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Unusual presentation of more common disease/injury

Acute encephalitis as initial presentation of primary HIV infection

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Summary

Acute encephalitis is a life-threatening condition. A wide variety of infectious agents are implicated and in many patients no cause is found. HIV acute seroconversion illness can rarely present as acute encephalitis. Although most experts agree in starting antiretroviral treatment in severe acute HIV infection, the evidence of the benefits are still lacking. The authors report a case of severe acute encephalitis as a primary presentation of HIV infection in which introduction of highly active antiretroviral treatment resulted in clinical recovery. This case highlights the need to consider HIV infection in the differential diagnosis of treatable viral encephalitis.

BACKGROUND

Early HIV invasion of the central nervous system is recognised. Neurological manifestations can occur in up to 17% of cases of acute HIV infection (AHI), and are associated with more aggressive evolution of the disease.[1 2] Among the neurological complications of AHI, acute encephalitis is one of the most severe, and the affected are at greater risk of death.[3 4] Highly active antiretroviral treatment (HAART) can potentially change favourably the clinical evolution in severe AHI.[5]

This case highlights the importance of considering HIV infection in the differential diagnosis of acute encephalitis and also the possible role of HAART in changing the prognosis of this severe complication.

CASE PRESENTATION

A 51-year-old previously healthy housewife was admitted to the emergency department with a 1 week history of fever, headache and fluctuating disorientation. She had been a habitual heavy drinker (more than 100 mg/day). There was no recent history of travel. On admission she was confused, disorientated, but able to follow simple commands. Neurological examination was otherwise unremarkable, with normal cranial nerves, normal power and sensation and flexor plantar response. Her vital signs were stable and the general examination did not disclose any clinical stigmata of immunosuppression. The complementary exams were negative except for peripheral blood thrombocytopenia (table 1). A lumbar puncture showed lymphocytic cerebrospinal fluid (234 lymphocytes cells/mm^3), increased protein (137 mg/dl) with normal glucose (61 mg/dl).

She was admitted to the infectious disease ward with a presumptive diagnosis of herpes simplex virus (HSV) encephalitis and commenced intravenous acyclovir. Repeated HIV ELISA was indeterminate but HIV western

Table 1 Investigation panel

Admission	
Haematology	N: blood count except for thrombocytopaenia 35 000 cells/mm^3; N: blood times
Biochemistry	N: renal function, hepatic function, pH
HIV ½	Indeterminate ELISA, negative Western Blot
Urine (drugs of abuse)	Negative
CSF	↑lymphocytes (234 cells), ↑protein (137 mg/dl), N glucose (61 mg/dl)
Chest x-ray	Normal
Cranial tomography of the brain	Normal
1st/2nd Week	
Brain MRI	Normal
EEG	Generalised diffuse slowing activity
Microbiology (blood/CSF)	Toxoplama, Koch bacillus, Borrelia, Mycoplasma, Adenoviruses, CMV, EBV, HSV, VRDL, HBV, HCV, VRDL/RPR, Enterovirus, JC
HIV ½	Indeterminate ELISA, negative Western Blot
3rd Week	
HIV ½	Positive ELISA and Western Blot
Haematology	N: blood count except for thrombocytopaenia 64 000 cells/mm^3

CMV, cytomegalovirus; CSF, cerebrospinal fluid; EBV, Epstein–Barr virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HSV, herpes simplex virus; JC, John Cunningham; N, normal, RPR, rapid plasma reagin; VDRL, venereal disease research laboratory test; ↑, increased.

blot was negative (table 1). Her clinical condition worsened in the following week, with progressive deterioration of consciousness (Glasgow Coma Scale of 7), *generalised asymmetric hypertonia*, and bilateral *Babinski's sign*. The general examination revealed oral candidiasis. Extensive study for HSV and other common and possible infectious agents was negative (table 1).

Brain MRI was unremarkable, although with moderate motion artifacts. The EEG showed generalised diffuse slowing activity consistent with a diffuse cerebral abnormality.

The indeterminate HIV test, the absence of an identified infectious agent and also the appearance of oral candidiasis, led to consideration of encephalitis related to AHI. The result of p24 antigenaemia, a marker of viral replication was not available; nor was testing of HIV in the cerebrospinal fluid. She started a scheme of antiretroviral drugs with good central nervous penetration: zidovudine (300 mg twice *a day)*, lamivudine (150 mg *twice a day)* and lopinavir/ritonavir (400/100 mg twice a day).

Over the following 2 weeks, she experienced a continuous progressive improvement in neurological and cognitive function and was discharged four weeks after the initial admission, with normal cognitive function, and capable of autonomous ambulation, although with frequent episodes of orthostatic hypotension.

Seroconversion to both HIV 1 and 2 occurred in third week of hospitalization (ELISA, Western Blot). The viral load was 6645 cells/mm^3, CD4+ lymphocyte count 537 cells/mm^3 and CD8+ lymphocyte 1113 cells/mm^3. The platelet count increased to 64000 cells/mm^3.

DISCUSSION

HIV invasion of the central nervous system occurs early, during seroconversion or 'window-phase' when the antibody *tests* are still negative.[6 7] The non-specific signs and symptoms of AHI are often not recognised.[8 9]

Contrary to the majority of clinical manifestations of HIV acute seroconversion illness, acute encephalitis can be a life-threatening condition.[3 4] Although the clinical relevance of HAART in AHI remains uncertain, it is accepted that at least patients with severe symptoms due to AHI may benefit from HAART.[5 10] Suspicious of acute HIV encephalitis offers an opportunity to discuss the opportunity of introducing HAART to minimise the risk of clinical deterioration.

It can take up to 6 months to develop *detectable* HIV antibodies, implying a long period with a false-negative test.[11] More sophisticated methods of detection of HIV in early phases, such as p24 antigenaemia, are not immediately available in most health facilities. In such a situation, the decision to start HAART when there is a suspicious of AHI solely depends on the clinical impression and on the exclusion of other condition that might explain the clinical findings. Acyclovir treatment is mandatory until laboratorial exclusion of HSV infection, which is the most common cause of acute encephalitis. Some findings in this patient raised a strong clinical suspicious of acute encephalitis as a manifestation of AHI: the presence of thrombocytopenia, which is a common finding in AHI; the development of oral candidiasis, a sign of immunosuppression in adults[10–12] and the indeterminate HIV ELISA test. Knowing that acute encephalitis may be fatal, the presence of a clinically aggressive evolution justified initiation of HAART, which was associated with progressive clinical improvement.

This case illustrates the need to include AHI in the differential diagnosis of acute neurological disorders, particularly acute encephalitis, and also the possible role of HAART in changing favourably the clinical evolution of this complication.

Learning points

- The possibility of misdiagnosis of acute encephalitis as a primary manifestation of HIV infection is strong.
- Acute encephalitis in the HIV seroconversion phase is a severe and potential lethal complication.
- Antiretroviral treatment with good central nervous penetration has the potential to change favourably the course of acute encephalitis in HIV infection.

Competing interests None.

Patient consent Obtained.

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