

# Sporadic Burkitt's lymphoma presents as an isolated orbital disease

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## Abstract

Burkitt's lymphoma is a highly aggressive non-Hodgkin's lymphoma and the fastest growing, that accounts for 3% to 5% of all lymphomas. Three clinically subtypes have been described: endemic, sporadic, and immunodeficiency-associated. The sporadic form typically presents as an abdominal mass. Orbital involvement has rarely been reported. In this case report, a 66-year-old man presented with a three-week history of vision loss and painful proptosis of the left eye. Neuro-imaging revealed a well-circumscribed solid mass of the left orbit, for which a biopsy under general anesthesia was performed. The diagnosis of Burkitt's lymphoma was confirmed by immunohistochemistry. Chemotherapy was initiated with good clinical outcome, though there was no improvement in his visual acuity. In conclusion, Burkitt's lymphoma must be considered in patients who present with painful proptosis and vision loss, as it is one of the fastest growing and chemosensitive malignancies, which can lead to irreversible vision loss.

## Introduction

Burkitt's lymphoma (BL) is a highly aggressive, small, non-cleaved B-cell non-Hodgkin's lymphoma that was first described in 1958 by Denis Burkitt; it often presents as a mandibular malignancy or as an

acute leukemia.<sup>1</sup> Though it was originally thought to represent two different lymphoproliferative disorders, BL was classified as a single mature B-cell neoplasm entity by the World Health Organization (WHO) on the basis of shared molecular and genetic features.<sup>2</sup> Three different clinical variants of BL have been described: endemic, sporadic, and immunodeficiency-associated. The endemic form is most commonly observed in equatorial Africa as a facial bones mass.<sup>3</sup> In the sporadic form, which follows no specific geographic or climatic distribution, typically presents as an abdominal mass that frequently involves the ileocecal region of the bowel; ocular and orbital involvement is rare.<sup>4</sup> The immunodeficiency subtype is frequently observed in the setting of human immunodeficiency virus (HIV) infection.<sup>5</sup> We present a case of sporadic orbital Burkitt's lymphoma with vision loss and painful proptosis, with response to chemotherapy.

## Case Report

A 66-year-old male patient with a history of arterial hypertension was admitted to the Ophthalmology Emergency Department with vision loss and painful proptosis of the left eye for three weeks.

Approximately a month earlier, he received oral antibiotics for a presumed preseptal cellulitis. On examination, his best corrected visual acuity was 20/30

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**Conflict of Interest:** The authors report no conflicts of interest.

**Contributions:** All authors contributed equally.

**Accepted for Publication:** April, 2019

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in the right eye and hand motion in the left eye. He had a dense afferent pupillary defect of the left eye and severely restricted ocular motility and inferior displacement of the left globe (Figure 1). Hertel exophthalmometry revealed 6mm proptosis of the left eye.



**Figure 1**

*Upon external examination, the patient was found to have proptosis of the left globe with inferior displacement and restricted motility.*

Slit-lamp biomicroscopy demonstrated engorgement of conjunctival vessels, chemosis and palpebral edema. Dilated funduscopy demonstrated optic nerve edema and engorgement of retinal veins; there were no chorioretinal folds.

Computed tomography (CT) scan of the head and orbit identified an orbital mass of 4 x 2.2 cm with defined margins. This mass was located in the superotemporal left orbit with resultant anteroinferior displacement of the globe. No intracranial structural pathology was noted (Figure 2). Magnetic resonance imaging (MRI) confirmed the left orbital mass as described in the CT scan (Figure 3).

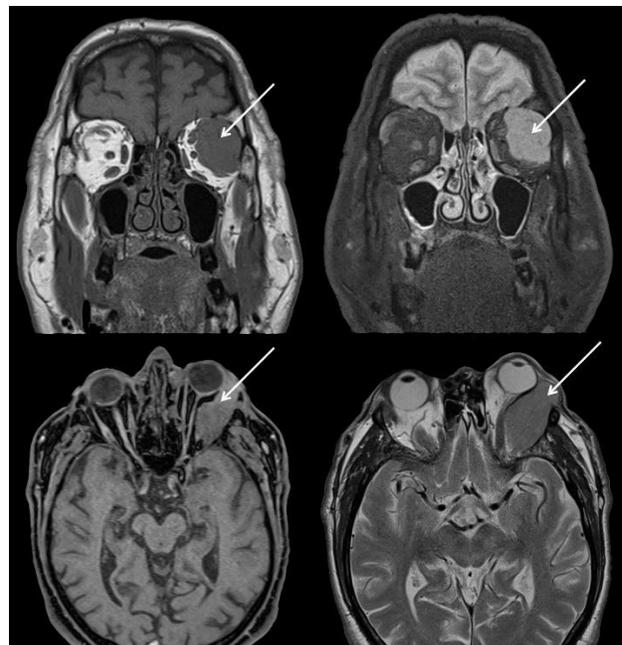
This mass was excised under general anesthesia using an anterior orbitotomy approach via the upper eyelid crease. A 3.5 x 3 x 2.5 cm soft mass was excised.

Histomorphological analysis of the excised tissue revealed medium-sized cells with round nuclei, basophilic cytoplasm, and an increased number of mitotic figures. A “starry-sky” appearance characteristic was found. Immunohistochemical evaluation of the tumor cells was positive for CD45, Bcl-6, CD10, CD20 and CD79, and negative for TdT (Terminal deoxynucleotidyl transferase), CD5, and CD23. The Ki-67 cellular proliferation index was close to 100% (Figure 4).



**Figure 2**

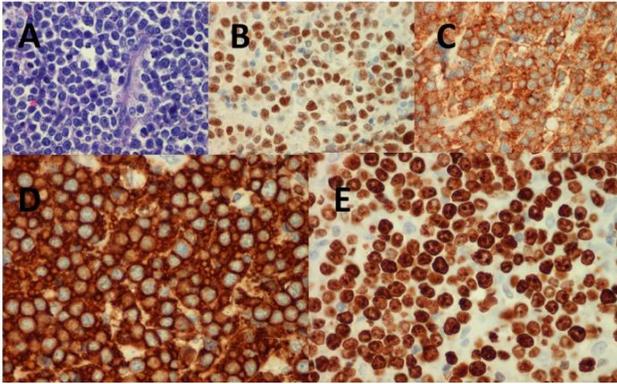
*CT scan demonstrated a left orbital mass (arrow) with defined margins.*



**Figure 3**

*MRI scan demonstrated a left orbital mass (arrow on T1 weighted coronal image, upper left; arrow on T1 weighted axial image, lower left; arrow on T2 weighted coronal image, upper right; arrow on T2 weighted axial image, lower right).*

Upon confirming a diagnosis of BL, the patient was sent to the Oncohematological Department, where basic serological testing was within the normal ranges, and lumbar puncture and bone marrow aspirate revealed no lymphomatous involvement. [18F]-2-deoxy-d-glucose (FDG) positron emission tomography



**Figure 4**  
Light microscopy of hematoxylin and eosin stained sections demonstrated medium-sized lymphocytes with high mitotic index (A). Immunohistochemistry demonstrated that the tumor was positive for Bcl-6 (B), CD20 (C), and CD79 (D). The tumor demonstrated a high Ki-67 cellular proliferation index (E).

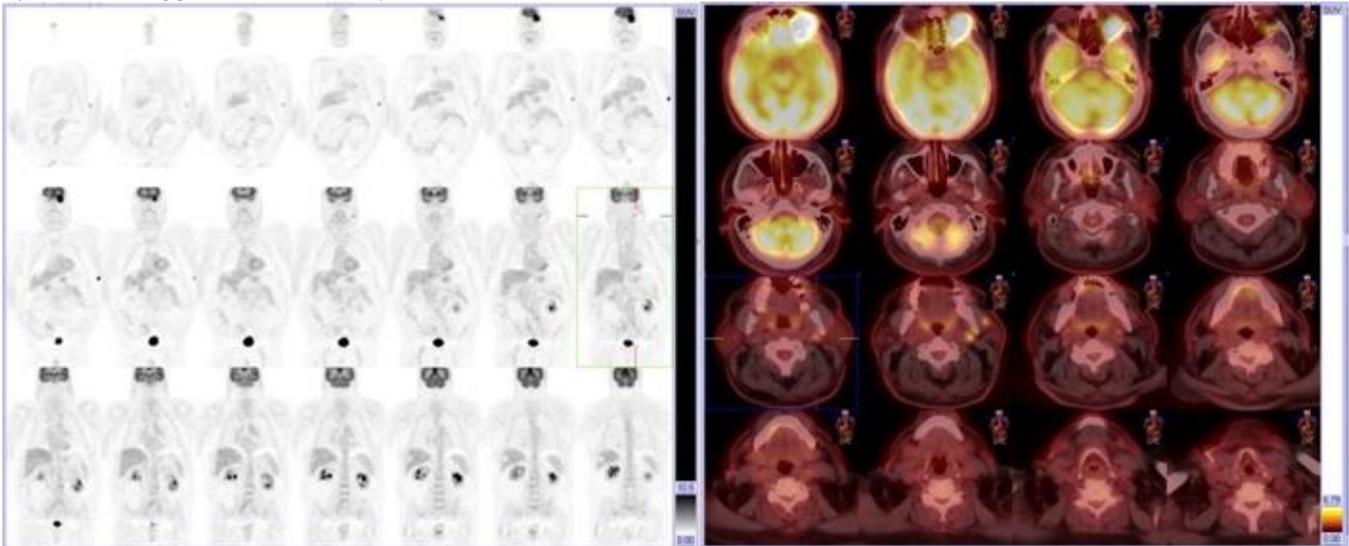
(PET) demonstrated intense hypermetabolism (maximum Standardized Uptake Values [SUVmax] 31.5) within the biopsied intraconal orbit mass and moderate hypermetabolism (SUVmax 8) in two left-side levels IIA cervical lymph nodes (Figure 5). After diagnosing clinical stage IA BL (Ann Arbor Staging System), an aggressive Dose-Adjusted EPOCH-R

chemotherapy (etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone, and rituximab) was initiated for six cycles with triple intrathecal therapy. Three months after the initiation of chemotherapy, palpebral edema, proptosis, and strabismus resolved, although there was no improvement in the patient’s visual acuity. One year after treatment, the patient was in remission, with no pathological findings in PET imaging (Figure 6). The proptosis and strabismus remained resolved, the optic nerve remained pale, and visual acuity remained poor.

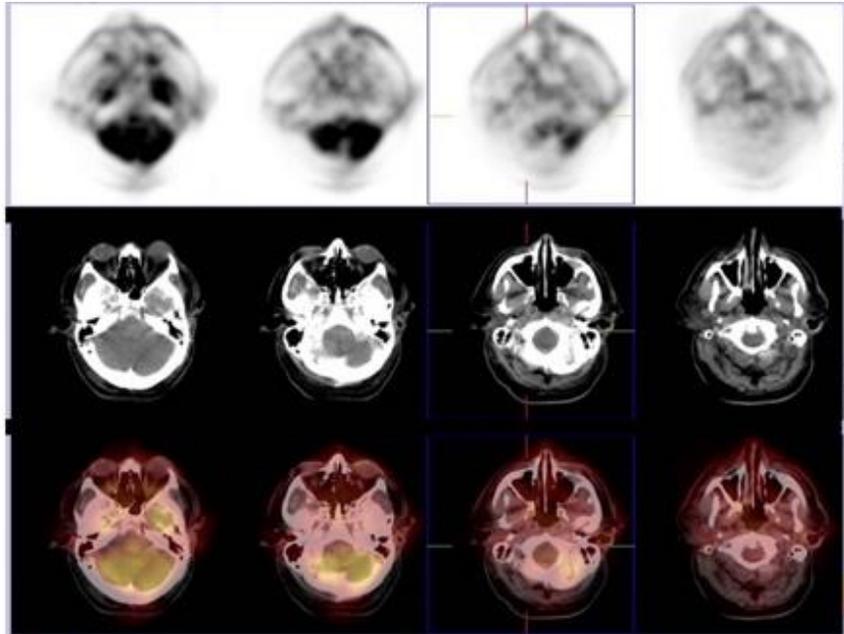
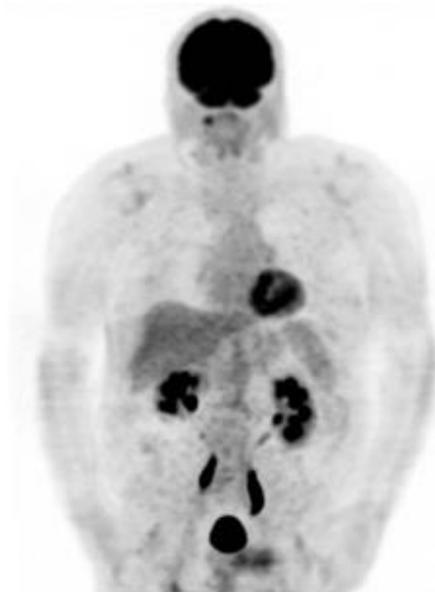
## Discussion

BL is a highly aggressive non-Hodgkin’s lymphoma that accounts for 3% to 5% of all lymphomas.<sup>6</sup> It is one of the fastest growing and very aggressive malignances, characterized by explosive growth with a doubling time of 24 hours.

Orbital involvement of BL is rare, but has been reported. Sporadic orbital BL has been reported in a 31-year-old woman and in a 2-year-old girl.<sup>7,8</sup> Immunodeficiency-associated orbital BL has been reported in a 35-year-old woman.<sup>9</sup> Histologically,



**Figure 5**  
[18F]-2-deoxy-d-glucose position emission tomography suggests tumoral lymph node involvement.



**Figure 5**  
*[18F]-2-deoxy-d-glucose position emission tomography suggests tumoral lymph node involvement.*

BL shows medium-sized cells with abundant, basophilic cytoplasm, round to oval nuclei with clumped chromatin and multiple nucleoli. A “starry sky” appearance has been described in this type of non-Hodgkin’s lymphoma because of its abundant proliferative rate, frequent apoptosis, and numerous macrophages containing ingested apoptotic tumor cells. Immunological analysis shows that BL cells express surface IgM, Bcl-6, CD19, CD20, CD22, CD10, and CD79a, and are negative for TdT, CD5, and CD23.<sup>10</sup>

Cytogenetically, 80% of BL cases harbor the reciprocal chromosome translocation t(8;14), resulting in the juxtaposition of the c-myc gene on chromosome 8 with IgH enhancer elements on chromosome 14 which drive c-myc mRNA and protein production.<sup>11</sup> In the remaining 20% of BL cases, translocations occurring between chromosomes 2 and 8, t(2;8)(p12;q24), or chromosomes 8 and 22, t(8;22)(q24;q11), place the c-myc gene adjacent to either kappa or lambda chain loci and enhancer elements, respectively.<sup>12</sup> The result is a deregulation

of the c-myc gene with effects on proliferation, apoptosis and cellular metabolism.

Clinical presentation is varied, but the most common symptoms include painless swelling of the lymph nodes in the neck, chest, abdomen, underarm, or groin; fever, sore throat; night sweats; fatigue; and weight loss or decreased appetite. The prognosis for many patients with BL has changed significantly with advances in chemotherapy that consists of the introduction of short, intensive chemotherapeutic regimens and an aggressive prophylaxis of central nervous system (CNS) involvement, with disease-free survival reaching 75% to 89% in pediatric patients with advanced-stage BL.<sup>13-15</sup> Adult patients, classically considered to have worse prognosis, also have shown a survival rates similar to pediatric population.<sup>16-17</sup> BL may be considered a curable malignancy and if there is no relapse one year after chemotherapy, the patient has a 90% chance of long-term survival. Our patient had excellent response to chemotherapy, without relapse after one year; however, there was no improvement in his visual acuity.

In conclusion, BL is a highly aggressive malignancy with high proliferation rates. Once thought to be incurable in adults, its chemosensitivity

has made complete remission and cures higher than other leukemias. Despite the advances in treatment, BL with orbital involvement may lead to irreversible vision loss. Therefore, in patients presenting with painful proptosis and vision loss, BL must be considered in the differential diagnosis because of its rapidly progressive nature and good response to chemotherapy, in order to minimize or prevent irreversible vision loss.

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