



Research Article

Burkitt's Lymphoma with Bilateral Cavernous Sinus Involvement: A Case Report

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Abstract

Burkitt's lymphoma is the commonest childhood malignancy in tropical Africa and is rare outside of Africa. Cavernous sinus lymphoma is a rare occurrence and Burkitt's lymphoma of the cavernous sinus is uncommon. We review the case of a 52-year-old non-african and immunocompetent woman who developed over a period of 2 weeks an ocular pain, diplopia and ptosis. Physical examination revealed breast tumors. CT scan and MRI disclosed a bilateral cavernous sinus mass and work-up of the tumor showed additional tumor within the pelvis. Biopsy of breast tumor showed findings consistent with Burkitt's Lymphoma and there was positivity to Epstein-Barr EBER-1. Chemotherapy led to complete and asymptomatic remission of the cavernous sinuses lesions. The disease had a highly aggressive course and the patient died 11 months after diagnosis. We discuss the MRI findings and the differential diagnosis of cavernous sinuses lesions. The case herein reported emphasizes this extremely rare location of Burkitt's lymphoma, the MR findings and the need of considering the diagnosis of Burkitt's Lymphoma in cavernous sinuses lesions.

Keywords: Non-Hodgkin lymphoma - Burkitt's lymphoma - cavernous sinus - lymphoma - brain neoplasm - MR.

Introduction

Burkitt's lymphoma (BL) is a peripheral B-cell lymphoproliferative malignancy.

BL is quite rare outside of Africa, uncommon in North America and in Europe, occurs in pediatric population, and is one of the fastest-growing

malignancies in the early-ages. The endemic form has a good prognosis and the association with HIV infection is frequent (1).

Disease confined to abdomen is seen in 50% of cases at presentation, most of them with bowel or mesenteric tumors

(2). Extranodal presentation of BL is rare. Although diplopia and ocular palsies have been previously reported in patient with BL, rarely bilateral cavernous syndrome is the initial manifestation in immunocompetent adults. Previous reports described BL of the skull base with invasion of the cavernous sinus (CS) especially in children (3 - 5). Four cases of CS initial presentation of sporadic BL have been recently described (6 - 9). We report an additional case presenting with unusual features.

Case Report

A 42-year-old woman without ongoing health problems developed within two weeks severe right orbital pain, associated with nausea, phonophotophobia, sweats, poor appetite, weight loss and lassitude. Two days later, she presented with a diplopia and a left ptosis. Neurological examination revealed incomplete palsy of the left III and right VI nerves, and sensory loss of the first and second division of the left trigeminal nerve. Physical examination revealed two breast masses of 10 cm of diameter and multiple axillary nodes, bilaterally.

Laboratory studies showed a hemoglobin count of 9,6 g/dl, normal white blood cells and platelet count, and a marked elevation in the level of lactate dehydrogenase (LDH) (1364 IU/L), which suggested the presence of tumor lysis syndrome. Other blood biochemical parameters were normal and there was no evidence of HIV infection. CSF

biochemistry and cyto-analysis were unremarkable.

CT and MRI of the brain demonstrated masses in the CS. On CT, the cavernous sinuses appeared enlarged and enhanced after contrast and there was no evidence of skull base or sellar destruction or erosion. On MR, there was symmetrical enlargement of both cavernous sinuses. The masses appeared isointense to the cortex on -T1- and T2-weighted images and FLAIR sequence, and enhanced slightly and homogeneously after gadolinium (Fig. 1-a-d). The cavernous sinus infiltration did not extend into the contiguous regions. Diffusion-weighted images (DWI) showed low signal intensity CS masses (Fig 1- e) and low ADC values. Magnetic resonance angiography (MRA) demonstrated displaced internal carotid arteries in their CS course (Fig 1-f). Additional tumor work-up showed on CT large pelvic mass with lymph nodes enlargement. Biopsy of the left breast nodule revealed BL. Infiltration consisted mainly of lymphoid cells with basophil cytoplasm, round or oval nucleus and many mitotic figures. Immunohistochemistry showed strong positivity for the B cell markers CD20, CD79A, CD10. Bone marrow aspiration biopsy disclosed massive proliferation of B great cells with positivity for CD20, CD10 cell markers and Epstein-Barr EBER-1 was detected immunohistochemically. On the basis of clinical, radiologic, cytologic, and immunophenotypic results, BL's stage IV with important bulk tumor was diagnosed, and chemotherapy type cyclophosphamide-vincristine regimen was initiated.

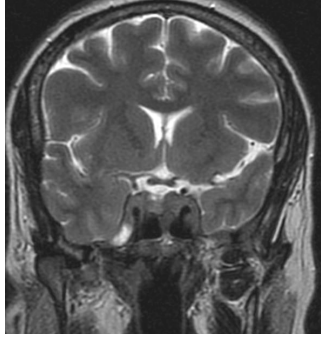


FIG 1 -a

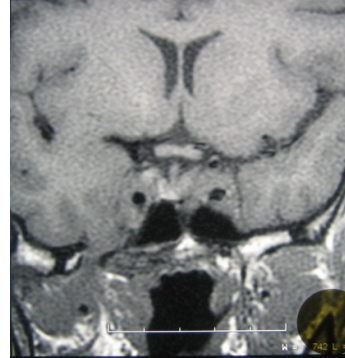


FIG 1-b

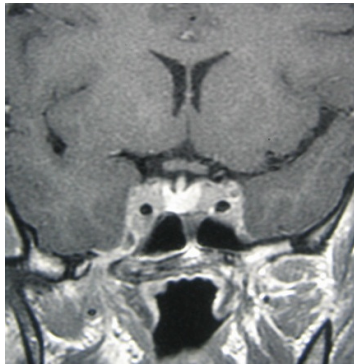


FIG 1-c

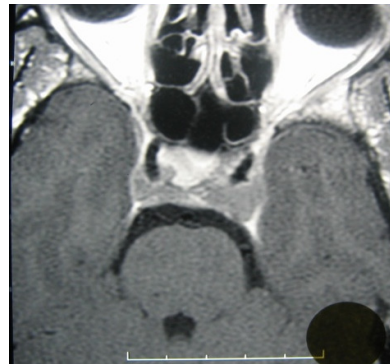


FIG 1-d

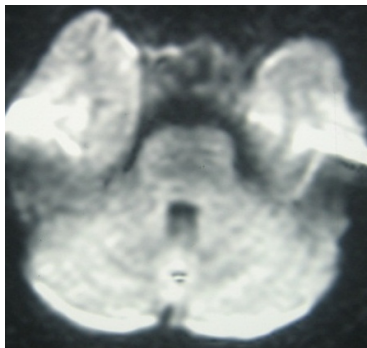


Fig 1-e

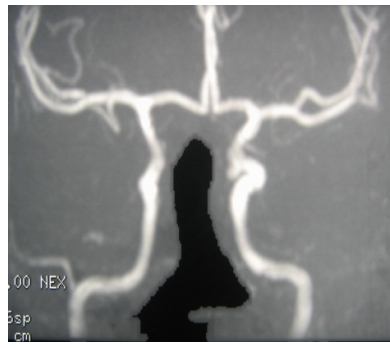


Fig 1-f

Fig 1 -MRI at Initial Presentation

- Coronal T1- (a) and T2-weighted images (b) show symmetrical enlargement of the cavernous sinuses by the lesion which has an homogeneous and isointense signal intensity to the cortex and complete encasement of the internal carotid artery (ICA) by the tumor.

- c. Coronal (same plane than Fig 1-b) and Axial (d) contrast-enhanced T1-weighted image shows slight and homogeneous enhancement of the masses.

- e- Diffusion-weighted image ($b = 1000s/mm^2$) shows low signal from the CS masses.

- f – MRA shows abnormal ICAs in their CS courses

Brain and diffuse meningeal involvement occurred six months later and the

patients died 11months after the initialization of treatment.

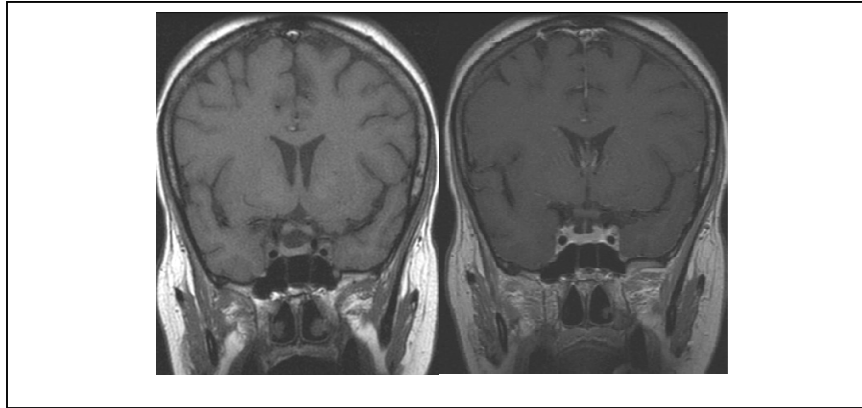


Fig 2 – a

Fig 2 – b

Fig 2 – MR follow-up, 3 Weeks after Initialization of Chemotherapy

Coronal T1 (a) and T1 after contrast-enhancement (b) images reveal the complete disappearance of the lesion. Both cavernous sinuses are free of tumoral invasion.

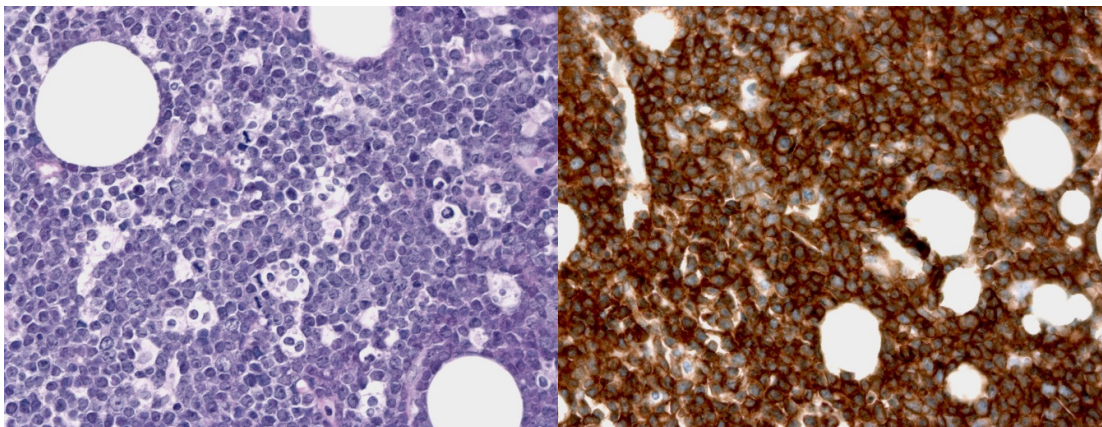


Fig 3-a

Fig 3-b

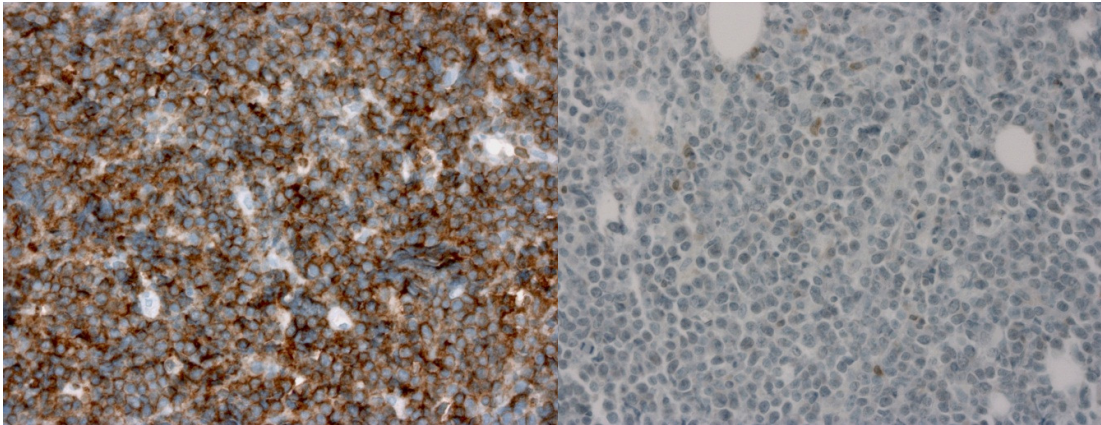


Fig 3-c

Fig 3-d

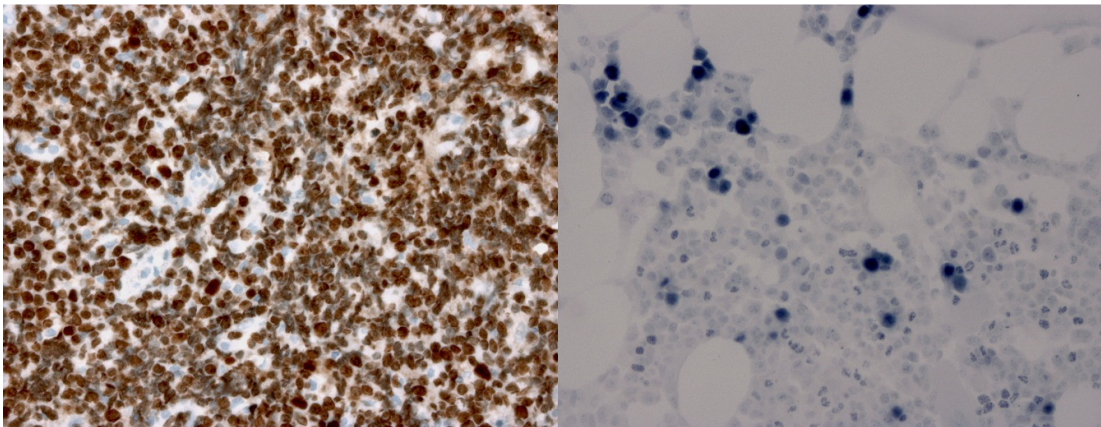


Fig 3-e

Fig 3-f

Fig 3-a to 3-b: Biopsy of the Left Breast Nodule

Histologically, Burkitt lymphoma is composed of uniform cells with small nucleoli and dispersed chromatin (3-a); tumor cells strongly express CD20 (3-b), CD10 (3-c) with a proliferation index of 100% with Ki67 (3-e).

Fig 3-f: Bone Marrow Biopsy

Scattered Burkitt lymphoma tumor cells are positive for EBV-1 situ hybridization

Discussion

More than 90% of primary Central Nervous System (CNS) lymphomas are histologically classified as high-grade B cell lymphomas and about 5-15% of these are of Burkitt's type (10). BL is characterized by rapid progression and early hematogeneous dissemination.

EBV viral antigens have been found in 50% to 90% of patients and are uncommon in the "sporadic form" (11). In the presented case, EBV antigen was detected immunochemically in B marrow cells.

Initial presentation with CNS or skull base involvement is a rare event, occurring more frequently in non-African form, and is

associated with the greatest risk of treatment failure. CS invasion as an initial presentation of BL has been reported only rarely. The clinical signs are those of a cavernous sinus syndrome (CSS), characterized by ocular motor nerves palsies involving the third, fourth and sixth nerves, as well as the first or second divisions of the fifth cranial sensory nerve in various combinations, and orbital pain. The pupil may be involved or spared (12). MRI findings may be useful for diagnosis (13).

Solitary primary BL of the CS has been reported in two cases and diagnosis was achieved by surgical biopsy of the lesion (6, 8) and bilateral and asymmetrical invasion of the CS as the initial presentation has been reported in another case (7, 9). Rare are the reports on MRI findings of BL of the CS, an appearance which is characterized by an isointensity to the brain on T1- and T2-weighted images. On post-contrast T1-weighted images, enhancement is always homogeneous, usually slight, as in our case. Rarely post-contrast enhancement is intense (6, 7). These radiological features are not specific, and slight enhancement is suggestive of lymphomas. Furthermore, low-signal on DWI is rarely observed in solid and enhancing intracranial tumors, especially intraaxial tumors. We could find no relevant report of DWI in cavernous sinuses lymphomas.

Our case is unusual by the bilateral and symmetrical CS involvement, the occurrence in an immunocompetent non-African woman and the association to EBV antigenicity.

Patients with increased tumor bulk and widely disseminated diseases have lower response rates as in our case.

Numerous causes for CSS have been reported and fall into categories of tumors (30%), infectious and inflammatory lesions, as well as vascular lesions. Lymphomas constitute 6% of all lesions (12).

Bilateral CS involvement suggests especially **lymphomas**, and **infectious** diseases, more rarely CS fistulas. More common infectious lesions involving the CS are aspergillomas or mucormycosis. They

occur in immunocompromised and diabetic patients and arise as a result of extension from the paranasal sinuses, and orbital involvement is usually associated. Thrombosis of the CS may also be bilateral, complicating bacterial or fungal invasion of the sinuses and imaging consists in lack of enhancement inside the CS and increased enhancement along the lateral border of the CS. In these cases of CSS, CT and MR provide useful information to the diagnosis. Bilateral CS tuberculomas are very uncommon and are associated with the enhancement of the adjacent thickened dura (14). Non-infectious inflammatory lesions such as sarcoidosis have also to be considered.

Metastatic disease of the CS is not an uncommon cause of CSS. Its presentation, however, occurs almost exclusively as a unilateral, rapidly progressive painful ophthalmoplegia and is an extremely rare cause of bilateral CS involvement (9; 15). Carotid cavernous fistulas cause also CSS, may be bilateral, and are associated with particular orbital congestion and bruit. Presence of signal voids inside the CS on T2-weighted images is a very specific feature (16). In these CS lesions, MRI may be useful for diagnosis (13).

Meningioma remains the most frequent tumor in this location. CS meningioma is associated with the enhancement of the dural attachment and in only rare cases invades the sellae and both cavernous sinuses. When the enhancement is not typical for a meningioma, a work-up for lymphomas must be realized.

In CSS in relation to BL, biopsy of associated locations usually allow the diagnosis as in the literature and herein reported case (7). When cavernous sinus lesion is solitary, surgical biopsy of this location is necessary (6)

Conclusion

Primary CNS involvement of Burkitt Lymphoma is rare, occurs more frequently in sporadic form and cavernous sinus involvement as initial presentation is uncommon.

Burkitt Lymphoma should be considered in the differential diagnosis and a work-up of the tumor must be realized when cavernous sinus enlargement is present at MRI with the herein described signal.

Since BL has the higher growth rate of any tumor, rapid diagnosis and immediate treatment are important and likely to improve outcome.

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