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Case report

Hemiballistic movements in a newly HIV patient

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ABSTRACT

Infections of central nervous system (CNS) include a broad group of conditions and pose a particular challenge to physicians, especially in immunocompromised individuals.

This case refers to a 26-year-old male patient with a history of smoked hashish and drug abuse admitted to the infectious disease department with hemiballismus of left hemibody and a positive HIV serologic test. A magnetic resonance imaging (MRI) study showed lesions at lower left and right cerebellar hemisphere, one of them thalamus – mesencephalic suggesting an opportunistic infection or an HIV associated encephalopathy. Lumbar puncture, brain biopsy and successive neuroimaging were not conclusive for one disease and despite the use of directed therapy for cerebral toxoplasmosis, meningeal tuberculosis, anti-retrovirals and sedative medication, after over 6 weeks of hospitalization pallidotomy was performed. After 5 months of oral and surgical treatment the patient showed clinical, immunological and radiological recovery.

Introduction

Neurologic disease is the clinical presentation of HIV infection in about 20% of persons, while 60% will have neurologic dysfunction during the course of their illness [1].

Since the combination of antiretroviral therapy (ART), the neurologic complications associated with HIV have been progressively shifted from opportunistic infections, related with severe immunocompromised status, to those related to treatment.

Despite the use of effective ART, the neurologic disorders associated with HIV infection (focal or disseminated lesions) are still a serious burden worldwide. Opportunistic infections of the CNS account for the greatest proportion of neurologic disease burden in low income countries and four main groups of pathogens are involved: fungi *(Cryptococcus neoformans* meningitis, as an example), parasite (*Toxoplasma gondii* encephalitis), bacteria (*M. tuberculosis* meningitis, for example) and viruses such as those causing progressive multifocal leukoencephalopathy. Other neurologic complications of HIV not associated with opportunistic infections including malignancies, encephalopathy and dementia. The laboratory and neuroimages resources are available, in middle and high income countries, however the diagnosis and management of these cases, sometimes involving empirical and broad therapeutic choices is challenging. We describe a case of hemiballismus as a first manifestation of acquired immunodeficiency syndrome, refractory to medical therapy.

Case report

A 26-year-old man with a history of long standing smoked hashish, inhaled ketamine and lysergic acid diethylamide use was admitted to the emergency department with 5-days of uncontrolled, large amplitude movements of left hemibody and frontotemporal headache and photophobia in the last 12 days. On arrival, Glasgow coma scale was 8, he was afebrile; arterial pressure of 84/55 mmHg, with a normal capillary blood glucose level. Chest auscultation revealed rhonchi bilaterally. The patient had whitish lesions on the oral mucosa and on neurological examination he avoided eye contact, he had isocoric and symmetric pupils, without abnormal eye movement; fundoscopy revealed no papilledema, the speech was disorganized and he had ballistic movements of left hemibody, more severe in the upper limb.

Serum analysis showed hemoglobin 9.2 g/dL, normal white blood cell count, C-reactive protein and renal function, Lactic acid dehydrogenase was 798 U/L. The electroencephalogram was not conclusive due to the lack of conditions to perform a correct test.

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The HIV serology and confirmatory test were positive and other serologic exams showed: HBV immune, HCV negative, Toxoplasma IgG positive, EBV IgG positive, IgM negative, CMV and HSV 1/2 IgG/IgM negative and negative tests for syphilis. The first cranial CT (computed tomography) revealed a: slight hypodensity at lower left cerebellar hemisphere, with small dots among it – calcifications/petechial hemorrhages. Based on these results, anti-toxoplasmosis therapy (pyrimethamine 75 mg/day plus clindamycin 600 mg every 6 h and folinic acid 25 mg/day) and high doses of antiepileptics and neuroleptics were initiated. Twelve hours later he was transferred to the intensive care unit.

Successive brain MRI showed: lesions at lower left and right cerebellar hemisphere with adjacent parenchymal changes, one of them thalamus-mesencephalic with extension to the internal capsule, another one frontobasal, suggesting toxoplasmosis [Figs. 1 and 2].

A lumbar puncture was performed and cerebrospinal fluid (CSF) analysis showed: 5000 WBCs/μL (3150 neutrophils/μL, 1100 lymphocytes/μL), protein 232 mg/dL, Glucose 28 mg/dL, ADA 12.0 IU, HIV-RNA 1188 copies/mL; India ink test was negative; *Cryptococcus* antigen, V.D.R.L/FTA-abs, CSF culture and polymerase chain reaction (PCR) for *Toxoplasma*, HSV, CMV, VZV, JC virus, EBV, Enterovirus and *Mycobacterium tuberculosis* were all negative.

Serum HIV viral load was 1337147 copies/mL, cd4 40/mm3 and ART: tenofovir/emtricitabine 245/200 mg plus raltegravir 400 mg was initiated.

Despite anti-toxoplasmosis, ART, antimicrobials and antiepileptics, in the 24th day of hospitalization involuntary movements remained and a stereotaxic cerebellar biopsy was performed [Fig. 3]. The histologic result raised the hypothesis of Whipple's disease; however the upper endoscopy didn't show erythema and duodenum biopsy did not reveal PAS material. After one month of admission, another CSF was performed and the PCR for *Tropheryma whipplei* was negative and positive for *M. tuberculosis* with an undetermined Quantiferon test. Culture of bronchial aspirates didn't isolate *M. tuberculosis*, but anti-tuberculosis treatment with isoniazid 300 mg/day, rifampin 600 mg/day, pyrazinamide 1500 mg/day and ethambutol 1200 mg/day was started. The patient kept uncontrolled and refractory movements despite medical treatment, therefore stereotactic right pallidotomies were performed in the day 46 and 69 of hospitalization.

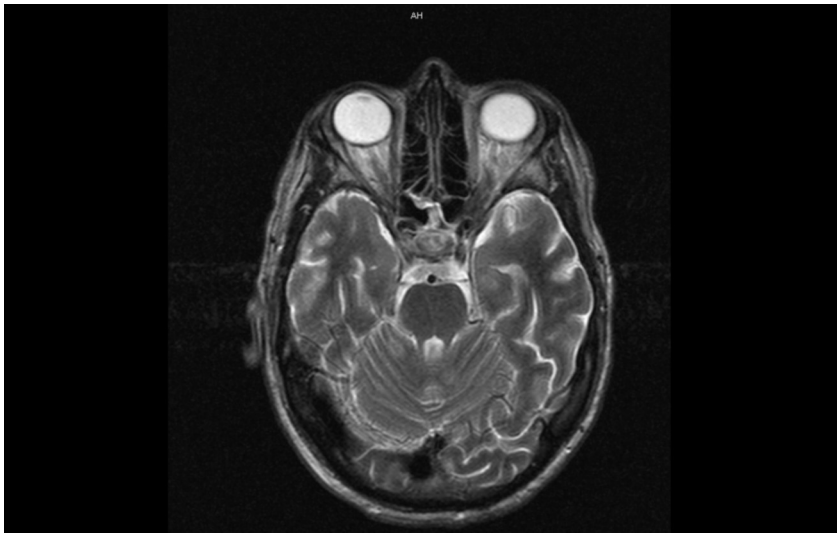

Fig. 1. Brain MRI March 2014(a).

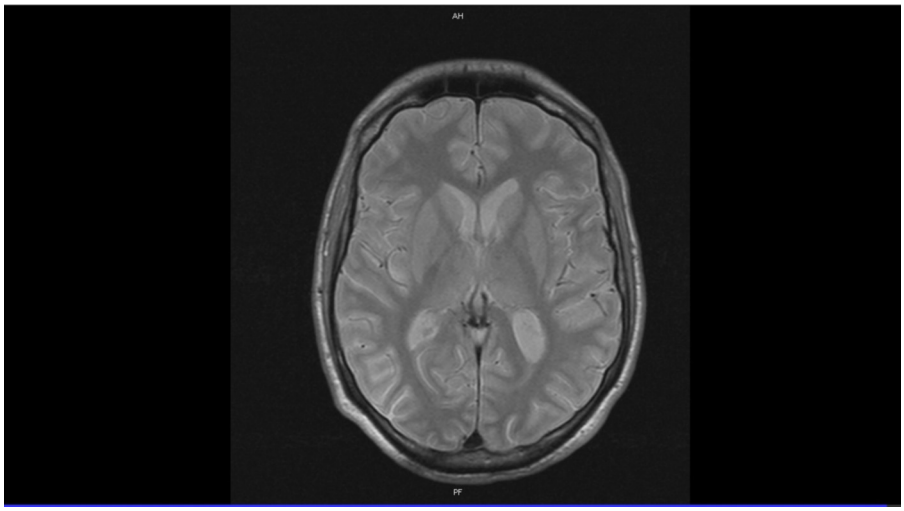

Fig. 2. Brain MRI March 2014(b).

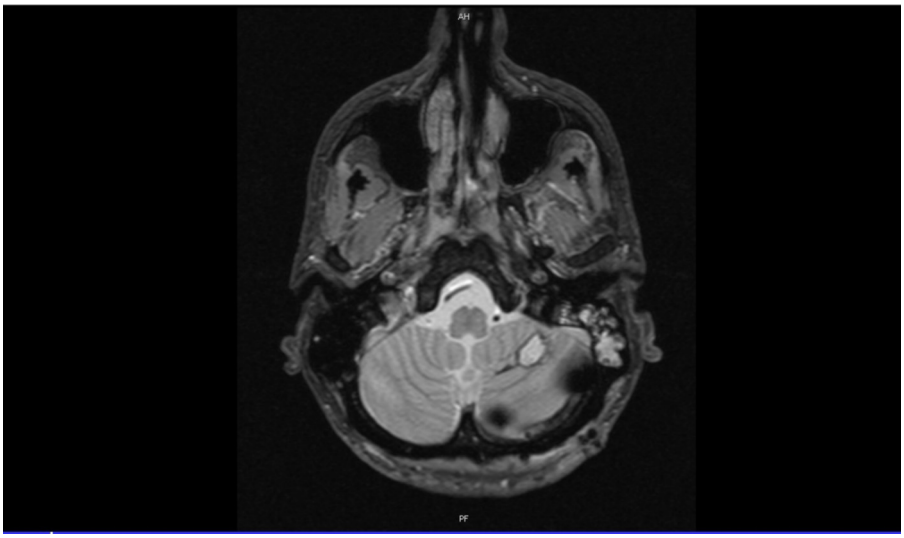

Fig. 3. Brain MRI after stereotaxic biopsy.

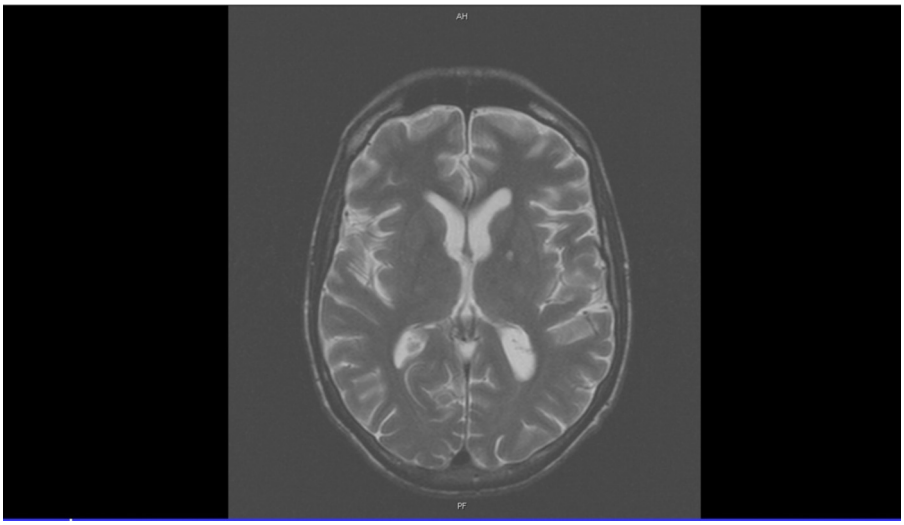

Fig. 4. Brain MRI July 2014.

During almost 12 weeks at intensive care unit, anti-epileptics were titrated, sedation reduced, while ballistic movements were progressively disappearing. The patient was referred for immunodeficiency consultation after 5 months of hospitalization and has been under anti retroviral therapy, after 12 months of anti-tuberculosis and almost one year of neurotoxoplasmosis maintenance treatment. In the last control he had cd4 count of 436/mm3 and undetectable viral load with a decrease in the left globus pallidus lesion and a right globus pallidus scar [Fig. 4], with no more choreiform movements, just a thin tremor on left hand.

Discussion

Hemiballistic movements are caused by a vascular lesion in the subthalamic nucleus in elderly people but more often by infections, neoplastic or immunologic disorders in younger patients [2]. In HIV patients who are unaware of their HIV status the first presentation can be a CNS opportunistic infection. The major disorders for those with less than cd4 200/mm3 are [3]: toxoplasmic or CMV encephalitis, cryptococcal meningitis, primary CNS lymphoma whereas tuberculous meningitis and PML are more frequently seen in patients with moderate immunosuppression.

Toxoplasmic encephalitis was considered here because of the clinical presentation, neuroimaging features, *T. gondii* IgG positive, despite a negative PCR in CSF. Some authors report 100% specificity but only 50% sensitivity [4] on *T. gondii* DNA (CSF) [5]. The diagnosis confirmation is still sought through clinical and radiological response after 2–4 weeks of specific therapy [6].

Another leading cause is the central nervous system tuberculosis, which can develop after mycobacteria's dissemination to the subarachnoid space or ventricles, or after a subependymal tuberculoma ("Rich focus") rupture into the subarachnoid space.

The hypothesis of tuberculosis infection was based on epidemiological and clinical criteria and cerebrospinal fluid analysis; neuroimaging findings of tuberculosis as: enhancing lesion, tuberculoma, abcess were not found but it could not excluded tuberculosis. Another challenge in the diagnosis is the wide variation in the sensitivity of CSF culture and PCR for *M. tuberculosis* [7], with significant discrepancies: 65–83% sensitivity between different type of measuring methods [8].

In HIV encephalopathy a wide range of neuroimaging features is present: diffuse cortical atrophy, ventricular enlargement or focal white spots in the white matter, as in this case. The HIV encephalopathy can present from mild to severe dysfunction in a newly HIV patient, with a nadir CD4 count very low and non specific CSF abnormalities. Nowadays, ART is the cornerstone of treatment for HIV-related encephalopathy; it induces remission and decreases the incidence of AIDS dementia complex.

Laboratory diagnosis of viral infections of the central nervous system by using a multiplex PCR screening assay was performed and enterovirus, EBV, HSV (1,2 and 6), CMV, VZV and JC virus were all negative, although there are some points to be considered. PCR can be performed rapidly and inexpensively and has become an integral component in the diagnosis of the CNS infections. Almost 90% of all of viral meningitis are caused by enteroviruses, followed by HSV-2 and VZV, EBV and HSV-1 [9]. Immunosupressed patients are susceptible to other viral infections, like Herpesvirus-6, JC virus or Varicela-zoster infections. The sensitivity of CSF PCR varies with different viruses; it can range from 75% for JCV virus to more than 94% for enterovirus, HSV1-2 or HHV-6; and can be influenced by the timing of specimen collection in relation to onset of illness [10,11]; usually specificity is higher than 98%.

PCR testing on CSF specimens may provide better diagnostic yield, however it is important to remember that the presence of viral nucleic acid in CSF does not exclude another primary etiology that could have triggered a secondary latent viral reactivation; on the other hand a negative PCR does not rule out CSF infection. In cases like HHV-6 encephalitis the diagnosis can be more challenging since HHV-6 is integrated into host chromosomes and it viral DNA will be present in CSF even though there is no viral replication [12].

Hemiballism is seen as a movement disorder in HIV patients [13]; usually one side of the body is compromised and the clinical onset is acute or subacute. In the majority of cases there are multiple lesions affecting the contralateral subthalamic nucleus, globus pallidus, or the internal capsule [14]. The opportunistic infections, particularly toxoplasmosis, are the main cause of choreiform movements, but other causes can be HIV encephalitis, viral encephalitis, PML or drug toxicicty [15]. The management of these cases involves treatment of opportunistic infections, symptomatic treatment and ART.

In the majority of cases hemiballismus is self-limiting or can be controlled with orally medications, therefore surgery as ventrolateral thalamotomy and posteroventral pallidotomy is reserved for intractable cases [16,17]. There are just a few series about the immediate and medium term success of this technique in patients with Parkinson's disease [18]. Most of them agree that the daily time spent with dyskinesias was significantly reduced and remained decreased throughout the follow up period (up to 2 years), although the improvement of postural stability and gait only lasted for 6 months [19]. The pallidotomy has not been described in the majority of case reports of hemiballismus in HIV patients [20], but it can be considered when the movements persist despite proper medication.

Conclusion

Brain lesions in HIV infected patients usually lead to an extensive list of differential diagnosis. In life saving situations, empirical therapy will determine patient evolution, despit its side effects. The great challenge in this patient after controlling the symptoms was deciding which treatment could be removed and which was the one responsible for the good outcome.

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