Orbital plasmablastic lymphoma with remission following chemotherapy

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ABSTRACT

We report the case of a middle-aged HIV-positive man who presented with proptosis and retro-ocular pain. On CT and MR imaging, a retro-orbital enhancing mass was seen, and PET/CT revealed this lesion as well as a similarly characterized mass in the nasopharynx to be hypermetabolic. Biopsy and subsequent pathological characterization revealed this mass to be plasmablastic lymphoma (PBL), a rare form of non-Hodgkin's lymphoma associated with HIV-infection. PBL is a diffuse B-cell lymphoma with characteristic cell marker patterns. The most common site of this malignancy is within the oral cavity. This case constitutes an unusual orbital manifestation of plasmablastic lymphoma as well as an unusual case in its response to chemotherapy. This case illustrates the importance of functional imaging with PET/CT in the diagnosis, management, and follow-up of plasmablastic lymphoma.

CASE REPORT

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A 43 year-old Caucasian man with a history of HIV with a CD4 count of 530 cells/mm3, not currently on HAART, presented with left-sided proptosis, headaches, and eye pain. Three months prior to this admission, he was seen for a jaw abscess for which his doctors prescribed clindamycin. CT scanning (Figure 1) and MR imaging (Figure 2) on this admission for proptosis revealed a left retro-orbital mass measuring 4.5 cm by 3.0 cm by 4.0 cm with bony erosion of the sphenoid wing and mass effect on the left globe and compression of the anterior left temporal lobe as well as a soft tissue mass near the right fossa of Rosenmüller in the right nasopharynx. PET/CT imaging revealed hypermetabolic activity of the left retro-orbital mass (Figure 3A) with a maximal SUV of 30.0 and right nasopharyngeal mass in the fossa of Rosenmüller (Figure 3B) with maximal SUV of 31.7 as well as diffuse lymphadenopathy in the neck, abdomen, and pelvis with maximal SUV of 4.5. Biopsy of the nasopharyngeal mass demonstrated proliferation of medium to large sized lymphoid type cells with prominent nucleoli and numerous mitotic figures on frozen section; these neoplastic cells are positive for CD10 and CD138 and weakly positive for CD79a, consistent with the diagnosis of plasmablastic lymphoma.

The patient was placed on a regimen of EPOCH chemotherapeutic agents (etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone) and pegfilgrastim. Follow-up MR imaging (Figure 4) demonstrated a precipitous reduction in the size of the lesion at two months, and PET/CT at five months does not show any recurrence or metastatic disease. At ten months, however, PET/CT revealed areas of hypermetabolic activity suggestive of recurrence of PBL most prominently in the retromandibular and posterior cervical lymph nodes (Figure 5) with a new lesion in the Rosenmüller's fossa of the left nasopharynx. No recurrence of the orbital

lesion was noted, however. The patient continues to be followed up with PET/CT routinely and otolaryngology is expected to biopsy the new hypermetabolic lesions and assess whether these regions of high SUV indicate recurrence or a new primary cancer such as nasopharyngeal carcinoma.

DISCUSSION

This case is an unusual example of plasmablastic lymphoma, originating in the right nasopharynx of an HIV-positive man. The lesion spread to the left retro-orbital region. Possible explanations of his initial clinical presentation include a host possible conditions ranging from orbital cellulitis, a retro-ocular hemangioma or AVM, a spheno-orbital meningioma, cavernous sinus thrombosis, Grave's disease to, most rarely, lymphoma. The lack of bony erosion on CT imaging in this case argues against the presence of hemangioma and the retro-orbital position and discrete mass supports diagnoses other than orbital cellulitis, Grave's disease or cavernous sinus thrombosis.

While there are several potential causes for the initial CT and MR imaging appearance of an enhancing mass located in the retro-orbital region (highlighted in the differential diagnosis table) that could explain this patient's proptosis and constellation of symptoms, functional imaging was able to provide clues to support the eventual diagnosis. Initial imaging with PET/CT demonstrating hypermetabolic activity largely restricted the differential diagnosis in this patient to malignancy and also suggested these lesions to be primary within the head rather than metastatic disease from elsewhere. Etiologies possible of producing this set of imaging findings therefore include glioblastoma multiforme, primary CNS lymphomas, and spheno-orbital meningioma. The clinical team could narrow the diagnosis in this case because of the presence of a lesion within the nasopharynx, biopsy could be performed. Pathological examination of this lesion made the definitive diagnosis of PBL. The presence of lymphadenopathy with hypermetabolic uptake of FDG in addition to the nasopharyngeal and retro-orbital masses supported the early initiation of chemotherapy. Unlike many reported cases of PBL, this patient's lesions responded well to EPOCH chemotherapy with complete remission on PET/CT at five months. Unfortunately, recurrence of hypermetabolic lesions was seen at ten months on PET/CT. Nevertheless, this duration of remission is greater than most reported cases, yet no clearly established response rates exist for EPOCH chemotherapy in PBL cases. This case demonstrates the utility of PET/CT imaging in the staging of this rare cancer as well as its usefulness in assessing for recurrence.

Plasmablastic lymphoma (PBL), an aggressive non-Hodgkin's lymphoma, is a recently identified form of diffuse large B-cell lymphoma (DLBCL) first described in 1997; this clinical entity is extremely rare with only about 60 cases reported [1]. On pathology, it is characterized by immunoblastic morphology of large cells with abundant cytoplasm and eccentric nuclei with positive staining for CD138 and VS38c [1,2]. These neoplastic cells do not express CD20 and CD45. PBL, like other Non-Hodgkins Lymphomas (NHL) is seen with greater frequency in immunosuppressed HIV patients and may even constitute the initial presentation of HIV, but approximately ten percent of cases of PBL occur in HIV-negative individuals [3,4]. Epstein-Barr Virus (EBV) and Human Herpes Virus 8 (HHV-8) may be responsible for initiation of neoplastic activity in PBL as identified in 76% and 37% of cases, respectively [1]. PBL classically manifests in the form of oral lesions and even led to its naming by the World Health Organization as plasmablastic lymphoma of the oral cavity, but more evidence suggests that extra-oral presentations of PBL occur with substantial frequency including cases of orbital, cutaneous, gastrointestinal and other manifestations [1,5-7]. One review of the literature demonstrates oral lesions to comprise three-quarters of PBL cases [4]. A few cases of orbital PBL similar to that reported here exist in the literature [8,9].

Prognosis is generally poor, yet poorly quantified in the literature; a meta-analysis reports a death rate of 60% at 10 months follow-up and another study reports an average survival time of six months [1,8]. There exists little evidence to support a particular treatment approach to manage PBL. PBL may respond to HAART therapy in HIV-positive as suggested by one case report and a meta-analysis demonstrating greater survival in HIV patients receiving HAART [1,10]. CHOP (cyclophosphamide, adriamycin, vincristine, and prednisolone) multi-agent chemotherapy is also purported to promote remission of PBL, but success rates vary in the literature and most cases recur [4]. One group reports success with HAART combined with CHOP in treating PBL [11]. As utilized by the clinical treatment team in this case, EPOCH chemotherapy is a standard chemotherapeutic regimen for HIV-associated lymphomas and has demonstrated varied efficacy in a small number of cases [12,13]. Spontaneous remission has even been reported in one particular case [14].

We report here the imaging findings of a rare case of orbital PBL. MR Imaging in this case demonstrates excellent response to EPOCH chemotherapy with reduction of the retro-ocular lesion. Imaging also clarified the extent of invasion of this lesion and provided reassurance of non-parenchymal involvement. PET/CT is of the utmost importance in following up the progression of this disease, especially in light of PBL's highly aggressive nature. Close monitoring of this patient has revealed potential recurrence of PBL and will continue to play an important role in assessing this patient's needs for chemotherapy and radiotherapy. In addition, PET/CT in this case has provided probable sites of malignancy to be biopsied to better stage this patient's cancer.

TEACHING POINT

Plasmablastic lymphoma may manifest in extra-oral locations such as the orbit, most commonly in patients with a history of AIDS. On imaging, PBL appears as a soft tissue mass differentiated from several other etiologies by avid FDG uptake on PET/CT scanning and is definitively diagnosed by characteristic histological markers on pathological examination.

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FIGURES

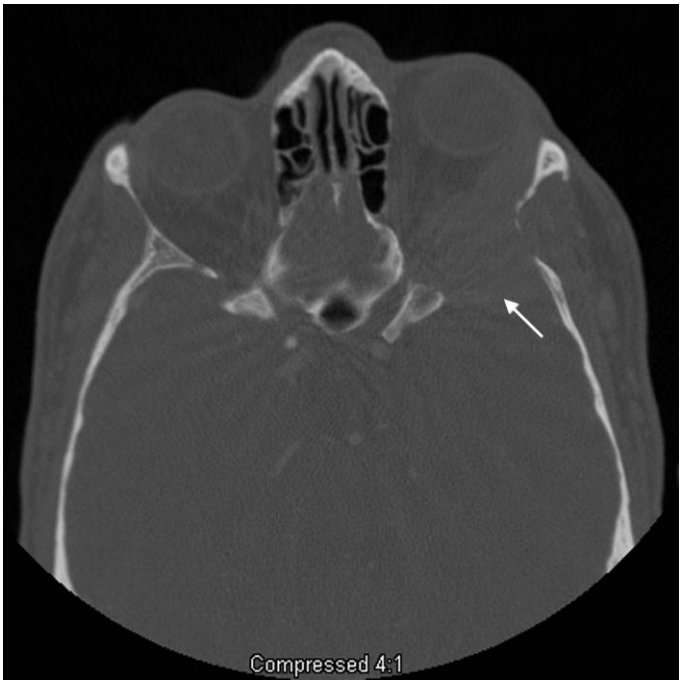


Figure 1. 43 year old male with history of HIV who presented with retro-ocular pain and proptosis was initially imaged with CT of the head and neck. Seen here is an enhancing mass measuring 3.8 x 2.7 x 3.6 cm located at the juncture of the lateral wall of the left orbit with destruction of the bone (arrow). (Protocol: kV: 120/mA 176/1825msec, Slice thickness: 0.6mm, FOV: 20cm, bone window)

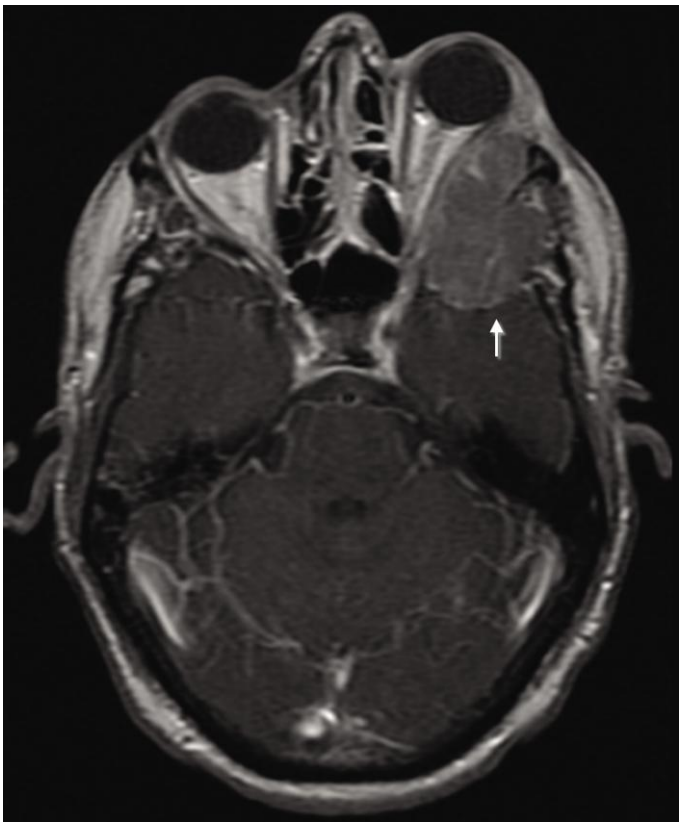
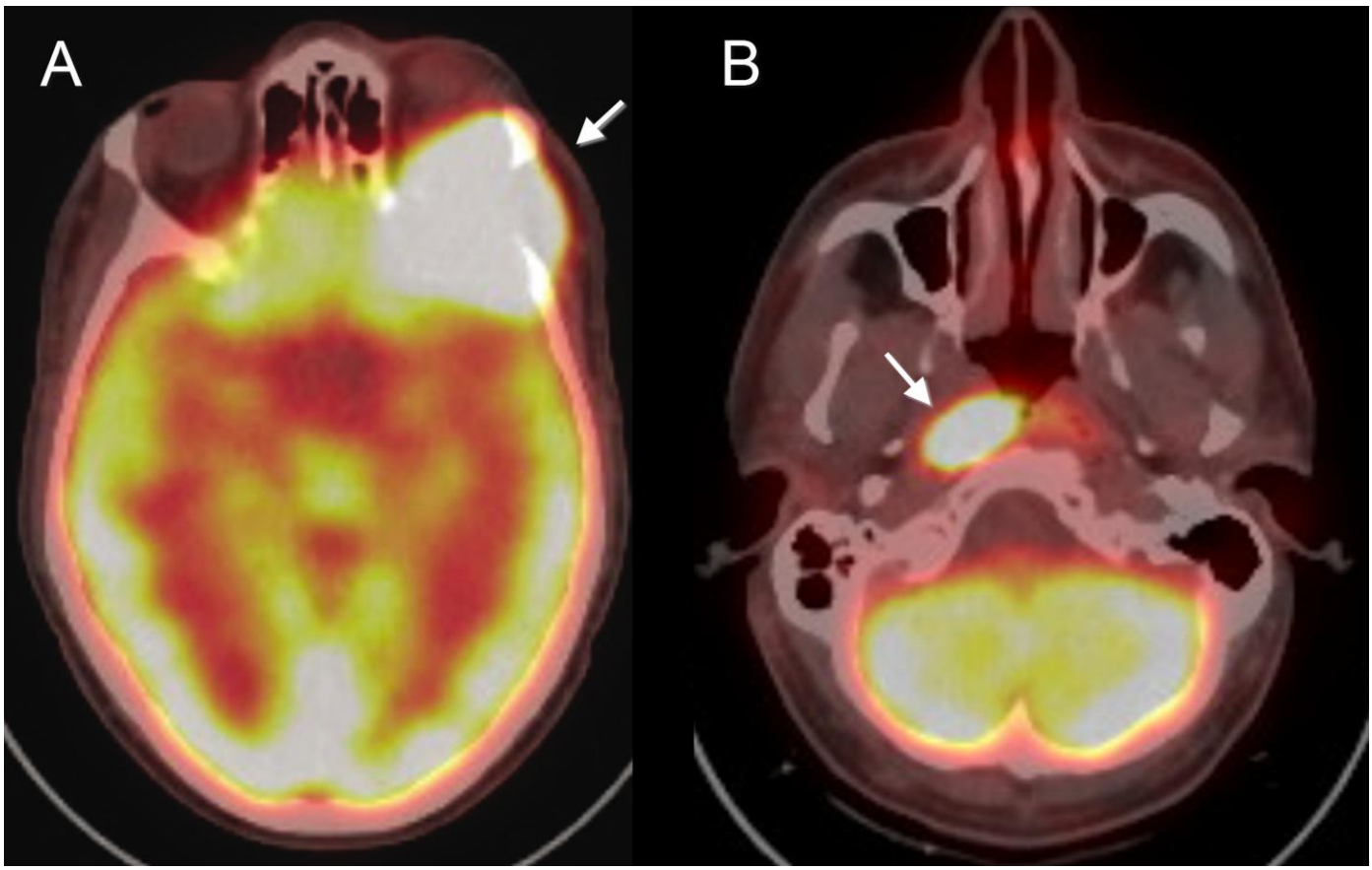


Figure 2 (left). 43 year old male with history of HIV later determined to have plasmablastic lymphoma underwent brain and orbital MRI study on a 1.5T scanner with Gadolinium contrast after initial presentation and discovery of mass on CT. Identified here on post-gadolinium T1-weighted imaging is a soft tissue mass lesion (arrow), measuring 4.5 x 3.0 x 4.0 cm causing bony erosion of the sphenoid wing and significant mass effect on the orbital structures and resulting in proptosis of the left globe. The mass impinges on and displaces the optic nerve and pushes on the maxillary sinus. There is no evidence of brain parenchymal invasion. (Protocol: TR: 617, TE: 20, Slice thickness: 5mm, FOV: 24cm)

Figure 3 (bottom). 43 year old male with history of HIV later determined to have plasmablastic lymphoma underwent PET/CT scanning shortly after initial presentation and discovery of mass on MRI and CT. (A) Observed is a markedly hypermetabolic left retro-orbital mass, maximum SUV of 30.0, compatible with neoplasm (arrow). (B) There is a markedly hypermetabolic right nasopharyngeal mass, maximum SUV of 31.7 (arrow), compatible with neoplasm as well. (Protocol: 14.8 millicuries of F-18 labeled FDG for the uptake interval, both emission and transmission scans of the whole body from lower head to mid thigh were obtained. Emission and attenuation corrected 3-D cine, transverse, coronal and sagittal images were reviewed on a workstation. The standardized uptake values were calculated using the patient's ideal body weight. A low dose spiral CT scan from the lower head to mid thigh is fused to the PET data for anatomical localization as needed.)



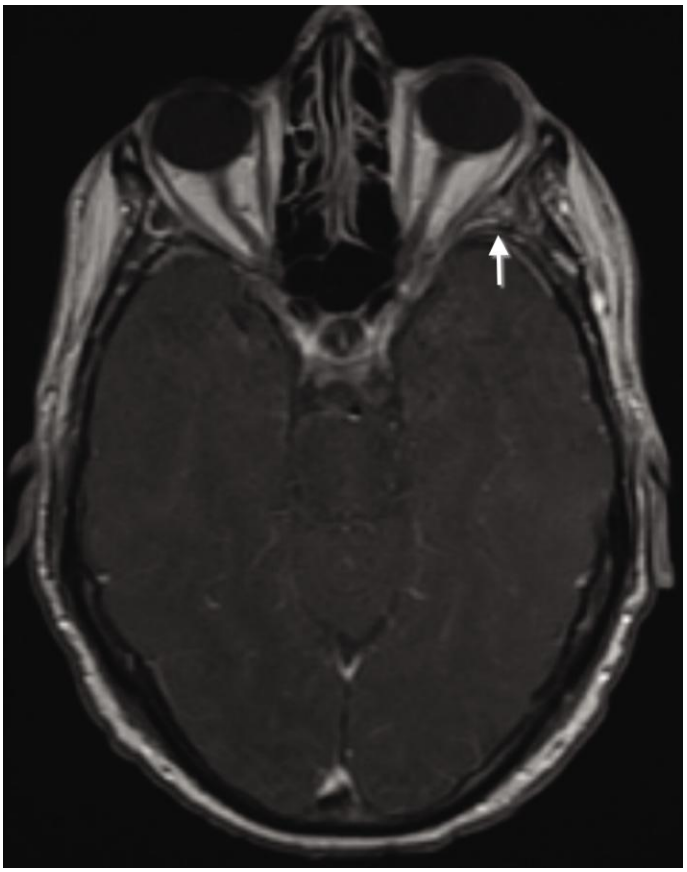


Figure 4. 43 year old male with history of HIV and plasmablastic lymphoma underwent repeat brain and orbital MRI at five months after initial presentation and imaging. There is marked improvement of the previously seen orbital left sphenoid enhancing lesion (arrow). Slight residual post gadolinium enhancement is identified. (Protocol: axial T2, TR:5867, TE:81, Slice thickness:5mm, FOV:24cm)

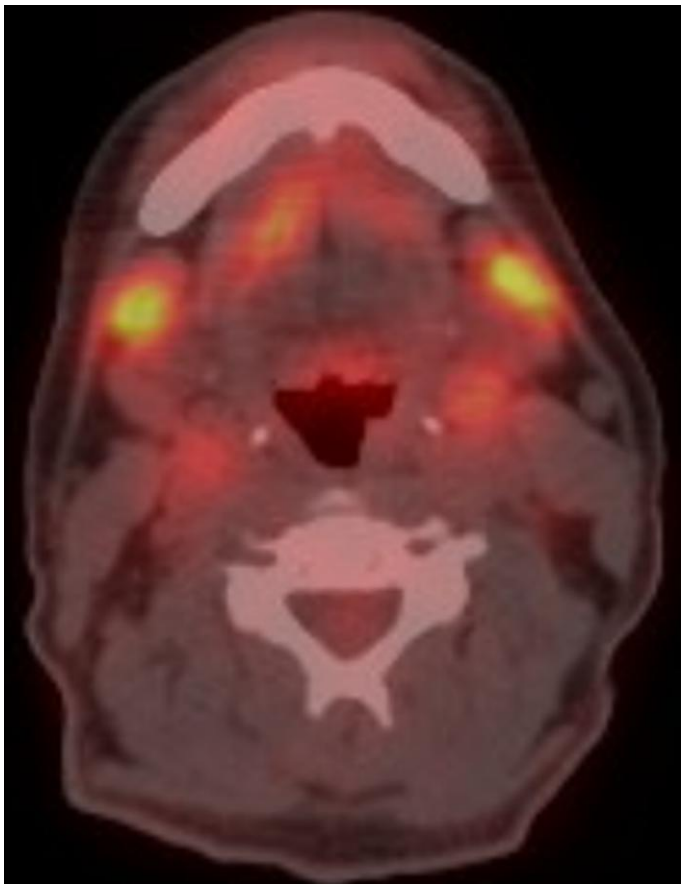


Figure 5. 43-year-old male with history of HIV with diagnosed plasmablastic lymphoma underwent PET/CT after five rounds of EPOCH chemotherapy ten months after initial diagnosis. Seen on this study is marked hypermetabolic activity within the submandibular glands bilaterally with a maximal SUV of 7.9. (Protocol: 14.8 millicuries of F-18 labeled FDG for the uptake interval, both emission and transmission scans of the whole body from lower head to mid thigh were obtained. Emission and attenuation corrected 3-D cine, transverse, coronal and sagittal images were reviewed on a workstation. The standardized uptake values were calculated using the patient's ideal body weight. A low dose spiral CT scan from the lower head to mid thigh is fused to the PET data for anatomical localization as needed.)

Etiology	Possible association with Epstein-Barr Virus (EBV), Human Herpes Virus 8 (HHV-8)
Incidence	Unknown Approximately 60 reported cases in the literature
Gender Ratio	5:1 (male:female)
Age predilection	Peak incidence at approximately 40 years of age
Risk factors	Untreated HIV infection, AIDS
Treatment	Radiotherapy Chemotherapy (CHOP, EPOCH) HAART
Prognosis	Poor, in general but may remit with treatment or spontaneously Average survival from diagnosis: 6 months
Imaging Findings	Oral or extra-oral mass-occupying lesion with enhancement on CT following administration of contrast, possible destruction of neighboring bone; MRI shows similar enhancement patterns; PET shows increased uptake of FDG by the tumor

Table 1. Summary table: Features of plasmablastic lymphoma

	MRI	CT	PET/CT
Non-Hodgkin's Lymphoma (e.g. Plasmablastic Lymphoma (PBL) and other Primary CNS Lymphomas (as differentiated by histopathology))	Mass lesion with Gd enhancement	Well-demarcated, homogenous mass Homogenous enhancement Bony erosion	High metabolic activity
Glioblastoma multiforme (GBM)	Hyperintense on T2w, Hypointense on T1w Gd Enhancing Cystic appearance with flow voids Peritumoral edema	Heterogeneous mass Inhomogeneous enhancement	High metabolic activity
Metastatic lesion (e.g. melanoma)	Multiple, well-marginated masses Peritumoral edema	Multiple, well-marginated masses	High metabolic activity
Spheno-orbital meningioma	Soft tissue tumor Gd enhancing meninges Parenchymal edema	Homogenous enhancement Hyperostosis	High metabolic activity
Cavernous hemangioma	Heterogenous mass often well-demarcated by hypointense rim of hemosiderin No surrounding edema	Round, oval homogenous lesion of slight hyperattenuation Occasionally calcifications present	Low FDG uptake
Orbital Cellulitis	Hypointense on T1w, hyperintense on T2w images	Increased density and swelling of anterior orbit	No increase in uptake
Hemangioblastoma	Generally superficial, cystic lesions Enhancement of the nodule, but not surrounding cyst Internal signal voids	Isoattenuating on nonenhanced CT Homogenous enhancement	No increase in uptake
Unilateral Cavernous Sinus Thrombosis	Flow voids within the cavernous sinus	Hyperattenuation within cavernous sinus	No increase in uptake
Intracranial abscess	Thin-walled mass with edema surrounding mass Thin wall occasionally seen, ring enhancement	Hypoattenuating mass Ring-enhancement	Less uptake than neoplasms
Arteriovenous malformation (AVM)	Flow voids	Enhancement of vessels	Low uptake in affected region

Table 2. Differential diagnosis of intracranial mass / periorbital mass

ABBREVIATIONS

AIDS = acquired immune deficiency syndrome
AVM = arteriovenous malformation
CT = computed tomography
FDG = fluorodeoxyglucose
HAART = highly active antiretroviral therapy
HHV-8 = human herpes virus 8
HIV = human immunodeficiency virus
MRI = magnetic resonance imaging
PBL = plasmablastic lymphoma
PET = positron emission tomography

KEYWORDS

Plasmablastic lymphoma; Magnetic resonance imaging; positron emission tomography; computed tomography; AIDS-related malignancy; orbital tumor

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