

CASE REPORT



The worst is yet to come: probable sporadic Creutzfeldt–Jakob disease in a well-controlled HIV patient

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ABSTRACT

We describe a case of probable sporadic Creutzfeldt–Jakob disease in the setting of well-controlled HIV and discuss whether exist, in fact, HIV-related factors that may predispose to the development of prion disease. To the best of our knowledge, this is the third report of this association.

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Introduction

Creutzfeldt–Jakob disease (CJD) is a rare, fatal, rapidly progressive neurodegenerative human disorder occurring in sporadic, genetic, and acquired forms. Sporadic CJD (sCJD), by far the most common form, is typically characterized by a rapidly progressive clinical course and widespread brain deposition of abnormal prion protein (PrP^{TSE}) aggregates leading to spongiform change, gliosis, and neuronal loss [1].

We describe a case of this rare disease in the setting of well-controlled HIV and discuss whether exist, in fact, HIV-related factors that may predispose to the development of prion disease. To the best of our knowledge, this is the third report of this association [2,3]. Another case of CJD had been recently described in a patient with a recent diagnosis of AIDS [4].

Case report

A 52-years-old Caucasian male with well-controlled HIV came to the emergency department presenting progressive imbalance, motor and cognitive deterioration and hypersomnia. Before being referred, he was evaluated by a psychiatrist who prescribed neuroleptics. On admission, he was in a state of mutism and did not obey to commands, although there were no vital signs abnormalities, meningism or focal motor deficit. His motor examination showed global deep tendon hyperreflexia and increased tone in all extremities with intermittent myoclonus.

Recent CD4 count was 495 μL^{-1} and HIV-1 RNA was undetectable. Initial laboratory work-up was unremarkable. Serum cryptococcal antigen, Toxoplasma IgM, Cytomegalovirus IgM, Herpes I and II and fluorescent treponemal antibody-absorption test (FTA-ABS) for syphilis were negative. Routine CSF analysis was normal: total protein 30 mg/dL, glucose 59 mg/dL (serum glucose, 80 mg/dL), 5 red blood cells, and 3 mononucleated cells. Opening pressure was 160 mmH₂O. CSF polymerase chain reaction for herpes simplex virus, cytomegalovirus, tuberculosis, and JCV were negative, as well as VDRL, cryptococcal antigen and bacterial and fungal cultures.

Diffusion-weighted brain MRI showed cortical gyri-form restriction on both hemispheres and on both caudate nuclei (Figure 1). EEG showed 1 Hz triphasic periodic sharp wave complexes (PSWC) (Figure 2) and CSF 14–3–3 protein level was elevated (77,849 AU/mL; reference value: <20,000 AU/mL). The combination of rapidly progressive mental state and motor deterioration and typical CSF, radiographic, and electroencephalographic features pointed to probable CJD according to CDC's criteria[5]. The patient died after 2 months of hospitalization from respiratory sepsis.

Discussion

Many diagnostic hypotheses should be considered in the context of an HIV-patient presenting with cognitive decline, e.g. HIV-associated encephalopathy, central

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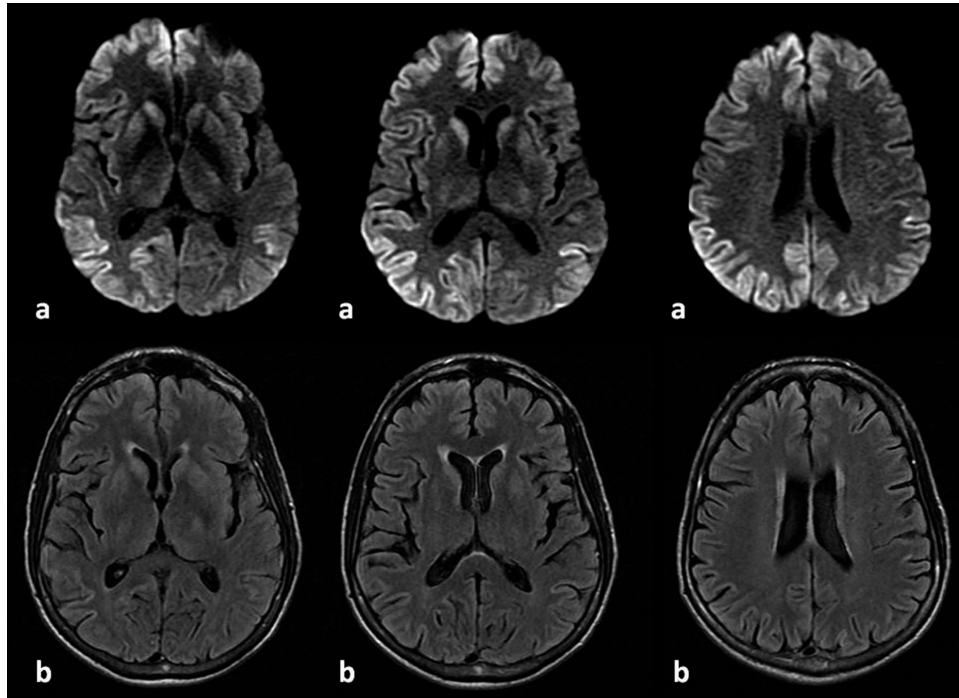


Figure 1. (a) Axial diffusion-weighted image (DWI) sequences show diffusion restriction of water molecules along the bilateral caudate and gyriiform cortical-restricted diffusion in the bilateral cerebral hemispheres. (b) Axial fluid-attenuated inversion-recovery (FLAIR) images sequences show discrete areas of hypersignal in bilaterally caudate nuclei, as well as in the cortical regions.



Figure 2. Electroencephalography (EEG) showing periodic sharp wave complexes (PSWC) every 1 s. There is also severe disorganization of the base rhythms, which are composed of irregular and diffuse slow activities.

nervous system opportunistic infections, and immune reconstitution syndrome. Although cognitive impairment can also be observed in patients with well-controlled HIV infection, rapidly progressive dementia is rare [4].

HIV-associated neurocognitive decline is characterized by subcortical dysfunction, attention, concentration and psychomotor impairment and mood disorder [6]. In this patient, rapid progression of the symptoms and the long period of well-controlled HIV infection made this diagnosis less likely. CNS opportunistic infections, on the other hand, were ruled out by neuro-image and CSF analysis.

Brain MRI also ruled out structural abnormalities such as tumour or stroke, but DWI and FLAIR sequences revealed bilateral diffusion restriction and hyperintensity in the caudate nuclei and cerebral cortex, the latter affected in a ribbon pattern (Figure 1). Cortical and basal ganglia involvement, with insula and cingulate cortices hyperintensity at DWI, in addition to involvement of the superior frontal gyri and cortical areas near the midline are the most common MRI pattern in sCJD [7].

Electroencephalography findings may provide additional supportive evidence for CJD. The most distinctive pattern is characterized by periodic sharp wave complexes that occur in the middle and late stages of the disease [8]. Our patient exhibited these classical EEG findings along with elevated CSF 14-3-3 protein which, although not specific, reinforces the clinical hypothesis of sCJD [5,9,10].

A well-controlled HIV-patient that developed sCJD was the subject of a recent report by Babi and colleagues [2]. The authors theorized that HIV infection could have predisposed to prion disease, based on the fact that both pathogens, despite being essentially different, depend on interfering with cholesterol cell efflux pathway for replication and infection[11]. HIV exploits the regulation of ATP-binding cassette transporter type 1 (ABCA1) functionality by displacing it from neuronal membrane lipid rafts to the intracellular compartments, and this effect on ABCA1 and lipid rafts was also observed in a prionic disease animal model [11,12].

Conclusion

As far as we know, this is the third report of sCJD affecting a chronic well-controlled HIV patient. Although shared cellular mechanisms had been demonstrated [2,12], no

causal link between HIV and spontaneous CJD has yet been firmly established.


Author contributions

Euripedes Gomes de Carvalho Neto and Matheus Ferreira Gomes – cared for the patient, acquisition of data, and literature review; Marina de Oliveira, Maryuris Isabel Niño Guete, Iuri Pereira Santos, and Mateus Damiani Monteiro – cared for the patient and literature review; and Fernando Gustavo Stelzer, Fernando Kowacs, and Liselotte Menke Barea – critical revision of manuscript for intellectual content and study supervision.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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References

- [1] Zerr I, Piero P. Chapter 9 sporadic Creutzfeldt–Jakob disease. *Handbook of clinical neurology*, Vol. 153 (3rd series). In: Pocchiari M, Manson J, editors. *Human prion diseases*. 2018;153:155–174. doi:10.1016/B978-0-444-63945-5.00009-X
- [2] Babi MA, Kraft BD, Sengupta S, et al. Related or not? Development of spontaneous Creutzfeldt–Jakob disease in a patient with chronic, well-controlled HIV: a case report and review of the literature. *SAGE Open Med Case Rep*. 2016;4:1–6.
- [3] van de Ven NS, Vera J, Jones JR, et al. Sporadic CJD in association with HIV. *J Neurol*. 2019 Jan;266(1):253–257.
- [4] Eimer J, Vesterbacka J, Savitcheva I, et al. Nonopportunistic infection leading to rapidly progressive dementia in a patient with HIV/AIDS. A case report. *Medicine (Baltimore)*. 2018 Mar;97(12):e0162.
- [5] Zerr I, Kallenberg K, Summers DM, et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt–Jakob disease. *Brain*. 2009;132:2659–2668.
- [6] Shapshak P, Kanguane P, Fujimura RK, et al. Editorial neuroAIDS review. *AIDS*. 2011;25:123–141.
- [7] Tschampa HJ, Kallenberg K, Kretzschmar HA, et al. Pattern of cortical changes in sporadic

- Creutzfeldt-Jakob disease. *Am J Neuroradiol.* 2007;28(6):1114–1118.
- [8] Wieser HG, Schindler K, Zumsteg D. EEG in Creutzfeldt-Jakob disease. *Clin Neurophysiol.* 2006;117(5):935–951.
- [9] Zerr I, Bodemer M, Gefeller O, et al. Detection of 14-3-3 protein in the cerebrospinal fluid supports the diagnosis of Creutzfeldt-Jakob disease. *Ann Neurol.* 1998;43(1):32–40.
- [10] Muayqil T, Gronseth G, Camicioli R. Evidence-based guideline: diagnostic accuracy of CSF 14-3-3 protein in sporadic Creutzfeldt-Jakob disease: report of the guideline development subcommittee of the American Academy of Neurology. *Neurology.* 2012 Oct 2;79(14):1499–1506.
- [11] Cui HL, Guo B, Scicluna B, et al. Prion infection impairs cholesterol metabolism in neuronal cells. *J Biol Chem.* 2014;289(2):789–802.
- [12] Cui HL, Grant A, Mukhamedova N, et al. HIV-1 Nef mobilizes lipid rafts in macrophages through a pathway that competes with ABCA1-dependent cholesterol efflux. *J Lipid Res.* 2012;53:696–708.