lesion of the orbit: a unique case report

Rui Liu^{1†}, Jing Li^{1†}, Tingting Ren¹, Hong Zhang² and Jianmin Ma^{1*}

Abstract

Background Eosinophilic angiocentric fibrosis (EAF) is a rare inflammatory lesion, especially in orbit. EAF is believed to be related to IgG4-related disease (IgG4-RD), but the clinical manifestations of systemic involvement are relatively rare and easy to be confused with tumors or other inflammatory diseases. Histopathological examination is the most important way of its diagnosis and differentiation.

Case presentation We presented a 55-year-old female patient presented with recurrent swelling of the right lower eyelid for more than 2 months. The pathological diagnosis was EAF. Positive immunostaining for IgG, CD34, κ , and λ , while negative immunostaining for IgG4.

Conclusions Complete surgical resection is the preferred treatment, histopathological examination is the main diagnostic standard.

Keywords Eosinophilic angiocentric fibrosis, IgG4-related disease, Histopathological examination, Diagnosis, Case report

Introduction

Eosinophilic angiocentric fibrosis (EAF) is a rare and slow progressive inflammatory disease. The main sites of involvement are the nasal cavity and sinuses, although rare cases can also occur in the orbit, upper respiratory tract, gingiva, and brain [1–4]. The etiology and pathogenesis of this disease are still unclear, and its clinical manifestations are nonspecific and diverse, making it easy to confuse with orbital inflammatory lesions or neoplastic lesions in diagnosis. In this paper, we report a case of orbital EAF and summarize the clinical characteristics

of the disease based on the literature to provide a reference for clinical diagnosis and treatment.

Case presentation

A 55-year-old female patient presented with recurrent swelling of the right lower eyelid for more than 2 months. She had a history of hypertension and hysterectomy. Ophthalmic examination showed binocular visual acuity of 1.0, normal intraocular pressure, and normal anterior ganglion and fundus. The tumor, which was tough, painless, and movable, was palpable near the zygomatic arch of the lower right eyelid. Laboratory examination showed the patient to be negative for syphilis antibody. Orbital magnetic resonance imaging (MRI) showed oval-like T1 and slightly shorter T2 signal shadows in the lower quadrant of the right outer orbit, with clear boundaries and significantly enhanced annular edges (Fig. 1A, B). To clarify the nature of the lesion, we removed the right orbital mass under general anesthesia with the patient's consent. The tumor was completely dissected during surgery. It

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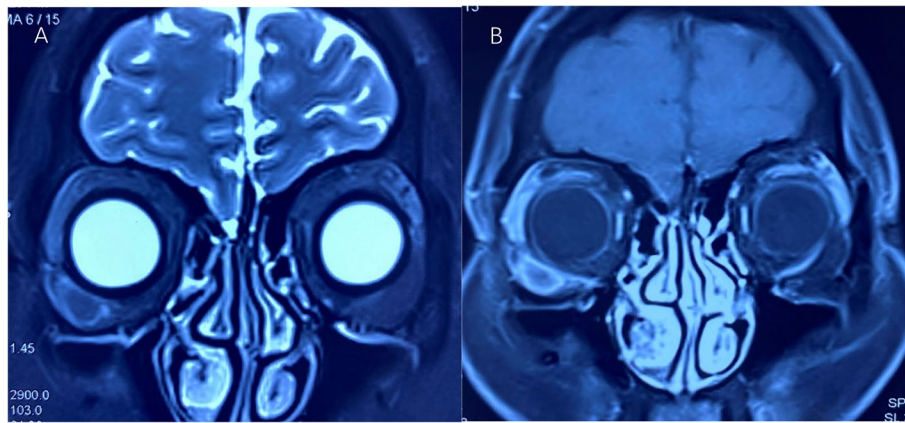


Fig. 1 MRI images of the orbit. **A** Orbital T2-weighted image (T2WI) shows clear tumor boundaries and slightly short T2 signal. **B** Enhanced orbital MRI scan shows significant enhancement of the tumor

was $1.6 \times 1.0 \times 1.0$ cm in size, gray, and homogeneous, with a clear boundary (Fig. 2A, B).

Histopathology

Histopathological examination of the resected mass showed infiltration of lymphocytes, plasma cells, and eosinophils in and around the vascular wall; fibrous-tissue hyperplasia; and fibrotic vascular-wall changes like onionskin, consistent with eosinophilic vascular-center fibrosis (Fig. 3A-F). Immunochemical (IHC) results were as follows: negative for immunoglobulin G4 (IgG4) and positive for IgG, CD34, κ , and λ . The patient took oral methylprednisolone after surgery, and the dosage was gradually reduced over the subsequent 3 months. Postoperative recovery was good, and no tumor recurrence was observed during 1-year follow-up.

Discussion

Orbital EAF progresses slowly. Its various clinical manifestations include diffuse inflammatory lesions or localized mass lesions, causing it to be easily misdiagnosed as

other diseases. It is also invasive, spreading easily to surrounding tissues and often causing bone damage, making timely diagnosis and treatment very necessary.

With this in mind, we collected a total of 18 cases of orbital EAF via a literature search and combined them with the above-described case for analysis to summarize the clinical characteristics of the disease [5–18]. Of the 18 cases, 6 involved naso-orbital–communication lesions and 12 involved localized orbital lesions (Table 1). Average age of onset was 47.67 ± 12.70 years. There were nine males and nine females for a male: female ratio of 1:1, indicating no significant gender difference. However, some studies have shown that women are more prone to EAF [11, 19]. The disease is commonly monocular in incidence, but binocular cases can also occur; the monocular: binocular ratio is 7:1. In 12 cases (66.7%), lesions were located in the orbit; in 2 (11.1%), they were in the lacrimal gland; and in 1 case each (5.6%), they were in the eyelid, conjunctiva, epicanthus and rectus. The main clinical manifestations were eyelid, orbital, or conjunctival swelling in ten cases (66.7%); eyeball protrusion in five

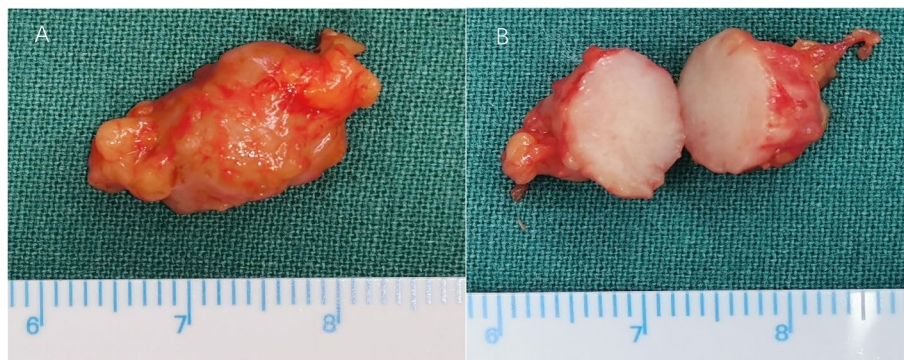


Fig. 2 General appearance of the mass. **A** Clear boundary. **B** Profile

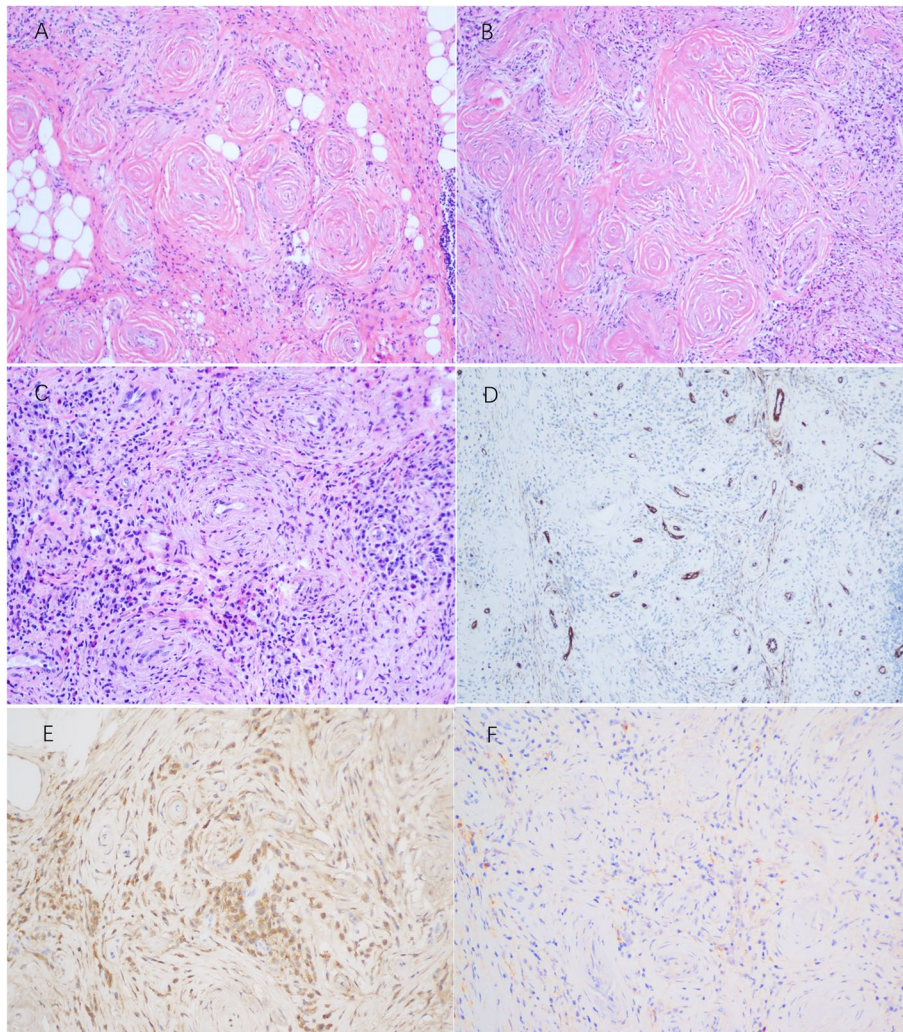


Fig. 3 Histopathological results for the lesion. **A** Fibrous-tissue hyperplasia is present, and the vascular wall shows scallion skin-like fibrotic changes. **B** Some of the fibrotic areas may be joined. **C** Additional infiltration of lymphocytes, plasma cells, and eosinophils in and around the vascular wall. **D** Positive expression of CD34 outlines the vascular endothelium. **E** Positive expression of IgG. **F** Negative expression of IgG

(33.3%); tearing, eyeball displacement, and headache in three (20.0%); and eye pain, limited eye movement, and vision loss in two (13.3%). Nasal congestion, nasal bleeding, loss of smell and other symptoms can also be associated with naso-orbital communication lesions. Studies have shown that nasal congestion is the most common symptom of nasal EAF, appearing in about 66.7% of cases [1]. Six cases had extraocular-muscle involvement, mostly of the internal rectus muscle. Six cases involved periorbital soft tissue, five involved bone destruction, two involved the optic nerve, and one involved the sclera.

EAF is believed to be a manifestation of IgG4-related disease (IgG4-RD) [3]. Chew et al. showed that about 30% of EAF meets the IgG4-RD standard of the 2019 European League Against Rheumatism (EULAR)/

American College of Rheumatology (ACR) classification scheme [4]. Of the 18 cases of EAF we reviewed, 3 had increased serum IgG4 levels, 5 had normal serum IgG4 levels, and serum IgG4 levels in the remaining 10 were unknown. Expression of IgG4 in tissues was increased in 10 cases, with the ratio of IgG4: IgG as high as 80%; it was normal in 2 cases and unknown in the remaining 6 cases. Antineutrophil cytoplasmic antibody (ANCA) was negative in 13 cases. We can therefore see that not all EAF is accompanied by increased IgG4 expression and local lesions are more common. In our case, IHC staining showed negative IgG4 expression, lesions were confined to the orbit, and no other parts of the eye or other bodily organs were involved. None of these findings supported a diagnosis of IgG4-RD.

Table 1 Clinical features of 17 cases of orbital EAF

| Case | Age | Gender | Laterality | Position | Clinical features | Destruction | Serum IgG4 | Tissue IgG4 | ANCA | Treatment | Prognosis | Follow-up |
|---------------|-----|--------|------------|--|--|---|-------------|------------------|----------|--|---------------------------------------|-----------|
| Our case | 55 | Female | Right | Orbital mass | Eyelid swelling | None | Negative | Negative | Negative | Surgery+glucocorticoid | No recurrence | 2 months |
| Headari [5] | 69 | Male | Left | Medial orbital mass | Periorbital edema, non-axial proptosis and lateral globe displacement, limited abduction | Medial orbital wall, inferior rectus, medial rectus muscles | Negative | Positive, 40–45% | Negative | Surgery+glucocorticoid | No recurrence | 4 months |
| Mansfield [6] | 37 | Female | Left | Lateral orbital mass | Periorbital swelling | Scleral thickening | Negative | Positive, < 10% | Negative | Biopsy+glucocorticoids+rituximab+ methotrexate / azathioprine | Multiple recurrence | 18 months |
| Okuyama [7] | 55 | Female | Bilateral | Upper eyelid conjunctivas | Conjunctival swelling | None | 179 mg/dl | Positive, 45% | – | Surgery | No recurrence | 6 months |
| Legare [8] | 58 | Male | Left | Orbit and sinuses illustrated a solid mass | Eyelid swelling | Nasal soft tissue, medial periorbital soft tissue, bony nasal destruction, nasal septum and anterior nasal cavity mucosa | – | Positive | Negative | Surgery+glucocorticoid/rituximab | Remission | 6 months |
| Gorostis [9] | 61 | Male | Right | Ethmoido-orbital mass | Visual loss, pain, proptosis, eyelid oedema, headache, nasal obstruction | Ipsilateral ethmoidal air cells and optic nerve, the periorbital fat, osteolysis of the lamina papyracea, medial oculomotor muscles | > 135 mg/dl | Positive, > 40% | – | Surgery+glucocorticoid/dapsone, Surgery+glucocorticoid/rituximab | Recurrence (5 years later), remission | 6 years |
| Chen [10] | 32 | Female | Left | Upper eyelid lesion | Bleeding, itching, clear discharge, headaches | Bilateral preperiorbital soft tissue swelling, maxillary sinuses, nasal cavity | Negative | Positive, 10% | Negative | Surgery+glucocorticoid/rituximab | Remission | 6 months |

Table 1 (continued)

| Case | Age | Gender | Laterality | Position | Clinical features | Destruction | Serum IgG4 | Tissue IgG4 | ANCA | Treatment | Prognosis | Follow-up |
|--------------------|-----|--------|------------|--|---|---|------------|---------------|----------|---|---------------|-----------|
| Faramarzi [11] | 35 | Male | Left | Medial canthal region mass, maxillary sinus mass | Progressive orbital swelling, left epiphora, proptosis, anterolateral globe displacement, nasal obstruction | Lamina papyracea | - | - | - | Septoplasty, left uncinectomy, middle meatal antrostomy, and anterior ethmoidectomy | No recurrence | 12 months |
| Radhakrishnan [12] | 38 | Female | Right | Inferior orbital mass | Limited abduction | Lateral rectus, inferior oblique muscles | - | - | Negative | Surgery+glucocorticoid | No recurrence | 3 months |
| Takahashi [13] | 43 | Male | Right | Medial rectus muscle lesion | Visual loss, eyelid swelling | Medial rectus muscle and optic nerve with soft tissue swelling of the ethmoid sinus | Negative | Positive | Negative | Surgery+intravenous methylprednisolone and oral diaminophenyl sulfone, cyclophosphamide | No recurrence | 18 months |
| Karligkiotis [14] | 46 | Male | Right | Orbital lesion | Proptosis, lateral globe displacement, right unilateral nasal obstruction, headache | Homolateral ethmoidal cells with oval configuration, right middle meatus, the ethmoid sinus | - | - | Negative | Surgery | Remission | 36 months |
| Deshpande [15] | 63 | Male | Bilateral | Nasal and lacrimal glands, lung | Ocular tearing, nasal congestion, anosmia | Nose, middle turbinates | 1490 mg/dl | Positive,80% | Negative | Surgery+glucocorticoid | - | - |
| Deshpande [15] | 31 | Female | - | Orbit, maxillary sinus, ethmoid, nasal | - | - | - | Negative | - | - | - | - |
| Deshpande [15] | 54 | Female | Right | Lacrimal gland | - | - | - | Positive,97% | - | - | - | - |
| Deshpande [15] | 55 | Male | - | Orbit | - | - | - | Positive, 68% | Negative | - | - | - |
| Kiratli [16] | 30 | Female | Right | Inferomedial orbit | Ipsilateral epiphora | Anterior ethmoid cells and right middle turbinate | - | - | Negative | Fluorocortolon+ desloratadine+ Steroid | No recurrence | 32 months |

Table 1 (continued)

| Case | Age | Gender | Laterality | Position | Clinical features | Destruction | Serum IgG4 | Tissue IgG4 | ANCA | Treatment | Prognosis | Follow-up |
|-----------------|-----|--------|------------|--|--|---|------------|-------------|----------|---------------|---------------|-----------|
| Azam [17] | 35 | Female | Right | Retrobulbar area of right orbit encasing the eyeball | Pain and right lower eyelid swelling | Subcutaneous fat | - | - | Negative | Surgery | No recurrence | 8 months |
| Leibovitch [18] | 61 | Male | Right | Medial orbit | Periorbital edema and painless proptosis | Fat, medial orbital wall and middle ethmoidal cells | - | - | Negative | Oral steroids | No remission | 6 months |

“-” stands for unknown

Histopathological examination is the main standard for diagnosing EAF. The typical pathological manifestations are massive infiltration of eosinophils, plasma cells, lymphocytes, and fibroblasts around small blood vessels; thickening of matrix; and characteristic rotation of onionskin-like collagen fibers and mesh proteins around occlusive blood vessels, accompanied by positive expression of IgG4 and IgG [1, 2]. EAF should be distinguished from orbital inflammatory pseudotumor, hemangioma, and granulomatous disease.

Complete surgical resection is the most important treatment method for this disease. Surgery combined with glucocorticoid therapy has a certain but not strong effect [5]. Rituximab is the most commonly used alternative or adjuvant drug when the patient does not respond to glucocorticoid therapy or when the side effects are relatively serious. Methotrexate and azathioprine are also used. However, when the degree of fibrosis is relatively severe, drugs seem to be ineffective [11]. Localized lesions have better prognosis and less recurrence. Diffuse inflammatory lesions involving the orbit or sinus take longer to treat, recur more frequently, and often require multiple operations. Studies have shown that 62% of sinus EAF cases undergo complete resection, with a recurrence rate of 20% [20]. Therefore, this disease requires close follow-up and observation and timely evaluation of recurrence. We followed up on our patient for 1 year without observing recurrence.

In conclusion, in this paper we report a case of localized EAF and summarize the current literature on this disease. In clinical diagnosis, EAF should be considered when a patient presents with an orbital mass. Complete surgical resection is the preferred treatment, histopathological examination is the main diagnostic standard, and close follow-up is very necessary. The relationship between EAF and IgG4-RD should be elucidated through additional case studies.

Abbreviations

| | |
|---------|------------------------------------|
| EAF | Eosinophilic angiocentric fibrosis |
| MRI | Magnetic resonance imaging |
| IHC | Immunohistochemical |
| IgG4-RD | Immunoglobulin G4 related disease |

Acknowledgements

Not applicable.

Authors' contributions

Rui L and Jing L wrote the manuscript; Tingting R and Hong Z helped collect and analyze the data; Jianmin M read and criticized the manuscript. All authors critically read and edited the manuscript. All authors read and approved the final manuscript.

Funding

Supported by Beijing Hospitals Authority' Ascent Plan (DFL20190201) and Natural Science Foundation of Beijing (7222025).

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

This article does not include the patients' names, portrait and other private information. Informed consent was obtained from the patient for publication of this article and any accompanying images.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 30 December 2022 Accepted: 13 February 2023

Published online: 23 February 2023

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