A challenging diagnosis of an uncommon manifestation of chronic graft-versus-host disease

Catherine Travaline DO, Sarah Wilson DO

Geisinger Medical Center, Danville, PA

Geisinger

Introduction

Allogenic hematopoietic stem cell transplantation (HSCT) can be a curative treatment option for patients suffering from a range of hematologic disorders. Chronic graft-versus-host disease (cGVHD) is a common and deadly complication of HSCT. It has been estimated that approximately 30-70% of all allogenic hematopoietic stem cell recipients who survive longer than 3 months after transplantation will develop cGVHD. Pulmonary manifestations of cGVHD are less common, occurring in approximately 2-5% of HSCT recipients. The diagnosis of lung cGVHD is challenging to make and often requires open lung biopsy. Here we report a case of a delayed diagnosis of pulmonary cGVHD in a patient who received an allogenic stem cell transplant one year prior.

Case Presentation

A 29-year-old male presented to the hospital with acute hypoxic respiratory failure requiring mechanical ventilation and veno-venous extracorporeal membrane oxygenation (VV-ECMO) due to persistent hypercapnia. His past medical history is significant for nodular sclerosing Hodgkin's lymphoma with multiple relapses status post chemotherapy and autologous stem cell transplant. His medical history is further complicated by the development of treatment-related myelodysplastic syndrome status post allogenic hematopoietic stem cell transplant, which was one year prior to this presentation.

Hospital Course:

- Started on empiric antibiotic therapy to cover pneumonia as well as steroids due to concern for possible GVHD
- Improved clinically and was able to be extubated, decannulated, and weaned off steroids
- Unfortunately, his respiratory status worsened after an aspiration event and he was subsequently found to have multiple molds on bronchial washing
- It was thought that his worsening respiratory status was due to aspiration pneumonia and possibly a fungal pneumonia; antibiotics were resumed, and antifungals started
- However, his respiratory status did not improve. A bronchial lung biopsy from two months prior was re-evaluated using stains to detect lymphocyte subsets and was significant for moderate CD8 positive cell infiltrates which is indicative of GVHD
- He was treated with steroids and photopheresis
- He improved and was ultimately discharged to a rehab facility then home

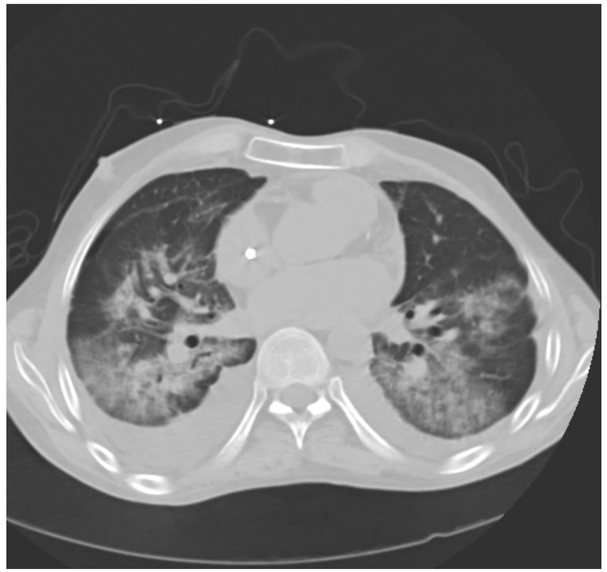

Figure 1-Ill-defined consolidation and ground-glass opacification suggestive of ongoing active inflammation.

The patient unfortunately returned to the hospital approximately one month later again with acute hypoxic respiratory failure. The etiology of his hypoxia was thought to be multifactorial in the setting of an acute bacterial infection and worsening of his cGVHD. During his second hospitalization the patient and his family decided to transition to a comfort-oriented approach to focus on quality of life. The patient was discharged and died at home approximately four days later.

Discussion

This case demonstrates the difficulty and importance of diagnosing cGVHD in patients with a history of allogenic stem cell transplant presenting with acute hypoxic respiratory failure. This patient had a lung biopsy two months prior to presentation that was not stained to look for GVHD. Given his history of aspiration and immunosuppression, the diagnosis of pneumonia had seemed much more likely. It was not until the patient continued to decline despite broad-spectrum antibiotics and antifungals that the possibility of cGVHD was revisited and his prior biopsy was re-evaluated to confirm the diagnosis.

Conclusion

Chronic graft-versus-host disease is a devastating complication of allogenic stem cell transplant. The diagnosis of cGVHD in the lung can be difficult to make due to nonspecific symptoms and wide range of disease severity. This case demonstrates the importance of keeping cGVHD high on the differential for patients presenting with acute hypoxic respiratory failure greater than three months after an allogenic stem cell transplant, as earlier diagnosis improves outcomes.

References

1. Lee SJ. Have we made progress in the management of chronic graft-vs-host disease? *Best Practice & Research Clinical Haematology*. 2010;23(4):529-535. http://www.sciencedirect.com/science/article/pii/S1521692610000770. doi: https://doi.org/10.1016/j.beha.2010.09.016.
2. Verleden SE, McDonough JE, Schoemans H, et al. Phenotypical diversity of airway morphology in chronic lung graft vs. host disease after stem cell transplantation. *Mod Pathol*. 2019;32(6):817-829. doi: 10.1038/s41379-019-0203-2 [doi].
3. Balassa K, Danby R, Rocha V. Haematopoietic stem cell transplants: Principles and indications. *Br J Hosp Med (Lond)*. 2019;80(1):33-39. doi: 10.12968/hmed.2019.80.1.33 [doi].
4. Socie G, Ritz J. Current issues in chronic graft-versus-host disease. *Blood*. 2014;124(3):374-384. doi: 10.1182/blood-2014-01-514752 [doi].