

CASE REPORT

Posterior reversible encephalopathy syndrome in a patient with HIV/AIDS and immune reconstitution syndrome: a case study and literature review

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Abstract

The etiology of posterior reversible encephalopathy (PRES) is typically multifactorial. Patients with HIV are at risk for the development of this syndrome. We review 17 published cases of HIV and PRES and describe the second reported case of PRES in the setting of HIV and immune reconstitution syndrome (IRIS). IRIS has not yet been described as a risk factor for PRES.

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic syndrome characterized by altered mental status, seizures, headaches, cortical blindness and classic posterior cerebral edema on radiographic imaging. The mechanism of cellular injury is related to breakdown of the blood brain barrier resulting in vasogenic edema. Immunosuppressed patients are at increased risk of PRES [1–3]. HIV infection has been associated with PRES either via endothelial inflammation or immune activation [4]. There are 17 previously reported cases of HIV and PRES and only one other case of PRES and immune reconstitution syndrome (IRIS) has been described in the literature.

CASE PRESENTATION

A 39-year-old man with previously untreated HIV was admitted with 1 year of progressive weight loss, altered mentation and

recurrent thrush. On presentation, he was hemodynamically stable with significant cachexia, confusion and mild desaturations with ambulation. His CD4+ count was 9 cells/μl and HIV RNA level >1.5 million copies/ml. Extensive workup for co-infections was initially negative (including cryptococcal antigen, CSF PCR for HSV, EBV and JC virus). Computed tomography (CT) of the chest/abdomen/pelvis revealed diffuse lymphadenopathy and an initial MRI brain was unremarkable. The patient was started on fluconazole, prophylactic azithromycin and trimethoprim/sulfamethoxazole. Once medically stabilized, he initiated HAART therapy (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate), and was discharged with close outpatient monitoring.

The patient returned 10 days later with fever to 103 °F, night sweats, cough, headache, myalgias, diarrhea and abdominal pain. He was found to have axillary lymphadenopathy, tense ascites and renal failure (Cr 1.5 mg/dl, baseline 0.9 mg/dl). Initial blood and sputum cultures were positive for *Mycobacterium avium-intracellulare* (MAI). Subsequent biopsy of a large right

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axillary lymph node also revealed MAI. His acutely worsening condition was felt to be consistent with IRIS in the setting of disseminated MAI and the recent initiation of HAART therapy. He began anti-mycobacterial treatment with clarithromycin and ethambutol and high dose steroids (dexamethasone 4 mg BID) to control his IRIS. Due to renal failure, his HAART therapy was altered to include dolutegravir, abacavir and lamivudine.

Over the next 3 days he was noted to have persistent hypertension up to 180/90 mmHg and worsening renal function with a creatinine to 2.8 mg/dl. He developed severe headaches, confusion, fluctuating visual changes, a new left homonymous hemianopsia, and one witnessed seizure. MRI brain showed multifocal T2/FLAIR hyperintensities favoring the parietal and occipital lobes with evidence of parieto-occipital hemorrhage (Fig. 1). His blood pressure was medically controlled with

clonidine and amlodipine. His neurologic symptoms improved over 1 week, at which point steroids were switched to oral prednisone and slowly tapered. Repeat MRI after 8 days from the initial seizure showed marked improvement with some residual hemorrhage and diffusion restriction in the right parieto-occipital region. His neurologic symptoms and reversible MRI findings were consistent with PRES. CNS IRIS and posterior multifocal leukoencephalopathy (PML) were considered on the differential, however, the symmetric and posterior distribution, rapid improvement and negative JC virus made these diagnoses less likely. At 1 year he had near complete resolution of neurologic symptoms with a mild stable left homonymous hemianopsia.

DISCUSSION

PRES is a clinico-radiological entity characterized by headache, seizures, focal neurologic deficits and classic neuroimaging findings of bilateral subcortical parieto-occipital vasogenic edema that resolves or improves with management of underlying etiologies [1]. PRES has been described in patients with severe hypertension, renal failure, immunosuppression, organ transplantation, cytotoxic chemotherapies, eclampsia, sepsis, blood transfusions, hypercalcemia and high dose steroids [1, 5–8]. Despite the reportedly high prevalence among patients with autoimmune disorders and immunosuppression, only 17 other cases of HIV and PRES have been reported in the literature, one of which presented with concurrent IRIS. Given the relatively recent discovery of PRES and the clinical and radiographic similarities to PML, PRES is likely more common than currently reported among HIV patients [9].

Like most patients with PRES, our patient had a combination of associated conditions including an acute hypertensive episode, renal failure, immunosuppression, systemic infection and steroid use. Nearly all documented cases of HIV and PRES present with multiple potential risk factors (see Table 1) including hypertension (13/18), renal failure (9/18), systemic or

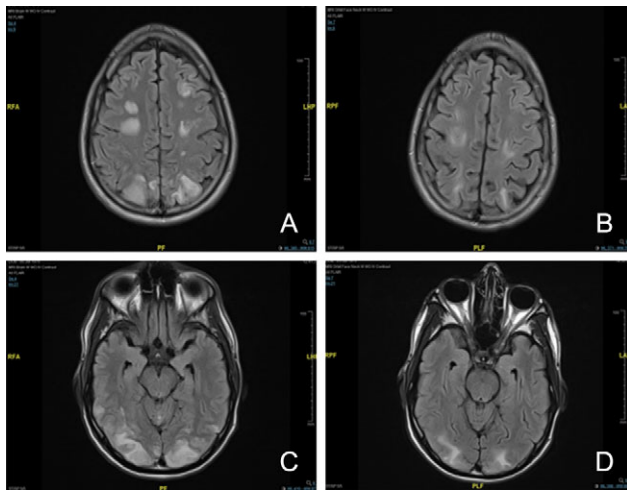


Figure 1: FLAIR MRI Brain showing bilateral parieto-occipital hyperintensities in the cortical and subcortical white matter (A, C) with significant improvement after 8 days (B and D).

Table 1: Comparison of 18 reported cases of HIV and PRES, including demographics, the presence of established risk factors and systemic disease if identified

Case	Age	Sex	CD4 (cells/ul)	On HAART	Acute HTN, max SBP	Renal failure	Hypercalcemia	Steroid admin.	Systemic disease/co-infection	Reference
1	40	M	<200	+	+220					Giner et al. [16]
2	40	M	284	+	+240	+				Ridolfo et al. [14]
3	50	F		+	+210					Ridolfo et al. [14]
4	28	F	28		+215	+				Chang et al. [18]
5	39	F	112		+152	+				Sasson et al. [19]
6	33	F	56		+186				Bd	Saeed et al. [20]
7	12	F	>200		+144		+			Frank et al. [21]
8	37	M	26		+183	+			TTP	Sylvester et al. [22]
9	54	M	173	+	+170			+	VZV	Sasson et al. [23]
10	26	F	2		+198	+	+		Hc	Stevenson and Taylor [24]
11	12	M	168		+	+			TTP	Kahn et al. [9]
12	48	M		+	+	+		+	TB, VZV	Kupper et al. [25]
13	30	F	<180	+		+			TB	Guerriero et al. [26]
14	32	F	290	+						Nightingale et al. [4]
15	56	F	438	+						Wilbanks and Hayat [27]
16	39	M		+			+		MAI	Choudary and Rose [28]
17	22	F	<75						MAI, IRIS	Hanna et al. [29]
18	39	M	9	+	+180	+		+	MAI, IRIS	Weiss, this case

Abbreviations: HTN, hypertension; SBP, systolic blood pressure (mmHg); Bd, blastomyces dermatididis; Hc, histoplasmosis capsulatum; TTP, thrombotic thrombocytopenic purpura; VZV, varicella zoster virus.

opportunistic infection (11/18), recent HAART therapy (3/18), chronic HAART therapy (6/18), steroid administration (3/18) and hypercalcemia (3/18). The 11/18 patients had documented CD4 counts <200 cells/ μ l. Of those patients with hypertensive episodes (SBP > 140 mmHg), median systolic blood pressure was 192 mmHg. Systemic diseases present included MAI (three cases), tuberculosis (two cases), thrombotic thrombocytopenic purpura (two cases) and varicella zoster virus (two cases). Two cases occurred in patients on long-term successful anti-retroviral therapy with unexplained hypertensive crises and two cases were documented in patients with HIV and no other risk factors.

The underlying pathophysiology of PRES is controversial. Three main mechanisms have been hypothesized including (i) hypertension induced hyperperfusion and vasogenic edema, (ii) cerebrovascular endothelial cytotoxicity, and more recently proposed (iii) immune mediated endothelial damage [4, 7]. The immune mediated pathogenesis suggests that pathological activation of T-cells leads to inflammatory cytokine production, endothelial damage and ultimately disruption of the blood brain barrier [7, 10, 11]. The relationship between HIV and PRES is not fully understood. The HIV virus alone may be a risk factor for PRES, as HIV precipitates cytokine mediated inflammatory pathways resulting in damage to cerebrovascular endothelial cells [4, 12, 13]. Anti-retroviral therapies, specifically protease inhibitors, have also been associated with hypertension and endothelial dysfunction directly or by way of metabolic derangements which may further predispose patients to the development of PRES [14–16].

In addition to one other documented case, our patient also had IRIS, a condition characterized by T-cell activation and paradoxical clinical deterioration after initiation of HAART therapy [17]. Though IRIS has not yet been described as a risk factor or etiology for the development of PRES, it shares the characteristic systemic aberrant T-cell activation seen in other predisposing conditions and supports an autoimmune pathogenesis.

HIV has been associated with PRES, a neurotoxic condition caused by damage to the blood brain barrier. IRIS may be an unrecognized risk factor via massive T-cell activation. Clinicians should consider PRES in patients with HIV and IRIS who develop acute neurologic symptoms. Favorable outcomes are reported with management of underlying etiologies.

CONFLICT OF INTEREST STATEMENT

Authors have no relevant financial or non-financial relationships or conflicts of interest to disclose.

FUNDING

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ETHICAL APPROVAL

None required.

CONSENT

The patient consented to be included in this case report. No PHI is included.

GUARANTOR

Dr Zoe Weiss.

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