NEUROLOGIC EMERGENCIES IN THE BONE MARROW TRANSPLANT PATIENT

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Bone marrow transplants are indicated in patients with hematologic malignancies and are associated with a high incidence of neurologic complications. Emergent presentations of neurologic dysfunction must be approached systematically as this patient population is at risk for various neurologic problems depending on where they are in the course of treatment and the status of their immune systems. It is important to keep in mind that most patients undergoing a bone marrow transplant have aggressive underlying malignancies and new neurologic symptoms at any time during their treatment can be related to new parenchymal or leptomeningeal metastases. Several of the **cytotoxic drugs** used result in acute neurologic conditions. High dose cytarabine is used as part of induction regimens, consolidation regimens or for peripheral stem cell mobilization. It can lead to an acute cerebellar syndrome and patients with renal failure and older age are at highest risk. Busulfan is used as part of some myeloablative regimens and is associated with seizures. Immunosuppressant drugs like tacrolimus and cellcept are used after transplant and can cause RPLS.

Following myeloablation, patients are at risk from numerous CNS disorders due to a depleted marrow, immune suppression and re-activation of latent viruses. **Thrombocytopenia** from a high dose chemotherapy regimen can result in spontaneous intracranial hemorrhage. Most commonly, these are subdural hematomas, but parenchymal hemorrhages and subarachnoid hemorrhages can also occur. Patients will typically require frequent platelet transfusions to maintain a platelet level above 50,000 to minimize expansion of the hematoma and to prevent recurrence. Patients with large hemorrhages, significant neurologic symptoms or herniation syndromes may require surgical evacuation of the bleed.

Opportunistic CNS infections in this population can have high morbidity and mortality. Prompt recognition and treatment is critical to prevent neurologic deterioration and death. The two most common causes of encephalitis after transplant are *Toxoplasma gondii* and *Aspergillus*. Toxoplasma can present with mass lesions and symptoms of a focal encephalitis. CNS Aspergillus infection results in multiple mass lesions involving cortical and deep structures. In both, definitive diagnosis requires a brain biopsy, but CSF PCR of toxoplasma is highly specific.

Re-activation of latent viruses, CMV and HHV6 can cause encephalitis. Early identification and treatment with ganciclovir and/or foscarnet can help minimize neurologic symptoms, although with a significant rate of drug related adverse events. CMV may have an associated retinitis and can be diagnosed by CSF PCR. HHV 6 typically occurs within 100 days of transplant and presents with an amnestic syndrome that progresses into a limbic encephalitis, often with status epilepticus. This has been termed post-transplant acute limbic encephalitis (PALE) and is fatal in almost half of patients. Re-activation of the JC virus and development of progressive multifocal leukoencephalopathy (PML) can occur related to prior therapies with monoclonal antibodies, immune dysregulation form the underlying hematologic malignancy and compounded by marrow ablation. VZV re-activation can cause an acute encephalitis or acute weakness due to a myelitis. In the post-transplant setting, chronic immune suppression can lead to EBV infection of B cells and a primary CNS post-transplant lymphoproliferative disorder. Presentation and workup are similar to primary CNS lymphoma, but these tumors can respond to therapy with single agent rituximab.

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