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PML-IRIS in an HIV-2 infected patient presenting as Bell's palsy

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Abstract

We present the case of an HIV-2 infected patient who developed progressive multifocal leukoencephalopathy (PML) in the setting of immune reconstitution inflammatory syndrome (IRIS) presenting as Bell's palsy. The brain MRI showed a single lesion in the facial colliculus considered initially to be ischemic in nature. This case report should alert clinicians that PML can occur in the setting of HIV-2 infection. It also illustrates the difficulty of establishing the diagnosis of PML.

Introduction

Of all people living with the human deficiency virus (HIV), approximately 39 million are infected with HIV type-1 and 1–2 million with HIV type-2 (Campbell-Yesufu and Gandhi 2011, Wang, Wolock et al. 2016). HIV-2 is mostly endemic in West Africa and is less efficiently transmitted than HIV-1. Although AIDS may develop in HIV-2 carriers, it takes longer than in HIV-1-infected patients suggesting that immune factors limit viral pathogenesis. (Chan, Wakeman et al. 2008) In HIV-2 infection, humoral, innate and cellular responses are more robust and polyfunctional (Nyamweya, Hegedus et al. 2013). Progressive multifocal leukoencephalopathy (PML) is caused by JC virus (JCV), a ubiquitous polyomavirus which infects more than 50% of the adult population without causing any disease. PML usually occurs in immunocompromised individuals, such as those with advanced HIV-1 infection. (Berger, Aksamit et al. 2013) There are only few published cases of PML in HIV-2 infected patients. (Stoner, Agostini et al. 1998, Bienaime, Colson et al. 2006, Duque, Matos et al. 2010, Descamps, Peytavin et al. 2015) We report an atypical case of infratentorial PML in an HIV-2-infected patient from Cape Verde and reviewed the clinical features of all the reported cases.

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Conflict of Interest:

Fabian Sierra Morales, Carlos Illingworth, Kathie Lin, Ivia Rivera Agosto, Chloe Powell, Jacob A. Sloane, and Igor J. Koralnik declare that they have no conflict of interest.

Case report

A 65-year-old man with 13 years history of HIV-2 infection and chronic tremors presented with left facial weakness for 48 hours. His initial neurologic exam showed left facial weakness with involvement of the forehead and incomplete left eye closure. He had action tremors involving the right arm greater than the left one and were unchanged from previous neurologic exams. His serum HIV-2 viral load at symptom onset was 311 copies/ml and his CD4+ T-cell count was 361/ul, on elvitegravir, cobicistat, emtricitabine, tenofovir, and atazanavir treatment, up from 254/ul two months prior.

His facial weakness, which was considered to be caused by a peripheral seventh nerve palsy (Bell's palsy), worsened over 48 hours after admission. However, an MRI of the brain showed a non-enhancing lesion in the left facial colliculus, which was initially interpreted as a subacute infarct. There was also a region of hazy enhancement in the right pons that was unchanged from a study done 7 years prior to his current presentation. This finding was compatible with a capillary telangiectasia.

Of note, he had an episode of varicella zoster virus (VZV) thoracic radiculopathy four months prior to symptom onset. He was discharged home on 1 week p.o steroids and valacyclovir treatment for Bell's palsy.

Six weeks later, the patient developed progressive dysphagia to solid food. His neurologic exam showed left facial palsy and a weak gag reflex. A repeat MRI showed slight interval increase in the left facial colliculus lesion with new faint peripheral enhancement (Figure 1). He underwent a video oropharyngeal swallow study which revealed difficulty with initiation of swallowing, early spilling and delayed initiation. A lumbar puncture was performed to investigate possible infectious etiologies. CSF analyses showed 2 WBC/ul, elevated protein at 58 mg/dL, normal glucose, negative bacterial cultures and positive CSF JCV PCR at 34 copies/ml, establishing the diagnosis of PML. CSF PCR for TB, VZV, Toxoplasma Gondii, HSV, cytomegalovirus, and EBV were negative and the CSF VDRL was non-reactive and Cryptococcal antigen was not detected.

He remained on the same cART regimen and his dysphagia and facial weakness improved mildly three months after symptom onset.

Discussion

We describe a case of PML in a patient with HIV-2 infection. PML is usually a subacute disease with progressive focal neurological deficits related to the location of the lesions. The clinical manifestations are very diverse including motor weakness, gait abnormalities, visual field defects, cognitive and language dysfunction.(Berger, Aksamit et al. 2013) The presentation of PML in this patient is atypical in several aspects: 1) A single lesion was present in the left facial colliculus, affecting the seventh nerve nucleus and causing a neurologic deficit undistinguishable from a peripheral facial palsy. 2) The symptomatology occurred in the setting of immune recovery with CD4+ T-cell count going from 254/ul up to 361/ul on cART. This is consistent with PML-IRIS. Indeed, faint contrast enhancement was present in the PML lesion (Fig 1 B–D), which is one of the features of PML/IRIS.

Compared to the other 4 published HIV-2/PML cases, (Stoner, Agostini et al. 1998, Bienaime, Colson et al. 2006, Duque, Matos et al. 2010, Descamps, Peytavin et al. 2015) this is the only one presenting with a single lesion and in the context of IRIS. Of note, HIV-1 can also be the target of the recovered immune system in IRIS, causing fulminant HIV encephalitis. (Nath 2015) To our knowledge, there are no reports of HIV-2 being the sole target of IRIS in the CNS.

The clinical features of 4 previously reported cases of PML among HIV-2-infected patients are summarized in Table 1. CD4⁺ T-lymphocyte count and viral load were available in 3 of them: CD4 count was <100 cells/ul and plasma HIV-2 viral load ranged from 250–23,120 copies/mL. One patient had faint and irregular contrast enhancement in PML lesions on MRI, but there was no evidence of immune recovery (Table 1, case 1). Of note, none of these patients survived more than four months after symptom onset. Conversely our patient demonstrated clinical improvement at 3 months follow up. One possible explanation is his higher number of CD4⁺ T- cells at symptom onset and the presence of IRIS, which has been associated with better prognosis in PML patients. (Gheuens, Ngo et al. 2012)

Neurological complications can be seen in the setting of HIV-2 infection. Those include neurocognitive disorder, demyelinating encephalomyelitis, CNS toxoplasmosis, cryptococcal meningitis, and spastic paraplegia. (Moulinier, Lascoux et al. 2006, Choi, Townsend et al. 2011) In a study of 5401 patients in West Africa, encephalitis was more frequent in HIV-2 infection than in HIV-1 infection. (Lucas, Hounnou et al. 1993)

This case report also illustrates the difficulty of establishing the diagnosis of PML. Indeed, Bell's palsy and stroke were first considered more likely, and the correct diagnosis of PML was only established at the second hospitalization 5 weeks after symptom onset. This is consistent with our experience with diagnosis delay in PML both in HIV+ and HIV- individuals. (Miskin, Ngo et al. 2016) Finally, this case report should alert clinicians that the CNS complications of HIV-1 and HIV-2 infection overlap, and highlights the need to consider PML in HIV-2 infected patients with progressive focal neurological deficits.

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MRI findings after symptoms onset

Figure 1. MRI findings after symptom onset

MRI of left facial colliculus PML lesion 6 weeks after symptom onset. (A) Axial fluid-attenuated inversion recovery (FLAIR) image shows a lesion in the left facial colliculus (arrow). (B) Axial post-contrast T1 weighted images demonstrates faint peripheral enhancement in the lesion and hazy enhancement in the right pons (arrow) (the latter was compatible with a capillary telangiectasia that was unchanged from a study done 7 years prior to his current presentation). Sagittal and coronal post-contrast T1 weighted images (C

and D) demonstrate faint peripheral enhancement in the lesion (arrows) of the left facial colliculus.

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Characteristics of Previously Reported Progressive Multifocal Leukoencephalopathy (PML) Cases in HIV-2-Infected Patients

Table 1

Case	Reference	Age at PML diagnosis,	Gender	Initial presentation	CD4 count (cells/ μ l), HIV-2 plasma viral load (copies/ml)	Initial MRI findings	PML diagnosis	Treatment	IRIS	Outcome
1	Duque, Matos et al. 2010	51	F	Left hemiparesis	9/20,600	Multiple lesions in the brain and cerebellum. Faint and irregular contrast enhancement	CSF JCV PCR +	cART	No	Death after 4 months
2	Bienaimé, Colson et al. 2006	60	M	Dysarthria, ataxia and gait dysfunction	83/250	Multiple lesions in the right cerebellum, pons inferior and middle peduncles	CSF JCV PCR + Typical histopathology / In situ hybridization +	cART	No	Death after 2 months
3	Descamps, Peytavin et al. 2015	43	M	MR	85/23,120	NR	NR	cART	NR	Death after 4 months
4	Stoner, Agostini et al. 1998	NR	NR	NR	NR	NR	Typical histopathology / In situ hybridization +	NR	NR	Death after 3 months
5	Sierra Morales et al. 2017	65	M	Facial weakness and dysphagia	311/361	One lesion in the left facial colliculus with associated contrast enhancement	CSF JCV PCR +	cART	Yes	Clinical improvement

PML, progressive multifocal leukoencephalopathy; VL, viral load; CSF, cerebrospinal fluid; JCV, JC virus; cART, combination antiretroviral therapy; IRIS, immune reconstitution inflammatory syndrome; NR, not reported.