

Acute Intermittent Porphyria and HIV

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Case Report

HIV infection and porphyrias are described together in the same patient. In the literature reviewed, fewer than a hundred cases of porphyria cutanea tarda (PCT) in HIV + patients are described. The HIV population is considered a risk group for developing PCT because in the pathogenesis of this disease, viral infections such as HCV, HBV have been involved. However, the coexistence of acute intermittent porphyria (AIP)-HIV is a rare event, only 5 cases have been described. We report the case of a young woman, recently diagnosed with HIV infection and in whom, after the beginning of several lines of antiretroviral therapy (ART), a number of symptoms were triggered that finally led to the diagnosis of acute intermittent porphyria.

The porphyrias are a group of metabolic diseases caused by enzymatic defects in the synthesis pathway of porphyrins, whose final product is the heme group. This group is part of several heme proteins such as hemoglobin or the cytochrome P450 superfamily. The deficient enzyme in the acute intermittent porphyria (AIP) is the uroporphyrinogen I synthetase, with more than 342 mutations identified in the gene that encodes it following a pattern of autosomal dominant inheritance [1-3].

The HIV (Human Immunodeficiency Virus) population is considered at risk to develop a porphyria because in the pathogenesis of this disease, viral infections such as HIV or HCV (hepatitis C virus) itself have been implicated [4]. Moreover, many antiretroviral drugs can act as inducers of cytochrome P450, and theoretically trigger seizures [5]. A 36 year old woman without risk behaviors or relevant family history. Conization of the cervix was performed in 1998 by CIN II-III (Cervical intraepithelial neoplasia). In 2002 she was diagnosed with lymph node tuberculosis and HIV + (lymphocytes CD4: 277 elements/mm³ HIV VL (viral load): 304000 copies/ml) HCV and HBV (hepatitis B virus) negative. Treatment with zidovudine+lamivudine+abacavir+tenofovir DF (Disoproxil Fumarate) coformulated was initiated. In 2006 (VL HIV<50 copies/ml and CD4:744 elements/mm³) consulted with abdominal pain and vomiting that was only controlled with opiates. Additional tests were normal [analytical, fibrogastroscopy, abdominal CT (Computed Tomography) and colonoscopy]. The pain disappeared coinciding with menstruation, and this was repeated monthly. Months later, confusional features and tonic-clonic seizure activity was present. CSF (Cerebrospinal fluid) examination was normal as well as a cranial CT. Diagnosed with depression and somatoform disorder, corresponding treatment was begun. Days later brought a new

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episode of acute delirium, with progressive loss of strength in upper and lower extremities, paresthesias and abdominal pain. Examination showed widespread loss of strength, predominantly distal, severe muscle atrophy and inability to walk. The diagnosis was opiate withdrawal. Antiretrovirals were discontinued for 6 weeks. Upon resumption, the CD4 were 417 elements/mm³, and VL 100,000 HIV-RNA copies/ml. She was treated with lopinavir/ritonavir and tenofovir DF. She was diagnosed with generalized anxiety disorder. The patient developed amenorrhea. A year later with rehabilitation treatment she began to walk around although there was the syndrome of drooping feet and hands. After 18 months and the reappearance of menstruation, progressive loss of strength in all four extremities again developed, with paresthesias and dysesthesias, and the reappearance of abdominal pain. The electromyogram showed sensorimotor polyneuropathy markedly of movement, with axonal character of symmetric distribution and severe axonal loss in distal and proximal areas of the 4 limbs without evidence of denervation in bulbar and thoracic areas. Severe autonomic involvement (sympathetic/parasympathetic). While interned there was also hypertension, acute urinary retention and lability. Finally (almost 2 years after onset of symptoms and after passing through five hospitals), a change was accidentally observed in the color of the urine when sunlight shone upon it, which led to the suspicion, later confirmed, of the existence of AIP. Treatment was initiated with Hemin leading to the improvement of all symptoms. A family

genetic study was carried out, showing that the mother and sister had AIP data without treatment. Since then the patient continues with physical therapy and the periodic administration of hemin. In 2007, as a result of dyslipidemia, lopinavir/ritonavir was changed for fosamprenavir/ritonavir. A few months later, there was a new crisis so it was decided to change fosamprenavir/ritonavir for unboosted atazanavir that was poorly tolerated with the onset of jaundice and mild renal failure. As a result, monotherapy darunavir/ritonavir was decided upon, but after 24 hours, a new seizure developed and it was decided to withdraw the drug. Since then the treatment has been with raltegravir and tenofovir DF+emtricitabine without further complications (CD4:1010 elements/mm³ and VL HIV-RNA<20 copies/ml) to the present (September 2015).

About a hundred cases are described in literature of porphyria cutanea tarda (PCT) in HIV+ patients [6]. However, the coexistence of AIP and HIV is rare and found in only 4 cases of those reviewed [7-10]. Apart from the unusual nature of the occurrence, the

proof is in the diagnostic delay that was probably the result of the patient receiving antiretrovirals which acted as triggers of the crisis. The review consulted classified abacavir, didanosine, lamivudine, tenofovir DF and zalcitabine as safe in patients with AIP, while the use of nevirapine, amprenavir, indinavir, nelfinavir or ritonavir (full dose) is not recommended. Others such as efavirenz, saquinavir, stavudine, zidovudine, emtricitabine, lopinavir and raltegravir should be used with caution as there are no conclusive data about them [6,7] and in the case of fosamprenavir, atazanavir and darunavir there is no information other than that given in the current case. The case of darunavir/ritonavir is of particular importance if confirmed, given its wide use today, and it is worth being taken into account for future patients diagnosed with both diseases, especially if there are other therapeutic options [11,12].

We believe that in our patient the HIV infection probably exposed the genetic defect and some of the antiretrovirals received could have triggered the crisis.

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