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## Case report

# Pediatric conjunctival lymphoma associated with oral carbamazepine use



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## ABSTRACT

**Purpose:** To report a case of a pediatric patient diagnosed with conjunctival lymphoma associated with oral carbamazepine use.

**Observation:** An 11-year-old boy who presented with 5-month history of a small nasal conjunctival mass in the left eye that failed therapy with topical corticosteroids. Upon excision and molecular analysis, diagnosis of Follicular Lymphoma was favored. The patient was healthy and did not have any known risk factors except for a history of epilepsy treated with systemic carbamazepine.

**Conclusion and importance:** We report a case of a rare childhood conjunctival lymphoma. Conjunctival lymphomas may masquerade as chronic conjunctivitis, or scleritis that fail therapy with topical corticosteroids. Furthermore, our patient did not have any known risk factors such as old age, systemic lymphoma or immunosuppression. The patient did have a history long-term use of systemic carbamazepine. This is to our knowledge the first case conjunctival lymphoma that may be associated to the use of carbamazepine.

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## 1. Introduction

This case presents a rare diagnosis in a pediatric patient with a possible link to a systemic medication. Overall, 97% of conjunctival masses in children are benign and only 3% are malignant.<sup>1</sup> The differential diagnosis ranges from common cysts to reactive lymphoid hyperplasia (RLH) to malignant tumors such as lymphoma. Our patient, a healthy 11-year-old male presented with a conjunctival mass that failed to resolve with topical corticosteroid use. Upon excision and molecular analysis, diagnosis of Follicular Lymphoma was favored. In the absence of risk factors, history of ocular diseases, and absence of systemic lymphoma, we turned to the systemic use of carbamazepine for a possible link.

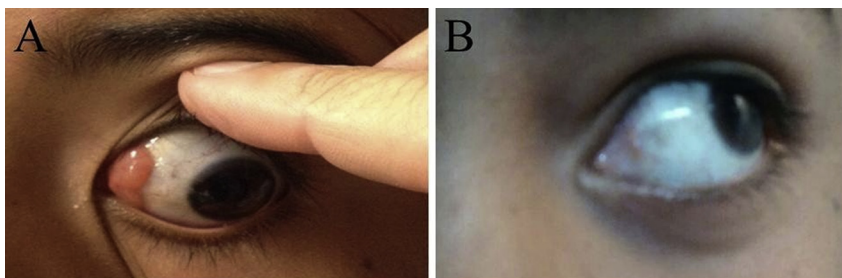
## 2. Case report

The patient provided written consent for publication of personal information including medical record details and photographs.

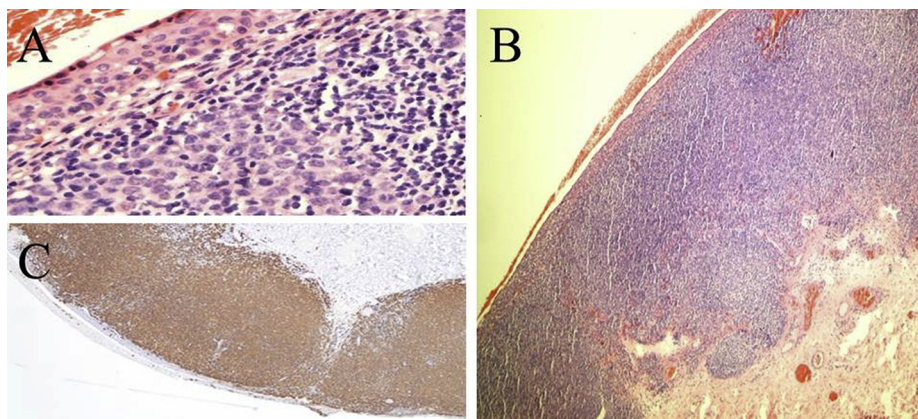
An 11-year-old boy referred to our Eye Clinic with a 5-month history of a small nasal conjunctival mass of the left eye. The mass had failed to resolve despite topical corticosteroid drops. He was otherwise healthy, with only a history of epilepsy treated with carbamazepine 200 mg in the morning and 300 mg in the afternoon for four years without any complications. He had no ocular history and no known allergies. On ophthalmological examination, his visual acuity was 20/20 (using Snellen chart) in each eye and the eye exam was normal bilateral except for an elevated pinkish mass in the conjunctiva of the left eye (Fig. 1A). Excisional biopsy was performed under general anesthesia. The lesion excised was an irregular fragment of tan gray mucosal soft tissue appearance measuring 0.8 × 0.6 × 0.3 cm. Histopathological examination of the mass showed dense nodular lymphoid infiltrate composed of a mixture of small lymphocytes with irregular nuclear contours and large transformed lymphoid cells with multiple prominent nucleoli (>15 per high power field) (Fig. 2A and B). Increased numbers of tingible body macrophages were noted in these areas. Immunoperoxidase studies showed increased number of CD20 (Fig. 2C) positive, Paired Box-5 positive B cells that were CD10 positive, B-cell lymphoma (BCL) 6 positive and BCL 2 negative. Ki-67 immunostain showed an abnormal pattern of staining in these nodules and a proliferation index of 30%. T cells were morphologically

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**Fig. 1.** A. The left eye prior to surgical resection. Note the pink nasal conjunctival mass. B. The left eye two years after surgical resection and radiotherapy. The patient has remained disease free.



**Fig. 2.** A. Microphotograph of the conjunctival biopsy specimen showing dense nodular lymphoid infiltrate (hematoxylin-eosin, magnification  $\times 40$ ) B. The dense nodular lymphoid infiltrates are composed of a mixture of small lymphocytes with irregular nuclear contours and large transformed lymphoid cells with multiple prominent nucleoli. Increased numbers of tinged body macrophages are noted in these areas (hematoxylin-eosin, magnification  $\times 400$ ) C. Immunoperoxidase studies showed increased number of CD20 positive.

unremarkable. Plasma cells were polytypic. Fluorescence in situ hybridization for Mucosa-associated lymphoid tissue lymphoma translocation 1 rearrangement was negative and Polymerase chain reaction analysis for Immunoglobulin Heavy Chain (IgH) Gene Rearrangement was positive. Which is consistent with a clonal B-cell population. These results were compatible with a lymphoproliferative disorder with involvement of B-cell lymphoma and a diagnosis of a Follicular Lymphoma was favored. The case was consulted with Dr. Elaine S. Jaffe (Center for Cancer Research, National Institute of Health) who agreed with diagnosis. Cerebrospinal analysis, bone marrow biopsy and total body position emission computerized tomography all were negative. He was treated with two cycles of radiotherapy of 1.5 Gy each for a total dose of 30 Gy. Two years after treatment, the patient's visual acuity was 20/20 and with no signs of lymphoproliferative disease (Fig. 1B).

### 3. Discussion

Carbamazepine is commonly used as an anti-epileptic medication. The use of this medication has been associated with the development of atypical lymphoid proliferation, cutaneous pseudolymphoma syndrome and lymphoproliferative disorders.<sup>2</sup> Interestingly, this drug and its main metabolite are excreted into tears in clinically significant amounts after oral intake.<sup>3</sup> The presence of carbamazepine in tears exposes the ocular surface to unknown phototoxic effects.<sup>4</sup> Review of available literature showed one case by Doughty et al. of a healthy 22-year-old male with conjunctival metaplasia associated with oral carbamazepine use.

The patient was symptom free and did not have any known risk factors for conjunctival metaplasia such as dry eye disease, contact lens wear or smoking. Further search of the literature shows an association of carbamazepine use with the development of systemic anaplastic large cell lymphoma.<sup>5</sup> This case did not show evidence of ocular involvement, yet it still highlights the possibility of carbamazepine inducing the development of lymphoma.

Our case has characteristics consistent with benign RLH as well as with follicular lymphoma. The histopathology examination showed an infiltrate mass with plasma cells and tinged bodies, both typically present in RLH. The presence of a clonal B-cell population favors the diagnosis of a lymphoma. In addition, the immunoperoxidase studies for CD10 and CD20 were both positive, which is characteristic but not exclusive of a follicular lymphoma.<sup>6</sup>

The mixed characteristics of the mass and the undetermined role of carbamazepine in its origin provided a clinical challenge. After discussing the benefits and risks with the child's family, a joint decision was made to treat. The patient was treated with two cycles of radiotherapy for a total dose of 30 Gy and has remained disease free for two years. Furthermore, after a discussion with the patient's neurologist, therapy was switched to lamotrigine 25 mg twice a day as alternative antiepileptic treatment. To our knowledge this is the first case report of a pediatric conjunctival lymphoma that may be associated to carbamazepine use.

### Conflict of interest

The authors declare no conflict of interest.

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