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LETTER TO THE EDITOR

Dengue encephalitis in allogenic hematopoietic stem cell transplantation recipient

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An altered mental state with or without neurologic signs have become more frequent in patients after hematopoietic stem cell transplantation (HSCT).[1] The neurologic problems are different according to the stage of transplant. In the pre-engraftment period, the occurrence is associated with toxicity of high-dose chemotherapy, bacterial infections, intracranial bleeding and other drug-related neurotoxicity. During the late post-transplant phase, with the use of immunosuppressive drugs and the occurrence of GvHD, the following neurologic complications can occur: central nervous system (CNS) infections, cerebrovascular disease, metabolic encephalopathy, calcineurin inhibitor neurotoxicity with thrombotic microangiopathy or posterior reversible encephalopathy syndrome and immune-mediate disorders.

In a retrospective analysis, CNS infection accounts for only 9% of CNS complications after HSCT.[2] In suspected CNS infection, it is important to perform the appropriate diagnostic procedures, which include an initial neuroimaging with MRI or CT scan and subsequent cerebrospinal fluid (CSF) examination.[3] The most prevalent etiologies are cerebral toxoplasmosis followed by aspergillosis.[4] Viral CNS infection after HSCT is uncommon. Herein we report the first case of dengue encephalitis in an allogenic HSCT patient.

A 65-year-old man with unclassifiable myelodysplasia/myeloproliferative disease underwent an ABO compatible matched-related peripheral allogeneic HSCT using myeloablative conditioning with fludabarine 150 mg/m^2 and melphalan 180 mg/m^2. GvHD prophylaxis was performed with cyclosporine and long-term methotrexate.

The complications during the immediate post-HSCT period were febrile neutropenia treated with broad spectrum antibiotics and platelet refractoriness with the need for a large amount of platelet transfusion support. The neutrophil engraftment occurred on D+17 and platelet recovery was on D+22.

Thirty-four days after transplantation, he was admitted with low-grade fever and altered mental status. Hemodynamic parameters were normal. On neurologic examination, Glasgow Coma Scale score was 13. He moved all limbs symmetrically on painful stimuli. The pupils were equal and reactive to light. Deep tendon reflexes were normal and plantar reflexes were extensor bilaterally. Meningeal signs were absent. The remainder of his physical examination was unremarkable.

The laboratory investigation revealed hemoglobin of 8.23 g/dL, white blood cell count of 18 890/mm^3 (neutrophils 42%, lymphocytes 10%, eosinophils 47%), platelet count of 338 100/mm^3, C-reactive protein (CRP) of 1 mg/dL, erythrocyte sedimentation rate of 22 mm. Renal and liver functions were normal. CSF analysis revealed an increase of proteins (166 mg/dL) with decrease in values of glucose (54.8 mg/dL) and pleocytosis. The CSF gram and culture resulted negative. Blood culture was sterile. Brain MRI revealed cortical and subcortical alterations suitable for age. Polymerase chain reaction (PCR) for cytomegalovirus (CMV), Herpes Simplex virus HSV-1 and HSV-2, Human Herpesvirus (HHV-6), Varicella Zoster Virus on CSF were negative. PCR for CMV on blood was also negative. Empiric acyclovir and meropenem were initiated due to the diagnosis of encephalitis without an etiology.

Considering the epidemiology in our city, Dengue, Chikungunya and Zika virus were considered among the possible hypotheses. Blood rapid test for Dengue resulted negative for antigen NS1. IgM and IgG serologies for Dengue were negative. PCR for Chikungunya and Zika virus were negative in CSF. The PCR for dengue resulted positive in CSF. The diagnosis of dengue encephalitis was performed and supportive care was preconized.

After 7 days, he evolved with a diffuse skin rash and liver dysfunction. A skin biopsy was made with the diagnosis of acute GvHD, clinical staging grade III. Then, prednisone 1 mg/kg was initiated. Despite steroid therapy, acute GvHD symptoms worsened and basiliximab was administered once a week for 2 weeks. The patient evolved with progressive deterioration of neurocognitive status and died 1 month later with a respiratory failure due to a bacterial pneumonia.

Dengue is the most common arboviral disease caused by four antigenically distinct dengue virus serotypes (DEN-1 to DEN-4). It is endemic in certain geographical parts of the world, like Southeast Asia, the Pacific, East and West Africa, the Caribbean and the Americas. In recent years, dengue-related neurological manifestations have been increasingly observed.[5] Dengue CNS involvement can be categorized into encephalopathy, encephalitis or immune-mediated syndrome.[6]

Dengue encephalitis is a neuronal infiltration by the dengue virus. It is a rare but important complication. Fever, headache and reduced consciousness are the features, corroborated by laboratory findings and neuroimaging (Brain MRI suggestive of viral encephalitis). The detection of virus (PCR, viral culture or immunocytochemistry for viral antigens) or detection of host immune response (MAC-ELISA) depends of the time of infection onset. In our case, the immunosuppression probably diminished the immune response.[5]

In a prospective study recently reported among arbovirus in oncohematological patients, three patients were diagnosed with dengue infection but none had neurological complications.[7] This case of dengue encephalitis in a HSCT recipient is important because it includes a new differential diagnosis of encephalitis in patients living in areas where these viruses are endemic or returning from endemic or epidemic regions.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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