CASE REPORT

EBV limbic encephalitis after allogenic hematopoietic stem cell transplantation

Encéphalite limbique à EBV après allogreffe de cellules souches hématopoïétiques

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Summary The clinical and radiological presentations of Epstein-Barr virus (EBV) encephalitis are pleomorphic, but a common and characteristic finding is an increased T2-weighted signal in the bilateral thalami and basal ganglia. We report here a case of post-transplant acute limbic encephalitis (PALE) syndrome that was possibly related to EBV infection. Six weeks after hematopoietic stem-cell transplantation, the patient developed confusion and anterograde amnesia. Brain magnetic resonance imaging (MRI) was performed and revealed bilateral hippocampal and amygdala signal abnormalities. The technetium-99m single-photon emission computed tomography (99mTc SPECT) imaging confirmed bilateral limbic structural involvement. The clinical, biological and radiological presentations were consistent with a diagnosis of EBV-induced PALE syndrome. To our knowledge, this is the first described case of PALE syndrome possibly related to EBV infection.

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Introduction

Epstein-Barr virus (EBV) infection of the central nervous system in the post-transplant immunocompromised host can lead to the development of intracranial tumors—such as
Post-transplant lymphoproliferative disorders (PTLD) and, more rarely, smooth muscle tumors—or to encephalitis or meningoencephalitis [1–3]. The clinical and radiological presentations of EBV encephalitis are pleomorphic, but there appears to be a predilection for the deep nuclei. Thus, a common and characteristic finding in such cases is an increased T2-weighted signal in the bilateral thalami and basal ganglia [4]. Also, in the rare reports of hippocampal involvement, it was not limited to the medial temporal lobe, but was associated with more extensive cortical lesions [5].

Hippocampus- and limbic-related structural involvement in patients following allogeneic hematopoietic stem-cell transplantation (HSCT) is more often related to human herpes virus-6 (HHV-6) infection, and leads to post-transplant acute limbic encephalitis (PALE) syndrome. However, we report here a case of PALE syndrome that was possibly related to EBV infection. To our knowledge, this is the first such described case with this association.

Case report

A 60-year-old EBV-seropositive patient, who had had aplastic anemia since 2004, underwent HSCT from a matched, unrelated EBV-seropositive donor in December 2007. The reduced-intensity conditioning regimen consisted of fludarabine, busulfan and rabbit antithymocyte globulins. Graft-versus-host disease prevention was based on cyclosporine alone. Engraftment was observed on day 11 concomitant with acute graft-versus-host disease (skin and gastrointestinal), which was treated with corticosteroids and daclizumab (anti-CD25 antibody).

Six weeks after HSCT, the patient developed confusion and anterograde amnesia. Brain MRI was performed (Fig. 1) and revealed bi-hippocampal and amygdala hypersignal on T2- and fluid-attenuated inversion recovery (FLAIR)-weighted MRI. Signal abnormalities were more pronounced on the left side. There was no contrast enhancement after gadolinium administration, but a technetium-99m single-photon emission computed tomography (99mTc SPECT) scan revealed bi-hippocampal and right-thalamic perfusion impairment.

Cerebrospinal fluid (CSF) analysis showed 96 lymphocytes. Real-time quantitative polymerase chain reaction (PCR) tests showed a high EBV DNA load (4.06 log_{10} copies/mL) in the CSF compared with only 2.7 log_{10} copies/mL in the blood, consistent with EBV reactivation in the CNS. PCR tests for other viruses, such as herpesvirus and enterovirus, were all negative. Indeed, the clinical, biological and radiological presentations were all consistent with a diagnosis of EBV-induced PALE syndrome, and the patient was treated successively with cidofovir, ganciclovir plus foscarnet, and rituximab.

The patient achieved a partial recovery with persistence of mild anterograde amnesia. Four weeks after PALE syndrome onset, MRI revealed atrophy of both hippocampi associated with T2- and FLAIR-weighted signal abnormalities that were more pronounced on the left side.

Discussion

The clinical, biological and radiological features of PALE syndrome have recently been precisely characterized by Seeley et al. [6] and are consistent with those of our present case: clinical features included pronounced anterograde amnesia and mild CSF pleocytosis. Also, the syndrome is accompanied by an MRI signature of bilateral, non-enhancing,
medial temporal lobe T2/FLAIR hyperintensities that are sharply demarcated by sparing of the parahippocampal gyrus. The $^{99m}$Tc SPECT scan confirmed bilateral limbic structural involvement revealing bi-hippocampal and right-thalamic perfusion impairment.

Although PALE syndrome is generally related to HHV-6 infection, biological etiological investigations were, in our case, all negative except for EBV. In addition, in our patient, the disease progression was also in accordance with those of previous reports—namely, partial recovery of the neuropsychological disorders after antiviral treatment and the development of limbic structural atrophy revealed by MRI [6].

Conflicts of interest

The authors report no conflicts of interest.

References