 HSV-1 Encephalitis Complicated by Cerebral Hemorrhage in an HIV-Positive Person

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Herpes simplex virus type 1 (HSV-1) is the most common cause of sporadic encephalitis in immunocompetent adults, it is an unusual cause of encephalitis in patients with HIV/AIDS. We report the case of a 56-year-old man with recently diagnosed HIV infection who presented with subacute mental status changes, fever, and temporal lobe abnormalities evident on brain imaging. Results of a polymerase chain reaction assay of the cerebrospinal fluid were positive for HSV-1. His course was complicated by 2 episodes of cerebral hemorrhage. He ultimately improved after surgical decompression, treatment with acyclovir, and a switch from a protease inhibitor–based antiretroviral regimen to one including an integrase inhibitor.


Key words: HIV/AIDS • Herpes simplex virus • Encephalitis • Cerebral hemorrhage • Acyclovir

Although herpes simplex virus type 1 (HSV-1) is the most common cause of sporadic encephalitis in immunocompetent adults, it is an unusual cause of encephalitis in patients with HIV/AIDS. We report the case of a 56-year-old man with recently diagnosed HIV infection who presented with subacute mental status changes, fever, and temporal lobe abnormalities evident on brain imaging. Results of a polymerase chain reaction assay of the cerebrospinal fluid were positive for HSV-1. His course was complicated by 2 episodes of cerebral hemorrhage. He ultimately improved after surgical decompression, treatment with acyclovir, and a switch from a protease inhibitor–based antiretroviral regimen to one including an integrase inhibitor.

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adverse effects associated with efavirenz could potentially complicate an assessment of the patient’s neurological status, the antiretroviral regimen was switched to tenofovir, emtricitabine, and lopinavir/ritonavir.

On hospital day 6, the patient became increasingly somnolent, and a head CT scan showed an acute hemorrhage in the left temporal lobe and basal ganglia (Figure 2). Five days later, he had another precipitous mental decline and was found to have an enlarging bleed in the same area. No deficiencies were found in his platelet count, prothrombin time/ partial thromboplastin time, or other coagulation studies (factor VII, VIII, XI, vWF studies; ristocetin cofactor test; and clot lysis test). The patient was taken to the operating room for urgent decompression and clot removal. Because of reports linking the use of protease inhibitors with increased bleeding risk in patients with hemophilia, the integrase inhibitor raltegravir was substituted for lopinavir/ritonavir. After receiving a 28-day course of intravenous acyclovir, the patient was discharged on a regimen of oral valacyclovir.

Over the next several months, the patient’s mental status gradually improved, although impairment in word finding, reading comprehension, and memory persisted. At his most recent outpatient visit, 3 months after admission, his CD4+ cell count was 406/µL and his HIV RNA level was undetectable.

DISCUSSION

T-cell–mediated immunity is essential for the control of HSV; thus, immunosuppressed patients, including those undergoing organ transplant and chemotherapy, are at increased risk for severe HSV infections. While HIV-infected persons are also at increased risk for severe mucosal HSV reactivation, HSV encephalitis is surprisingly rare in this population. In several large studies of HIV-positive patients who underwent neurological evaluation, the incidence of HSV encephalitis ranged from 0% to 3%. On the other hand, cytomegalovirus infection and other human herpesvirus infections appear to be much more common.

Even though HSV encephalitis is not considered an AIDS-defining illness, the vast majority of case reports in the literature involve patients who have CD4+ cell counts below 350/µL. In the HIV-positive population, the relative rarity of HSV encephalitis and the increased frequency of mucocutaneous disease are puzzling and deserve further investigation.

Unlike the acute meningoencephalitis seen in those with intact immune systems, HSV encephalitis in persons with HIV/AIDS can present in an atypical, subacute fashion with several days to weeks of confusion, depressive symptoms, and slowed mentation. Our patient presented with a 2-week history of memory impairment, possibly reflecting an attenuated immunological response to HSV infection as a consequence of his underlying HIV infection. In addition, stroke-like symptoms and seizures have also been reported to be frequently encountered.

This patient’s clinical course was complicated further by 2 episodes of intracranial hemorrhage. A survey of the literature found that while radiologically apparent intracranial hemorrhage is a rare sequela of HSV encephalitis, it has been well described that HSV causes a necrotizing encephalitis with evidence of hemorrhage seen in autopsy studies.

There have been several reports linking protease inhibitor use to an increased bleeding risk in hemophiliacs. (None of the reports have demonstrated consistent laboratory abnormalities of hemostasis, and the mechanism behind the association is still unclear.) Furthermore, the prescribing information for the protease inhibitor tipranavir cites a possible association between its use and intracranial hemorrhage, which prompted a black box warning from the FDA.

These issues led us to switch this patient’s ritonavir-boosted protease inhibitor to an integrase inhibitor, because we felt that a slight increase in the risk of bleeding might have converted a necrotizing encephalitis into...
a clinically important bleed.

There is no consensus on the most appropriate treatment of HSV encephalitis in HIV-positive persons. In most of the previous reports in this patient population, patients were treated with 14 to 24 days of intravenous acyclovir followed by a suppressive regimen of oral acyclovir. With this regimen, the patient has had a very good recovery, although memory deficits remain 1 year later.

While HSV is a common cause of encephalitis in immunocompetent persons, it is a surprisingly rare cause of encephalitis in the HIV-positive population. As this case demonstrates, HSV encephalitis in the immunocompromised person can present quite atypically, with symptoms such as subacute memory loss and seizure. This case was further complicated by 2 episodes of intracranial hemorrhage after the patient began an antiretroviral regimen containing raltegravir. Clinicians should remain vigilant for bleeding complications in persons with necrotizing encephalitis caused by HSV.

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