

# Running Head: Ocular Allergy after Mantel Cell Lymphoma Chemotherapy Allergic Bilateral Blepharoconjunctivitis and Periorbital Edema Following Rituximab, Bendamustine and Bortezomib Chemotherapy



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## Abstract

**Purpose:** To report a case of bilateral allergic blepharoconjunctivitis and periorbital edema following chemotherapy with combination regimen of rituximab, bendamustine and bortezomib.

**Case report:** A 59-year-old man presented with bilateral periorbital swelling and blurry vision following three cycles of rituximab, bendamustine and bortezomib combination chemotherapy for mantle cell lymphoma. At presentation, visual acuity was 20/25 and 20/20 in the right and left eyes, respectively. Slit lamp examination disclosed a bilateral periorbital myxedema of both upper and lower eyelids, as well as bulbar and palpebral conjunctivitis. The patient was prescribed conservative topical medications and monitored with serial ophthalmic examinations. At 6 weeks follow up, ophthalmic symptoms improved with the resolution of blepharoconjunctivitis and periorbital edema.

**Conclusion:** Bilateral allergic blepharoconjunctivitis and periorbital edema were reported following rituximab, bendamustine and bortezomib chemotherapy. Ophthalmic examination and preventive measures may be warranted particularly in patients with combination chemotherapy regimen.

**Keywords:** Blepharoconjunctivitis; Periorbital edema; Rituximab; Bendamustine; Bortezomib; Chemotherapy

## Introduction

Ocular toxicities of anti-cancer medications are often underestimated as compared to the more serious adverse effects in other organ systems [1-3]. Concurrent to the development of new chemotherapeutic agents and new combination regimens, there has been an increase in the number of reported ophthalmic adverse events following chemotherapy. Although there is a wide spectrum of ocular toxicities induced by cancer therapy [2-4] little is known about the ophthalmic toxicities of newer target-specific cellular molecules intended for specific molecular and biologic pathways. We present a subject with mantle cell lymphoma who developed bilateral allergic blepharoconjunctivitis and

periorbital edema following chemotherapy with combination regimen of rituximab, bendamustine and bortezomib.

## Case Report

A 59-year-old man with stage IV mantle cell lymphoma presented to the outpatient Eye Clinic at Stroger Hospital of Cook County with the complaint of bilateral periorbital swelling and pain, burning sensation, and blurry vision for 1 week. The symptoms started 1 week following the third cycle of rituximab, bendamustine and bortezomib chemotherapy, improved without medications in the time interval between the third and fourth

cycles, and progressed again right after the fourth chemotherapy cycle at the day of ophthalmic examination. There was no past ophthalmic history and his past medical history included peptic ulcer disease. His medications were tylenol, acyclovir, docusate-senna and pantoprazole. At the initial ophthalmic evaluation, visual acuity (VA) was 20/25 and 20/20 in the right and left eyes, respectively. There was a bilateral periorbital swelling and redness which was not tender on palpation. The patient's pupils were round and reactive without an afferent pupillary defect. Extraocular motility was full and visual fields by confrontation demonstrated no defect. Intraocular pressure was 12mmHg and 13mmHg in the right and left eye, respectively.

The slit-lamp biomicroscopy disclosed a bilateral periorbital edema of upper and lower eyelids, and bulbar and palpebral conjunctivitis. Anterior segment showed corneal irritation and dry eyes bilaterally, and dilated fundus examination was unremarkable. Review of systems disclosed right supraclavicular, infra auricular and bilateral axillary lymphadenopathies, and a rash in the upper chest and upper extremities. Due to temporal relation between the patient's ophthalmic presentation and chemotherapy, his symptoms were attributed to an allergic reaction to his chemotherapy regimen. Oral diphenhydramine, topical hydrocortisone lotion, ocular cyclosporine and artificial tears were prescribed. The patient was instructed to perform warm compresses and lid scrubs daily, and to return to the clinic two weeks later for follow up or sooner if urgent symptoms including further vision loss and eye pain occurred. At 6 weeks follow up, patient showed improvement with resolution of blepharoconjunctivitis and periorbital edema in both eyes.

## Discussion

Conjunctivitis concurrent with periorbital edema have been reported following chemotherapy with 5-fluorouracil and methotrexate [5]. Moreover, ifosfamide [6] Deoxycoformycin [7] doxorubicin [8] Cytosinarabioside [9] docetaxel, [10] and cyclophosphamide [11] have also been associated with conjunctivitis. Other chemotherapeutic drugs, such as carboplatin, [12] have been linked to periorbital edema. To our knowledge there have been no reports of bilateral allergic blepharoconjunctivitis and periorbital edema following chemotherapy with combination regimen of rituximab, bendamustine and bortezomib.

Rituximab is a monoclonal antibody against the CD20 antigen of B cells and is used to treat non-Hodgkin B-cell lymphomas. The most common reported ophthalmic side effects of rituximab include transient ocular edema, conjunctivitis, burning sensation, and transient visual changes, [13] similar to the ophthalmic symptoms of the patient in the current study. Bendamustine is nitrogen mustard which is used in the treatment of chronic lymphocytic leukemia and lymphomas [14]. To our knowledge, there have been no reported ocular adverse effects of bendamustine, but other agents with similar mechanism including cyclophosphamide may cause blepharoconjunctivitis

and reversible blurred vision [15]. Bortezomib is a proteasome inhibitor and is approved for treating multiple myeloma and mantle cell lymphoma [16]. There have been no reported ocular adverse effects for bortezomib.

The exact underlying mechanism of bilateral blepharoconjunctivitis and periorbital edema in the patient in the current study is not clear; however, since the ophthalmic symptoms started right after each exposure to chemotherapy medications, it is more likely that the chemotherapy medications caused the symptoms. Furthermore, both the ophthalmic symptoms and the skin reactions in the upper chest and upper extremities happened simultaneously, which is suggestive of allergic reaction to combination chemotherapy. It is not clear if either rituximab or bendamustine monotherapy or the combination chemotherapy caused the ocular symptoms in this patient; however, it is probable that the combination therapy may have increased the risk for development of ocular toxicities.

## Conclusion

In summary, bilateral allergic blepharoconjunctivitis and periorbital edema were reported following rituximab, bendamustine and bortezomib chemotherapy. Ophthalmic examination and preventive measure of allergic reaction may be warranted particularly in patients with combination chemotherapy regimen.

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