



Case report

Sixth nerve palsy in sporadic Burkitt Lymphoma

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ABSTRACT

Purpose: To describe a unique presentation of Central Nervous System Burkitt Lymphoma.**Observations:** A 59-year-old male presented with new onset binocular horizontal diplopia five days after initial presentation with abdominal distension, weight loss, and night sweats. He was diagnosed with Burkitt Lymphoma with base of skull metastasis that was initially visible only on PET scan and subsequently resolved with chemotherapy.**Conclusions and Importance:** Burkitt Lymphoma (BL) is an aggressive type of B-cell, non-Hodgkin, lymphoma that arises due to a translocation of the MYC proto-oncogene. Although central nervous system (CNS) involvement has been described previously with BL, isolated sixth nerve palsy as the initial sign of CNS metastasis is rare. Suspicion should remain high for metastatic disease in patients presenting with acute-onset neurologic complaints even when initial imaging is negative as timely treatment can prevent poor outcomes.

1. Introduction

Burkitt Lymphoma (BL) is an aggressive type of B-cell, non-Hodgkin, lymphoma that typically arises due to a translocation of the MYC proto-oncogene.¹ There are three known subtypes of BL: endemic, sporadic, and immunodeficiency-related. The sporadic variant of BL accounts for only 1–2% of Non-Hodgkin Lymphoma in adults and typically presents as an abdominal tumor.¹ Although central nervous system (CNS) involvement has been described previously, isolated sixth nerve palsy is rare.² We report binocular, horizontal diplopia due to isolated CN VI palsy as the presenting sign for CNS BL. To our knowledge, this is the first such case to be reported in the English language ophthalmic literature.

2. Case report

A 59-year-old male presented with new onset binocular horizontal diplopia. Past medical, surgical, social, and family history were non-contributory. The patient presented with abdominal distension, three weeks of weight loss, and night sweats. Computed tomography of the abdomen showed a terminal ileal and ileocecal valve mass extending to

the cecum with mesenteric metastatic implants, adenopathy and ascites. A biopsy of the terminal ileum and two small nodules in the sigmoid colon showed Burkitt lymphoma, with the neoplastic cells expressing CD20, CD10, BCL-6, MYC, and FOXP1.

Five days after initial presentation, the patient developed diplopia. Neuro-ophthalmic exam showed visual acuity of 20/30 in the right eye (OD) and 20/20 in the left eye (OS). Intraocular pressure measured 23 mm Hg OD and 22 mm Hg OS. Both pupils measured 4mm in the dark and 2mm in the light, with no relative afferent pupillary defect (RAPD). Motility examination showed a 14 prism diopter incomitant esotropia in primary gaze with an abduction deficit of –3, consistent with a 6th nerve palsy OS (Fig. 1). No motility deficits were present OD. Slit lamp and fundus examinations were unremarkable bilaterally.

Initial cranial magnetic resonance imaging (MRI) was negative, but positron emission tomography (PET) scan showed multiple areas of osseous involvement, including increased uptake in the skull base, specifically near the left cavernous sinus (Fig. 2). Repeat cranial MRI then showed abnormal tissue in the left cavernous sinus (Fig. 3). The body PET scan showed diffuse uptake in abdomen consistent with lymphomatosis, hepatic involvement, left internal mammary chain of nodes and multiple areas of osseous uptake. CSF analysis was negative

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Fig. 1. Patient demonstrates a left incomitant esotropia and an abduction deficit consistent with a 6th cranial nerve palsy OS.

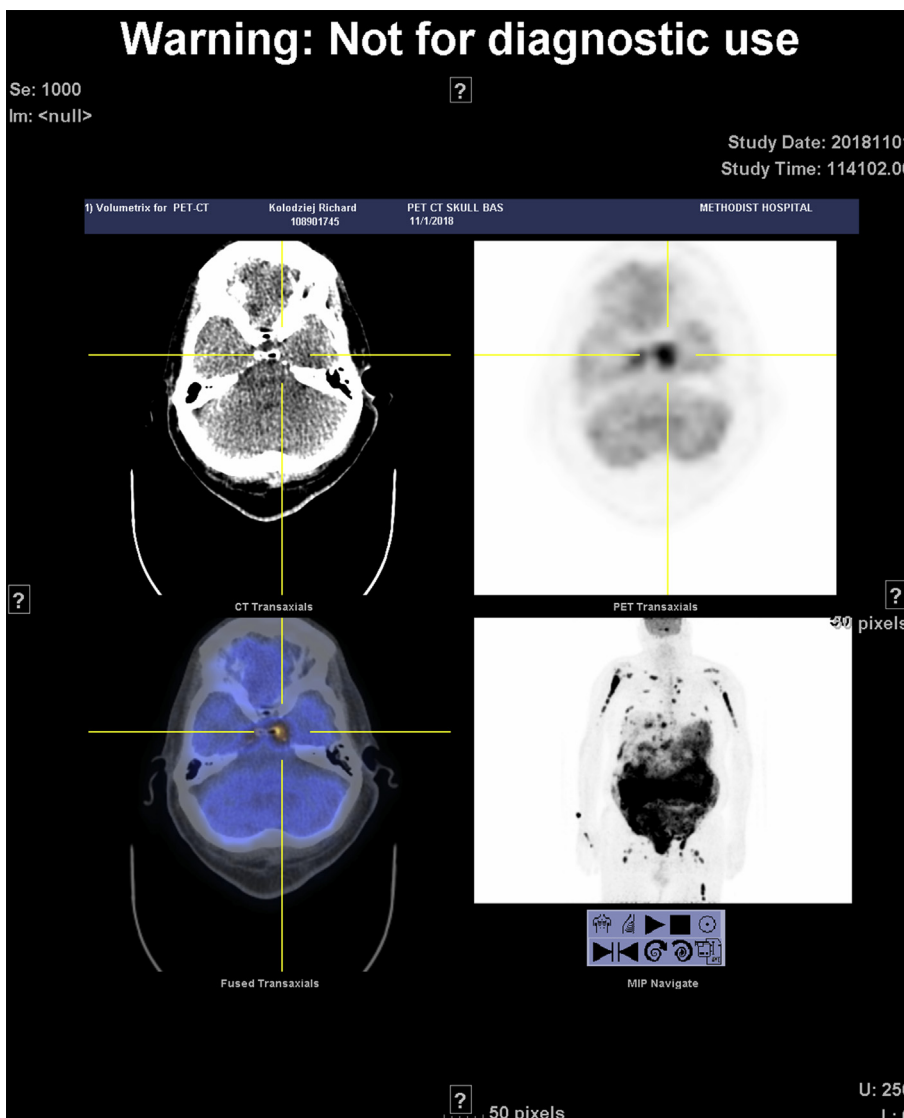


Fig. 2. PET scan showing increased base of skull uptake.

for any malignant cells confirmed by flow cytometry.

The patient was treated with intrathecal methotrexate and cytarabine and four cycles of chemotherapy with C3D226 R-CODOX-M (Rituximab-cyclophosphamide, doxorubicin, vincristine-methotrexate). This regimen has been shown to markedly improve rates of remission,

progression-free survival and overall survival in BL.³⁻⁵ Intrathecal methotrexate is used as a prophylactic or treatment agent for CNS spread in BL.⁶ Although previous intrathecal regimens for CNS BL (including methotrexate and cytosine arabinoside) had some initial success, CSF relapse occurred in up to 60–100% of these patients.⁶ In

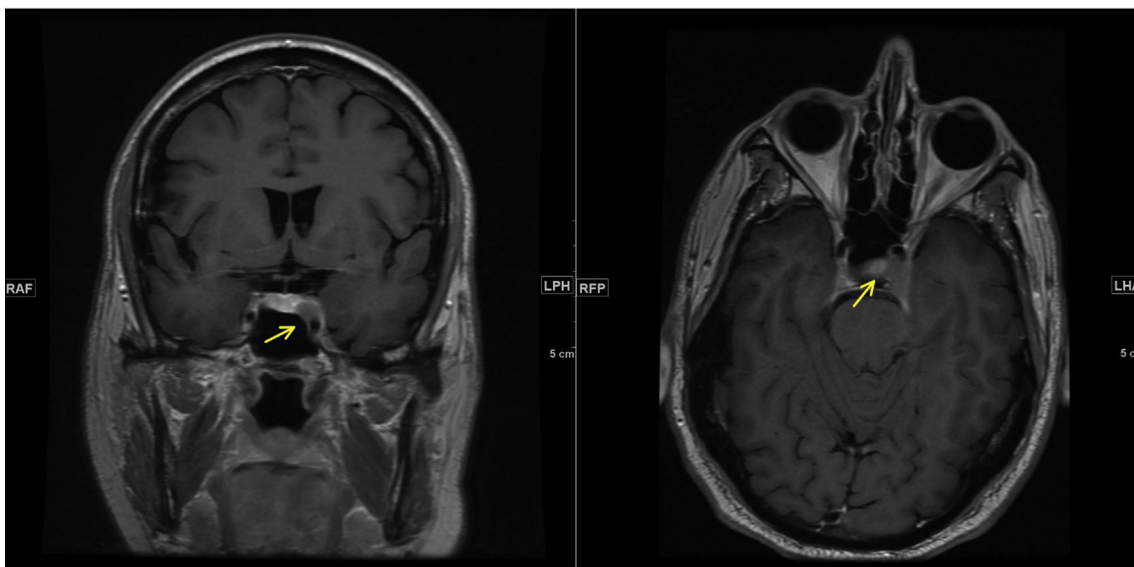


Fig. 3. MRI showing heterogenous signal intensity with decreased enhancement of the lesion in the left cavernous sinus compared with normal enhancement on the right side.

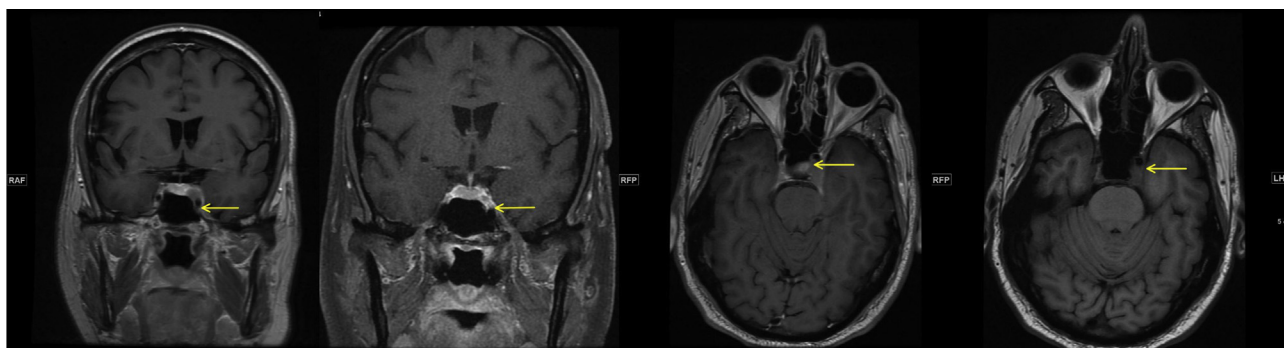


Fig. 4. MRI sequences showing left cavernous sinus tissue before and after treatment of Burkitt lymphoma with R-CODOX-M Rituximab. (Image credits to Dr. Kuang-Chun Hsieh, Department of Neuroradiology, Houston Methodist).

contrast, intensive R-CODOX with methotrexate has achieved about an 88% remission rates with 71–75% progression free survival and 77–80% overall survival at 5 years.^{4,5} Post-treatment cranial MRI showed an interval decrease in abnormal tissue in the left cavernous

sinus (Fig. 4).

At a 3 month follow up visit (Fig. 5), the abduction deficit had improved and the residual small angle esotropia was treated with prism. His clinical course while on chemotherapy was complicated by



Fig. 5. In primary gaze, a small esotropia continues to persist after chemotherapy. Left gaze shows improvement in abduction of the left eye consistent with resolving 6th cranial nerve palsy.

Table 1
Burkitt lymphoma involving the cavernous sinus.

	Patient	Neuro-Ophthalmologic Presentation	Imaging (MRI)
Liang Y et al. ¹⁴	29yo male	CN III palsy	No corresponding lesion was seen – MRI only showed diffuse abnormal signals in bones
Rasper M, Kesari S ¹⁵	33yo female	Diplopia (CN unspecified), blurred vision, retro-orbital headache	Bilateral enlargement and enhancement in the pituitary gland, cavernous sinus, and optic nerves
Kalina P et al. ¹⁶	4yo female	Left CN III and IV palsy, headache	Mass in cavernous sinus and sphenoid sinus
Seixas DV et al. ¹⁷	11yo male	Right cranial nerve III palsy	Enlarged right cavernous sinus
Moghaddasi M et al. ¹⁸	47yo female	Left CN III, IV, V ₁ , V ₂ , VI palsy, headache, nausea	Bilateral enlargement of the cavernous sinus
Tanaka Y et al. ¹⁹	62yo female	CN III, IV, and IV palsy, ptosis, frontal headache	Swelling of the optic nerves, and external ocular muscles, exophthalmos and bilateral tumors in the cavernous sinus
Huisman TA et al. ²⁰	12yo male	Cranial nerve III palsy, exophthalmos, headache	Homogenously enhancing mass in right cavernous sinus (treatment with NHL-BFM-1995 protocol was ineffective: patient died of progressive liver failure within 3 months of diagnosis)
Lee AG et al. ²¹	9yo male	Vertical diplopia, CN III palsy and CN VI palsy OS.	Bilateral cavernous sinus lesions

E. coli bacteremia, tumor lysis syndrome, lactic acidosis, neutropenic fever, thrombocytopenia and anemia. He was adequately managed for his systemic complications and was in complete remission after his last cycle of chemotherapy in February 2019. His last PET scan showed resolution of all the previously noted hypermetabolic lesions and nodes including the skull base involvement.

3. Discussion

Burkitt lymphoma (BL) is an aggressive, B-cell, non-Hodgkin lymphoma. Endemic BL is one of the most common childhood cancers in tropical Africa and as classically described by Burkitt, involves the jaw.⁷ The immunodeficiency-related type of BL occurs frequently in patients with human immunodeficiency virus (HIV) and often presents with abdominal symptoms and extranodal disease. Similarly, the sporadic variant of BL (as in our patient) commonly presents in adults with bulky abdominal tumor, B symptoms, and evidence of tumor lysis.⁸ CNS involvement by BL is seen in up to 38% of cases.⁹

CNS BL can be diagnosed via cerebrospinal fluid (CSF) analysis or neuromaging.¹⁰ However, CSF cytology and initial cranial CT/MRI scans may be normal in CNS BL and a high clinical suspicion should be maintained in these cases. In our patient, the CSF and initial cranial MRI were negative. PET scan however showed skull base hypermetabolic activity that was confirmed by repeat cranial MRI demonstrating the lesion in the left cavernous sinus corresponding to the left sixth nerve palsy.

Skull base tumors comprise a vast array of masses arising from neurovascular structures or meninges, the cranial base itself, or subcranial structures.¹¹ The most common skull base tumors, particularly in the anterior and middle fossas, are meningiomas.¹² Metastases to the skull base arise most commonly from breast, lung, and prostate cancer.¹³ Although lymphomas comprise approximately 5% of skull base metastases, to our knowledge there have been only eight previously reported cases of cavernous sinus syndrome from sporadic BL (Table 1). Most cases involved multiple cranial nerves or CN III. To our knowledge, this is the first case of an isolated sixth nerve palsy as the presenting sign of CNS sporadic BL in the English language ophthalmic literature.

Patient consent

The patient consented to publication of the case orally. This report does not contain any personal information that could lead to identification of the patient.

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Authorship

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

Declaration of competing interest

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