Autoimmune Encephalitis with Catatonic Features after Hematopoietic Stem Cell Transplantation: Case Review and Review of Literature

Alice Luo MD, Mark Wiener MD, Martin Chin MD
Memorial Sloan Kettering Cancer Center, New York, NY
Weill Cornell Medicine, New York, NY

Background

- Hematopoietic Stem Cell Transplantation (HSCT) is a potentially curative treatment for many hematologic disorders.
- Neurological complications after HSCT occur with an incidence of 3-44 percent.[1]
- Complications include central nervous system (CNS) infections due to immunosuppression, neurotoxicity from conditioning agents and immunosuppressants, and autoimmune phenomena including manifestations of graft versus host disease (GvHD), myasthenia gravis, cytokine release syndrome, and autoimmune encephalitis.
- Cases of autoimmune encephalitis in the absence of CNS manifestations of GvHD are rare.
- Autoimmune encephalitis represents a group of disorders in which the immune system attacks CNS resulting in diffuse brain inflammation and symptoms can include confusion, loss of consciousness, amnesia, seizures, and psychiatric manifestations.
- Catatonia, a disorder with psychomotor signs of stupor, rigidity, and waxy flexibility, has been closely linked to a specific type of autoimmune encephalitis, anti-N-methyl-D-aspartate (NMDA) receptor encephalitis.[2]
- Currently, there are no reported cases of catatonia associated with post-HSCT autoimmune encephalitis.

Case Presentation

- 66-year-old male with no past psychiatric history and medical history of coronary artery disease requiring percutaneous intervention
- Presented to the hospital for allogenic-HSCT for progressive myelofibrosis
- Prior to HSCT, scored a 27/30 on Montreal Cognitive Assessment (MoCA)
- Conditioning treatment regimen: Busalfan, Melphalan, Fludarabine with rabbit antithymocyte globulin (rATG)
- Received allogenic-HSCT from his brother

Clinical Course

Post-HSCT: seemed to be recovering well, ambulating and tolerating PO → Day 16 post transplant: nursing documented acting strangely, lying in stool, oriented X3 → CT head revealed no acute process: normal ventricles, no hemorrhage, no mass effect

Day 17 post transplant: stooled on floor, impulsive – almost pulled out IV, word finding difficulty → Neurology consulted: MRI (no intracranial abnormality), vEEG (diffuse cerebral dysfunction), infectious workup (negative), CSF analysis → Day 20 post transplant: psychiatry consulted – Scored 13 on Bush-Francis Catatonia Rating Scale

After 2mg IV lorazepam challenge, Bush Francis Score decreased to 7 – no posturing and speaking to providers → Started on lorazepam 2mg IV q8hr: response lasted only for a few days → Titrated lorazepam to 18mg total daily dose and eventually tapered due to lack of response; amantadine started but discontinued soon after due to paranoia

Neurology suspected autoimmune encephalitis due to high protein on CSF and serum glutamic acid decarboxylase (GAD) antibodies → After steroids: responded to "yes" or no" questions → After 2 rounds of intravenous immunoglobulin (IVIG), he seemed more awake and responsive

After rituximab, made jokes, sang along to the Beatles, and engaged in meaningful conversations with others → 3 weeks later at outpatient Neurology appointment: remembered very little about hospitalization but no concerns for altered mental status or confusion

Serum and Cerebrospinal (CSF) Analyses

Serum	
Glutamic Acid Decarboxylase (GAD) Antibody	0.15
C-reactive Protein (CRP)	5.16
Erythrocyte Sedimentation Rate	53

CSF Analysis			
White Cell Count	1	Autoimmune Encephalopathy	Negative
Protein	68	B-D glucans	Negative
Glucose	78	Oligoclonal Bands	Negative
Gram Stain	Negative	JC Virus	Negative
Meningitis/Encephalitis	Negative	EBV	Negative

Diagnostic Criteria for Autoimmune Encephalitis[3]

Subacute onset of altered mental status, working memory deficits, or psychiatric symptoms

One of the following:
1. New focal CNS findings
2. Seizures not explained by known seizure disorder
3. CSF pleocytosis
4. MRI features

Reasonable exclusion of other causes

Discussion and Conclusion

- Only a few cases of autoimmune encephalitis reported post-HSCT. None of the cases reported catatonic features.

Case Series[4]
- 54 y/o M, 65 y/o F, 63 y/o F
- Antibody-associated
- Myoclonic jerks, hemiparesis, choreiform movements, visual loss, and paranesthesia

Case Report[5]
- 60 y/o F
- antibodies against NMDA-type-glutamate receptor
- Acute short term memory loss, emotional lability

Peds Cases[6,7]
- 5 y/o F
  - Anti-GAD antibodies
  - Seizures, AMS
- 7 y/o M
  - LGI1 antibodies
  - Attention deficit, abnormal movements, cognitive dysfunction

- Conditioning regimens, used to prepare the bone marrow to receive donor cells and to reduce the chance of rejection, increase risk of autoimmune reactions.
- Immune system dysregulation contributes to etiology of catatonia: acute phase reactants (*i.e.*, CRP) increased in catatonia and association of NMDA receptor encephalitis with catatonia.[2]
- Disruption of immune system may not only increase risk of autoimmune encephalitis post-HSCT but also increase risk of catatonia.
- Consideration that first line treatments of catatonia *i.e.*, lorazepam may not be fully effective until treatment of underlying autoimmune encephalitis.
- **Conclusion:** Consultation-Liaison psychiatrists are well-poised to recognize catatonia in a medically ill population i.e., post-HSCT patients and make an association between catatonia and autoimmune encephalitis.

References
1. Maffini E, et al. Neurologic Complications after Allogeneic Hematopoietic Stem Cell Transplantation. *Biol Blood Marrow Transplant.* 2017;23(3):388-397.
2. Rogers JP, et al. Catatonia and the immune system: a review. *Lancet Psychiatry.* 2019;6(7):620-630.
3. Graus F, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol.* 2016;15(4):391-404.
4. Hümmert MW, et al. Severe allo-immune antibody-associated peripheral and central nervous system diseases after allogeneic hematopoietic stem cell transplantation. *Sci Rep.* 2021;11(1):8527.
5. Toda J, et al. Limbic encephalitis with antibodies to N-methyl-D- aspartate (NMDA)-type glutamate receptor after allogeneic transplantation. *Int J Hematol.* 2020;112(2):254-257.
6. Nagai K, et al. Severe anti-GAD antibody- associated encephalitis after stem cell transplantation. *Brain Dev.* 2019;41(3):301-304.
7. Rathore GS, et al. Autoimmune Encephalitis Following Bone Marrow Transplantation. *Pediatr Neurol.* 2015;53(3):253-256.