Case report

A case of primary extranodal natural killer/T-cell lymphoma in the orbit and intraocular tissues with cerebrospinal fluid involvement

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ABSTRACT

Purpose: To report a rare case of primary orbital natural killer (NK)/T-cell lymphoma without nasal lesions but with cerebrospinal fluid involvement.

Observations: A 73-year-old woman was referred to the uveitis clinic with suspected unilateral acute uveitis in her right eye and a right orbital tumor. Epstein–Barr virus DNA was detected in the aqueous humor in her right eye, and orbital biopsy revealed the presence of extranodal NK/T-cell lymphoma (ENKTL), nasal type. Positron emission tomography showed significant 18F-fluorodeoxyglucose uptake in the right orbit, with no other signs of systemic involvement. Cerebrospinal fluid analysis demonstrated lymphoma cell infiltration. She was diagnosed with stage IV ENKTL and treated with orbital radiotherapy and systemic chemotherapy, with subsequent remission. However, the lymphoma relapsed in her left vitreous at 10 months after therapy, suggesting metastasis of lymphoma cells to the contralateral eye via the vitreous and cerebrospinal fluid.

Conclusions and importance: A few cases of ocular-tissue ENKTL have been reported, mostly involving invasion or dissemination of primary nasal lesions; in contrast, primary orbital and intraocular ENKTL has rarely been reported. To the best of our knowledge, this is the first report of a primary orbital ENKTL metastasizing to the vitreous of the contralateral eye. Although ENKTL is rare in the orbit and intraocular tissues, it should be considered as a possible differential diagnosis in patients with orbital tumors or intraocular inflammation resistant to steroid therapy because ENKTL has a very poor prognosis in the advanced stage.

1. Introduction

Lymphomas are the most common type of primary orbital malignant tumors. Most orbital lymphomas are non-Hodgkin's lymphomas, such as mucosa-associated lymphoid tissue lymphomas, which have a relatively good prognosis, while T-cell and natural killer (NK)/T-cell lymphomas are extremely rare.1,2

Extranodal NK/T-cell lymphoma (ENKTL), nasal type, formerly known as lethal midline granuloma, angiocentric T-cell lymphoma, or polymorphic reticulosis, is an uncommon disease that typically arises from the nasal cavity and paranasal sinuses.2,3 While most NK/T-cell lymphomas in ocular tissues occur as an invasion or dissemination of nasal ENKTL, a few cases of primary orbital or intraocular ENKTL have been reported.3,4

Here we report an extremely rare case of primary orbital NKTL that metastasized to the contralateral eye during the follow-up period, presumably via the vitreous and cerebrospinal fluid.

2. Case report

A 73-year-old woman noted blurred vision and swelling of her right eyelid. She was initially diagnosed with unilateral anterior uveitis and treated with topical steroids (0.1% fluoromethol), with no improvement of her symptoms. She was then referred to our clinic 1 month after starting local steroid therapy. Her vision was 20/100 in the right eye and 20/15 in the left eye, and the intraocular pressure was 30 mmHg in the right eye and 14 mmHg in the left. The right conjunctiva showed injection and chemosis. Her right cornea had 50–100 pigmented keratic precipitations and 2+ cells in her right anterior chamber, but there was no evidence of inflammation in her right vitreous, retina, or choroid. There was no evidence of inflammation in her left eye. She had no history of weight loss or night sweats and her body temperature was within the normal range. Magnetic resonance imaging (MRI) showed a poorly margined large mass surrounding her right eyeball, with no evidence of extraorbital tumor, suspected to be an inflammatory fluid involvement.
The patient was also seen by an otolaryngologist to confirm the absence of nasal or paranasal sinus involvement. A bone marrow biopsy was negative, but a PET scan demonstrated significant 18F-fluorodeoxyglucose uptake by the tumor surrounding her right eye. The tumor responded well to radiotherapy. Immunohistochemically, the tumor cells were positive for CD3ε, CD2, CD56, CD8, and TIA-1, and negative for CD4, CD7, and CD20. The Ki-67 index was > 90%. The tumor cells were also positive for EBV-encoded mRNA by in situ hybridization (Fig. 3). These results were consistent with a diagnosis of ENKTL. A positron emission tomography (PET) scan demonstrated significant 18F-fluorodeoxyglucose uptake by the right orbit, with no other systemic involvement. The patient was also seen by an ophthalmologist to confirm the absence of any structural damage in the retina or choroid. The patient remained alive 14 months after her diagnosis.

3. Discussion

This is a rare case of primary ENKTL involving the uvea and orbit with leptomeningeal dissemination. Lymphomas involving the orbit are generally low-grade B-cell lymphomas, with marginal zone lymphomas accounting for > 50% of cases.5 In contrast, ENKTL is extremely rare in the orbit, and most cases represent a direct invasion from the nose and paranasal sinuses.1-3 Since ENKTL usually has an aggressive clinical course compared with other types of orbital lymphomas, its early diagnosis and intervention is essential for improving prognosis of the affected patients.12

Given that primary ENKTL is uncommon in the orbit and intraocular tissues, its early recognition may be difficult for general ophthalmologists. Indeed, the current case was initially thought to be a pseudotumor with anterior EBV infection, and thus was treated with corticosteroids. EBV has been implicated in the development of a variety of
malignancies, including nasopharyngeal carcinoma, gastric cancer, and various types of lymphomas. Thus, lymphoma should be considered differential diagnosis, along with ocular inflammatory disease, when the EBV genome is detected in the aqueous humor, vitreous, or orbital tumor. Moreover, although most types of extranodal lymphomas respond to corticosteroid therapy, the orbital tumor in the current case deteriorated under treatment with high-dose steroids, which may be a characteristic of ENKTL. Hon et al. demonstrated two distinct categories of ocular ENKTL: uveitis/vitritis and orbital infiltration. In this case, the right orbital tumor was initially diagnosed as NK-TCL, and NK/T-cell lymphoma cells were then detected in the vitreous of the contralateral eye 10 months after therapy. This indicates that the primary orbital-type lymphoma had led to the uveitis/vitritis-type in the ipsilateral eye, as a result of direct invasion and metastasis to the contralateral vitreous via the cerebrospinal fluid. The patient was > 70 years old with stage IV, placing her in a high-risk group. Despite the recurrent lymphoma in her left eye and subsequent need for chemotherapy, she remained alive at 14 months after her diagnosis, suggesting that early intervention may have been effective in this case.

4. Conclusions
ENKTL should be considered differential diagnosis in patients with steroid-resistant orbital tumors. In the event of anterior uveitis or vitritis with an orbital mass lesion at presentation, orbital incisional biopsy, as well as quantitative PCR for EBV-DNA using aqueous or vitreous humor samples, is essential to facilitate an early diagnosis.

Patient consent
Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Conflicts of interest

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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