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Case Report

Yellow droopy eyes: A case of obstructive jaundice from Burkitt's lymphoma with involvement of bilateral cavernous sinus ☆

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ABSTRACT

Burkitt's lymphoma follows a lymphogenous spread early in the disease. The central nervous system can be involved via a hematogenous route but involvement of the cavernous sinus (CS) is rare and can be misdiagnosed as other pathology of primary neoplastic, infective, or vascular origin. We present a case of a 73-year-old gentleman with painless jaundice and subjective heaviness to his eyes that progressed to partial ptosis of the left eye, complete ptosis of the right eye with diplopia, found to have disseminated Burkitt's lymphoma with bilateral deposits to the CS. Early recognition of Burkitt's lymphoma with CS involvement is important as it often signifies disseminated disease with implications on chemotherapy regimen, treatment outcomes, and survival.

Introduction

Burkitt's lymphoma (BL) accounts for approximately 1%-5% of B-cell non-Hodgkin lymphomas (NHL). It more commonly affects males and is typically a condition of the pediatric population. The common subtypes of BL include endemic, sporadic, and immune-deficiency-associated variants. The sporadic subtype accounts for only around 1% of NHL in the adult population. The presentation of sporadic subtype can be variable but typically presents with abdominal symptoms including pain, gastrointestinal bleeding, and distention due to ascites [1]. While central nervous system (CNS) involvement occurs in 10%-20% in the sporadic subtype, involvement of the

Abbreviations: CS, Cavernous sinus; BL, Burkitt's lymphoma.

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cavernous sinus (CS) with neuro-ophthalmological presentations is very rare. Only a handful of BL with CS involvement has been documented in literature [2–5].

Case report

A 73-year-old man presented to the emergency department with concerns of 1 week history of painless jaundice and elevated liver functions test with an obstructive cholestatic pattern. Initial CT of the abdomen revealed intrahepatic duct dilatation (Fig. 1) with hypodense metastatic lesions causing mass effect on the common hepatic duct (Fig. 2), with a presumed primary cholangiocarcinoma. At the time of presentation, the patient also complained of subjective heaviness to his eyes; however, examination was unremarkable for cranial nerve deficit. The patient was admitted for further workup and received an ERCP and stent insertion which clinically improved the biliary obstruction. A cytology brushing taken at the time was undiagnostic.

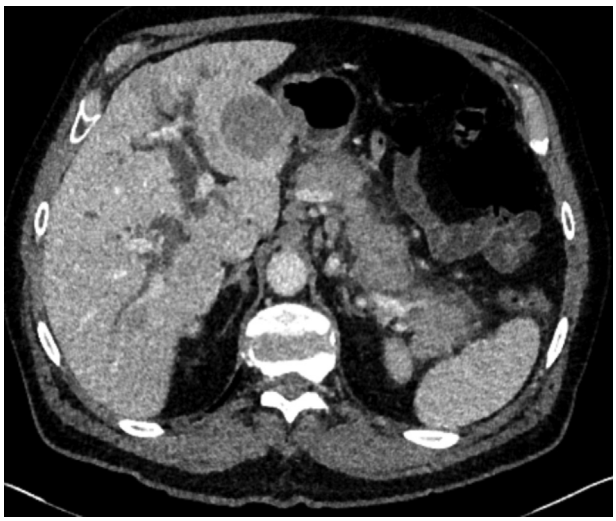

Fig. 1 – Intrahepatic dilatation with low-density hepatic lesions.

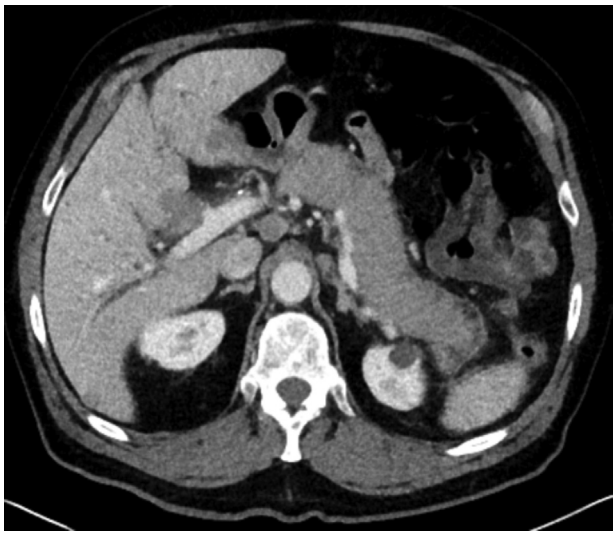

Fig. 2 – Segmentin IVa/IVb 25 mm hypodense hepatic lesion causing mass effect on common hepatic duct.

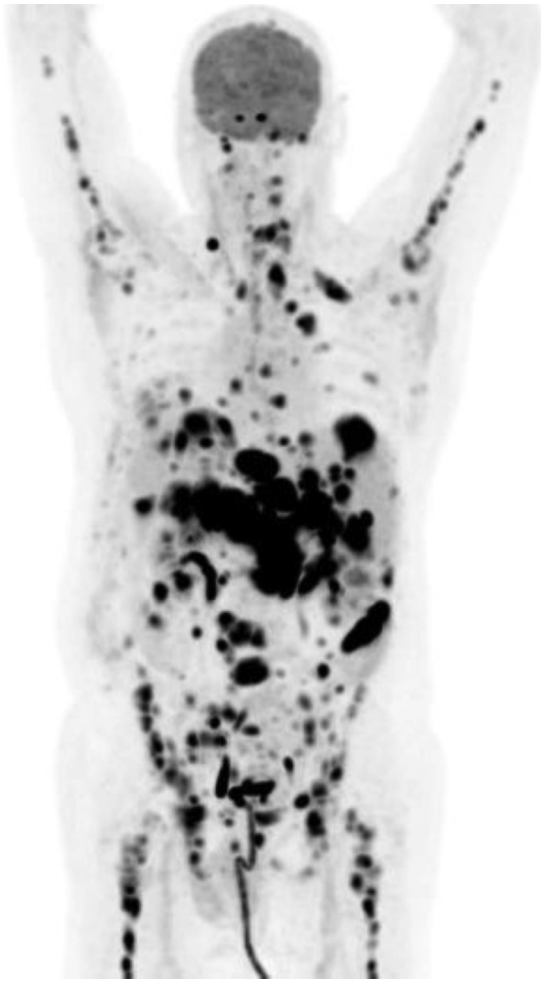

Fig. 3 – PET maximum intensity projection (MIP) showing diffuse nodal an extranodal disease.

Progressively during his admission, he developed partial ptosis of the left eyelid, complete ptosis of the right eyelid with binocular diplopia and retro-orbital pain. Examination was consistent with partial left and complete right CNIII palsy. CT scan did not reveal any intracranial lesions; however, MRI of the brain and orbits (Fig. 2) showed subtle bilateral nodular lesions involving the CS. Maximum intensity projection ^{18}F-FDG PET/CT attenuation corrected image of the body showed diffuse extensive nodal and extranodal disease involving multiple abdominal organs, bone, and soft tissues (Fig. 3). Staging ^{18}F-FDG PET/CT fused color images (Fig. 4) and attenuation corrected (Fig. 5) confirmed bilateral intense avidity of the CS.

The patient was further investigated with targeted fine needle aspiration biopsies of a left level III cervical node and of a hepatic lesion. Immunohistochemistry showed B cells with positive expression of CD10, CD19, CD20, and CD23. Ki67 proliferation index was 90% with rearrangement of *c-MYC* gene on FISH studies. The culmination of results confirmed BL.

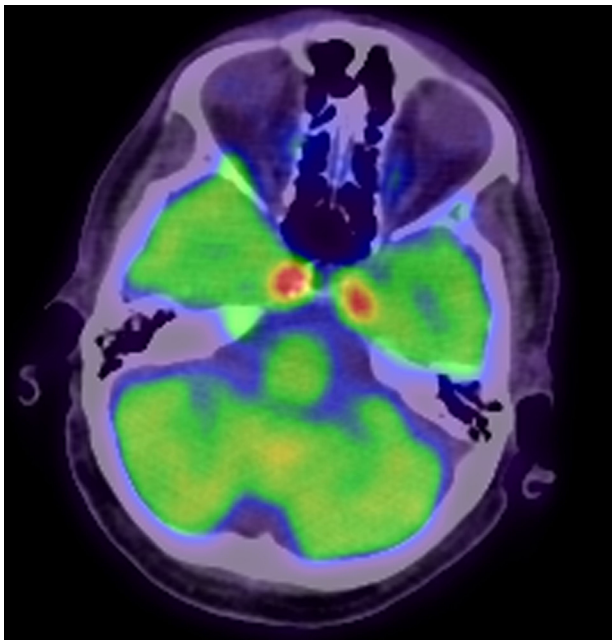

Fig. 4 – Axial ^{18}F-FDG PET/CT of the brain showing bilateral intense avidity of the cavernous sinus.

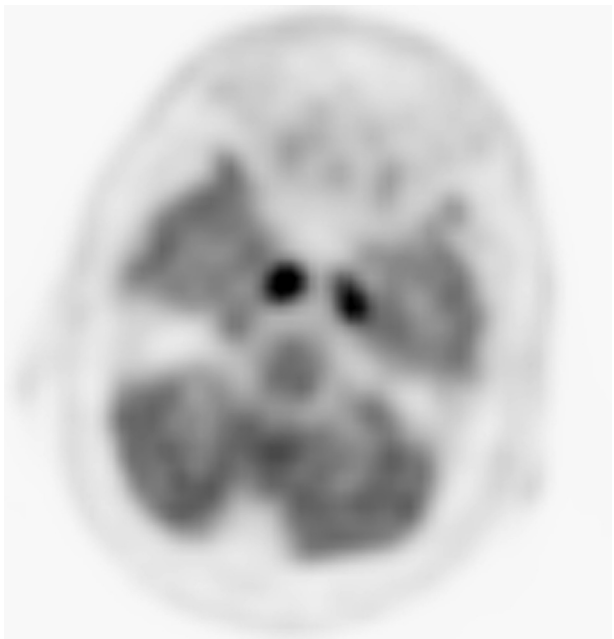

Fig. 5 – Axial attenuation corrected PET showing increased metabolic activity of bilateral cavernous sinus.

CSF analysis and flow cytometry on multiple occasions were negative for malignant cells. The patient was commenced on hyper-CVAD chemotherapy but clinical course was complicated by neutropenic sepsis requiring admission to intensive care unit. De-escalation to mini R-CHOP was well tolerated so he was escalated to R-CHOP for 2 cycles. Intrathecal methotrexate was also administered.

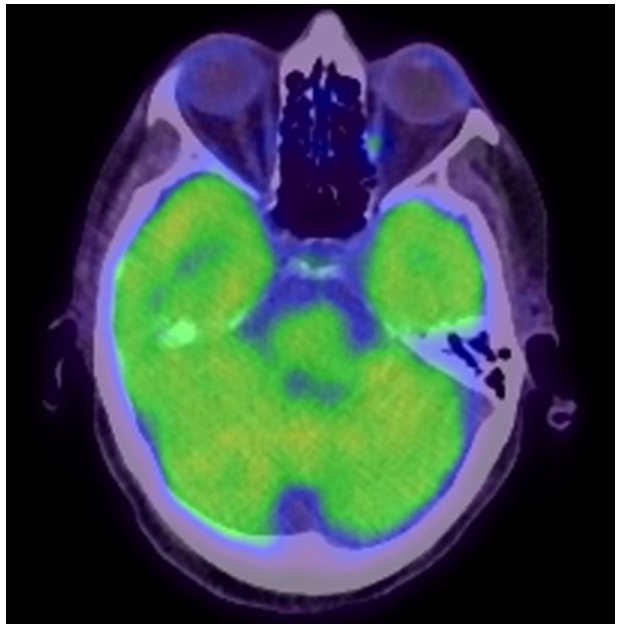

Fig. 6 – Axial ^{18}F-FDG PET/CT post chemotherapy showing return to normal metabolic activity of bilateral cavernous sinus.

Restaging ^{18}F-FDG PET/CT 1 month post chemotherapy showed complete resolution of generalized BL deposits, including the CS, with return to normal metabolic activity (Figs. 6 and 7). Clinically, the patient recovered full function of bilateral oculomotor nerves. At the time of writing, the patient remained in clinical remission.

Discussion

BL is a rapidly progressing and aggressive subtype of NHL with a doubling time of 24-48 hours due to the deregulation of proto-oncogene *c-MYC*, disinhibiting cell growth and division [6,7]. BL can be further divided into 3 recognized subtypes being endemic, sporadic, and HIV-associated BL. Sporadic BL, as in this report, comprises less than 1% of adult NHL patients and has a male and Caucasian predisposition [1,8]. In adults, it usually occurs before the age of 35, with a mean of 30 years [8]. Gastrointestinal symptoms such as abdominal pain, distension, bowel obstruction, nausea, and gastrointestinal bleeding typify the initial presentation of sporadic BL.

Burkitt's lymphoma rarely affects the CNS as a primary disease [9]. Its detection should therefore raise the suspicion of systemic dissemination, as demonstrated in this case. Typically, the sporadic BL disease follows a lymphogenous path of metastasis that leads to extranodal involvements of the kidneys, pancreas, liver, and lungs among organs. CNS involvement occurs later in the disease process, often via a hematogenous route [3,10], defining stage IV disease which accounts for 13%-17% of adult cases [11]. CNS involvement is usually leptomeningeal but only rarely involves the CS [12].

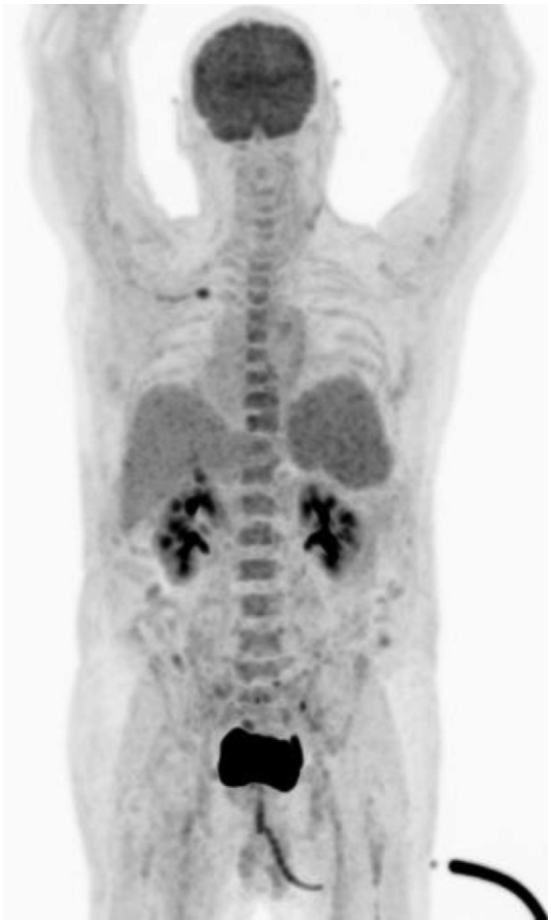

Fig. 7 – PET maximum intensity projection (MIP) showing resolution of diffuse sporadic Burkitt's lymphoma post chemotherapy.

A number of documented cases over the years have shown unilateral BL involvement of the CS [3,13–17]. Bilateral involvement of CS in adult sporadic BL has only been reported a few times in literature [2,4,5] Clinical signs of CS involvement can be variable but may be characterized by ophthalmoplegia involving cranial nerves 3, 4, and 6 as well as sensory deficits in the first and second divisions of cranial nerve five due to their intimate anatomical relation [4,10]. Associated headache and retro-orbital pain is also a common complaint [2,5,10,17].

Other differential diagnoses of CS syndrome include a primary neoplastic process, vascular lesions such as CS thrombosis, inflammatory conditions such as Tolosa-Hunt syndrome and sarcoidosis, and infectious processes such as bacterial and fungal infections. Further characterization with high-resolution MRI is mandatory to exclude pathology within or along the CS [10]. Imaging pattern of BL of the CS on MRI may be characterized by isointensity to the brain on T1- and T2-weighted images with slight homogenous enhancement on post-contrast T1 weight images [4].

Deregulation of the *c-MYC* proto-oncogene leads to increased cellular metabolism making BL a glucose-avid tumor with intense ^{18}F-FDG avidity. As such, ^{18}F-FDG PET/CT imaging plays a key role not only in the detection of suspected disease but has a role in disease monitoring [18]. BL has a favorable prognosis with the use of multi-agent chemotherapy regimens in children and young adults [11,19]. However, treatment of older adults can be difficult due to susceptibility to acute toxicities with increasing age [20]. As such, the regimen is dependent on individual risk profile and comorbidities. CNS involvement is an independent risk factor that is associated with poorer outcomes [21]. However, in this case, there was a marked reduction in ^{18}F-FDG avidity post-therapy, indicating a favorable prognosis.

In conclusion, we describe a patient with an unusual presentation of Burkitt's lymphoma. Our case demonstrates that CS involvement which is a rare finding in adult BL raises the suspicion of disseminated disease. However, due to its rarity, it can also masquerade as host of other differential conditions. Prompt recognition is important to avoid delayed diagnosis that can impact on management and overall survival outcomes for the patient. ^{18}F-FDG PET/CT also has an important role in the prognostication by monitoring response to therapy, even after a short period of time.

Patient consent

Written informed consent has been obtained from the patient to publish this case. All clinical information and radiological information in this case has been anonymized.

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