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Recurrent Lung Infections Post-Hematopoietic Stem Cell Transplant (HSCT) in a Patient with Chronic Lymphocytic Leukemia (CLL)

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Abstract

Hematopoietic stem cell transplantation (HSCT) is an essential therapy for malignant and non-malignant hematologic, autoimmune, and genetic disorders. However, post-transplant complications, particularly pulmonary infections, remain a leading cause of morbidity and mortality. Case report: We present the case of a 70-year-old male with chronic lymphocytic leukemia (CLL) who underwent allogeneic HSCT several years ago. Post-transplant, he received intravenous immunoglobulin (IVIG) every six weeks for immune support. Despite this, he developed chronic obstructive pulmonary disease (COPD) without any smoking history and has experienced recurrent pneumonia requiring frequent hospitalizations. Extensive microbiologic and imaging evaluations repeatedly failed to identify a causative organism. The patient remains on chronic antibiotic therapy, nebulized bronchodilators, and antiviral prophylaxis with valacyclovir. This case underscores the vulnerability of post-HSCT patients to recurrent, often unexplained pulmonary infections despite ongoing prophylactic and supportive measures. Management focuses on infection prevention and treatment through broad-spectrum antimicrobials, immunoglobulin replacement, and respiratory support, while addressing physical, psychological, and nutritional needs. Discussion: In patients with CLL and T-cell-depleted HSCT, persistent immunodeficiency can lead to refractory pulmonary complications, significantly reducing quality of life and survival. Early recognition, aggressive management, and multidisciplinary care are essential to improving outcomes in this high-risk population.

Keywords: ***Hematopoietic Stem cell transplantation; Chronic lymphocytic leukemia; Pulmonary complications; Infections; Transplantation; Intravenous immunoglobulin; Graft-Versus-Host Disease.***

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1. Introduction

Hematopoietic stem cell transplantation (HSCT), which involves the transplantation of stem cells from the bone marrow or umbilical cord blood, can be used to treat malignant and non-malignant hematologic, autoimmune, and genetic diseases [1]. There are about 50,000 to 60,000 patients who undergo hematopoietic stem cell transplantation worldwide each year. The most common indications for HSCT are multiple myeloma and lymphoma, up to 65% (1). 15-40% of transplant recipients, who get admitted to the intensive care unit, have pulmonary complications from infectious and noninfectious causes [2]. Infections may develop within the first 100 days post-HSCT, up to 30% of patients [3]. However, pulmonary infections can occur late in the HSCT course [3]. Even in patients who have undergone T-cell-depleted allogeneic HSCT and receive regular intravenous immunoglobulin (IVIG) infusions, the incidence of frequent lung infections remains high; the occurrence of infections significantly affects patient survival [4].

Patients with chronic lymphocytic leukemia (CLL) have a profoundly weakened immune system, making them more vulnerable to opportunistic pathogens [5]. During the first 100 days, patients may be neutropenic and are vulnerable to a range of pathogens, including gram-positive and gram-negative bacteria (such as Staphylococcus species and Streptococcus species), E. coli, and Pseudomonas, as well as fungi and viruses [6]. After the first 100 days, recipients remain vulnerable to infections, especially those with chronic graft-versus-host disease (GVHD), who require prolonged immunosuppression [8]. The most common pathogens are encapsulated bacteria (Streptococcus pneumoniae and Haemophilus influenzae), fungi (invasive mold, aspergillosis, and mucormycosis), and protozoa (Pneumocystis jirovecii) [7], [8].

Noninfectious pulmonary complications are also a threat to post-HSCT recipients. They often overlap with lung infections, and it is crucial to distinguish them through diagnostic evaluations [9]. The most recognized noninfectious complications are idiopathic pneumonia syndrome, bronchiolitis obliterans, diffuse alveolar hemorrhage, or cryptogenic organizing pneumonia [10].

In the evaluation of HSCT patients, medical history should be thoroughly obtained along with clinical presentations, chest imaging, PFTS, sputum examination, and serologic studies [11]. Blood cultures should be performed routinely; however, they often offer limited diagnostic value, except when the pathogen has a high propensity for infecting the blood [11]. Sputum, quantitative real-time PCR (qPCR), blood biomarkers, and lung biopsy are essential for diagnosing specific pathogens [12]. Treatments for pneumonia that occurs after HSCT should be started immediately due to the life-threatening nature and complications in immunocompromised patients, such as those with CLL [4].

2. Case Report

A 70-year-old male patient with a history of CLL, gout, benign prostate hyperplasia (BPH), status post HSCT 10 years ago, and COPD presented to the ED with complaints of shortness of breath and fevers. Symptoms onset earlier during the day. Patient stated he had shortness of breath, O2 sat in the 80s, and a fever of 104°F while resting at home. The

patient rushed to an urgent care facility, then went home; however, the fever persisted, so the patient called EMS. When EMS arrived at the patient's home, his O2 saturation was 89%. The patient was placed on 2L NC, and his O2 sat improved to 92%. His temperature was 102°F, and he was experiencing wheezing. EMS started the patient on methylprednisolone 125mg and DuoNeb updrafts. His breathing improved, but he had a fever of 104°F en route. They started intravenous fluid and placed ice packs under the patient's axillary regions.

Initial studies in the emergency department revealed the patient's blood pressure to be 142/71 mmHg, heart rate 102 bpm, respiratory rate 20 bpm, temperature 104.5°F, and O2 saturation 92% on 2 liters of nasal cannula. WBC 7.9 × 10^3/uL, Hgb 13.6 g/dL. The rest of the complete blood count (CBC) was unremarkable. The comprehensive metabolic panel (CMP) results were significant, with a BUN of 24.0 mg/dL and a creatinine (Cr) level of 2.4 mg/dL. Respiratory was negative for any infections. Chest X-Ray revealed central vascular congestion, and bilateral airspace opacities may represent pulmonary edema or multifocal pneumonia. Urine and blood culture, BioFire, and MRSA panel ordered. Patient was to start Cefepime 2g IV q8h x 7days and Vancomycin HCL Rx to dose for empiric therapy while waiting for urine and blood culture results. Patient reported that within the last two months, he had four episodes of atypical pneumonia, and all the labs and chest imaging were unremarkable. The patient was also on his outpatient Cefdinir and Azithromycin for atypical pneumonia when he got admitted this time. The patient was also taking Valacyclovir orally daily for prophylaxis.

Urine culture and blood culture showed no growth. Computed tomography (CT) chest without contrast demonstrated scattered patchy ground-glass opacities, predominantly in the lower lobes, likely representing pneumonia/infection. However, a component of pulmonary edema cannot be entirely excluded. A more focal right lower lobe opacity, 1.0 x 0.9 cm, may be related or represent a pulmonary nodule. After one night in the hospital, the patient's condition improved, and he was able to breathe well on room air. He was stable for discharge home with Metronidazole 500 mg PO every 8 hours for 7 days and Levofloxacin 750 mg PO every 48 hours for 7 days (Figs. 1 and 2).

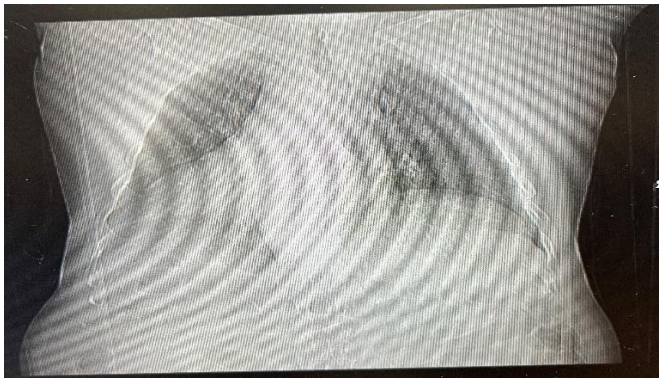

Fig. 1. Scattered patchy groundglass opacities predominantly in the lower lobes likely representing pneumonia/infection. More focal right lower lobe 1.0 x 0.9 cm opacity may be related or represent a pulmonary nodule.

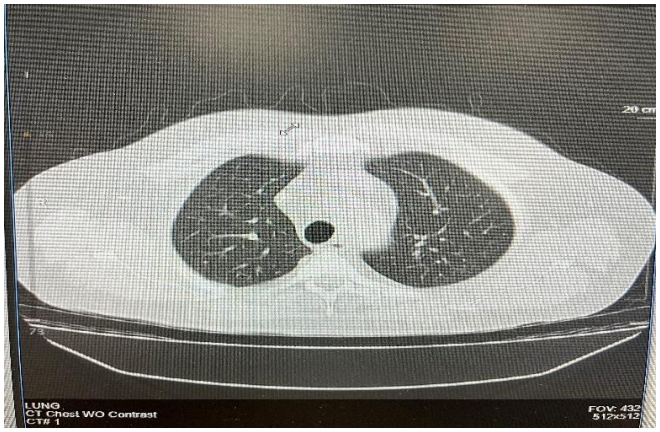

Fig. 2. Scattered patchy ground glass opacities predominantly in the lower lobes likely representing pneumonia/infection.

Patient stated that he stopped taking his over the counter (OTC) proton pump inhibitor (PPI), and he has had many episodes of pneumonia due to aspiration. He also commented that his chest CT scans from all hospitalizations consistently showed right lower lobe opacity, and blood cultures always came back negative, with normal lactic acid levels, white blood cell counts (CBC), and neutrophil counts. He also reported his COPD started to develop after HSCT. The patient has followed up with his primary care physician and oncologist at the University Medical Center for the last several years.

3. Discussion

This case is particularly unusual in terms of the patient with CLL status post HSCT, who has had many episodes of lobar pneumonia over the years, even though he has been on ongoing IVIG therapy [13]. The profound alterations in immune status associated with HSCT render the patient vulnerable to severe community-acquired pneumonia [13]. With CLL disease progression, cumulative and unanticipated immunosuppression occurs because of multiple treatment lines, and the risk of infection further increases [14].

CLL is the most common leukemia in adults in developed countries, and infection is the leading cause of death for these patients [15]. With improvements in the prophylaxis of post-HSCT infections and treatment of CLL over the last few decades, infection-related mortality has decreased [16]. Despite the introduction of numerous prophylactic strategies and advances in diagnosis and treatment, the leading infectious cause of death post-HSCT is pneumonia. Factors that enhance the recipient's vulnerability to pneumonia include protracted neutropenia before engraftment, impaired humoral and cellular immunity associated with the administration of exogenous immunosuppressive agents, and GVHD [17].

The most common infection of post-HSCT is bacterial pneumonia, which typically presents with fever; however, respiratory symptoms and signs may be absent in the neutropenic host. Presumably because of the paucity of neutrophils, chest X-ray abnormalities may be subtle or absent as well. In one series, the use of high-resolution CT imaging revealed evidence of pneumonia in more than 50% of febrile neutropenic patients with normal chest radiographs [18]. Broad-spectrum antibiotics should be initiated expeditiously in all suspected cases of bacterial pneumonia and in febrile, neutropenic patients without an identified site of infection. There is currently no consensus on the routine use of prophylactic antibiotics in afebrile, asymptomatic neutropenic patients during the pre-engraftment period [19]. Administration of intravenous immunoglobulin may reduce the risk of bacterial infections in the subset of allogeneic recipients who experience severe hypogammaglobulinemia during the first 100 days [19].

Pulmonary complications after HSCT are common, with an incidence of up to 60% and up to one-third of recipients require intensive care after transplantation [17]. Respiratory failure is the most common cause of critical illness (19). Pulmonary complications can occur early or late in the post-HSCT course, can have infectious and noninfectious etiologies, and can present with radiographic findings [1]. The pulmonary complications of HSCT also vary depending on the indication for, type of, and preparative regimen preceding HSCT [19]. Recipients of allogeneic transplantation experience more infection complications than recipients of autografts, not only because these recipients require chronic administration of immunosuppressants to treat or prevent GVHD, but also because GVHD itself causes an immunodeficient state by affecting the mucosal surfaces, the reticuloendothelial system, and the bone marrow [19]. These factors predispose allogeneic recipients to fatal viral pneumonias, multidrug-resistant bacteria, and invasive fungi [20].

Diffuse pneumonia is a common complication after HSCT; no infectious etiology is identified in up to half of these cases [21]. The term "idiopathic pneumonia syndrome" (IPS) reflects the diversity of clinical presentations and likely multifactorial etiologies [21]. IPS refers to "diffuse lung injury occurring after marrow transplant for which an infectious etiology is not identified" [21]. Bronchoalveolar lavage, rather than lung biopsy, was recommended as the primary diagnostic approach to exclude infection [22].

Supportive care in the post-HSCT period has changed the microbiology of pneumonia. Prophylactic administration of trimethoprim-sulfamethoxazole (TMP-SMX), antivirals, antifungals, and fluoroquinolones has decreased the incidence of *Pneumocystis jirovecii*, CMV, herpes simplex, and *Candida albicans* infections. Resistant gram-negative and gram-positive bacteria, viruses, and other fungi remain important pathogens [23]. Treatments focus on preventing and treating infections (antibiotics, antivirals, antifungals), managing side effects, promoting physical and psychological well-being, rehabilitation, chemotherapy, and targeted agents, as well as donor lymphocyte infusions. Additionally, treatments aim to prevent disease relapse through maintenance therapies and cellular treatments, provide palliative care, and offer nutritional support [24].

4. Conclusion

This case highlights the unusual number of episodes of pneumonia in a patient with CLL who underwent HSC. Despite regularly scheduled IVIG therapy, the patient continues to experience pneumonia infections without an identifiable infectious etiology. The patient may have idiopathic pneumonia syndrome, a reflection of the diversity of clinical presentations and likely multifactorial etiologies. Diffuse lung injury occurring after HSCT, it's not clear to identify an infectious etiology. Bronchoalveolar lavage, rather than a lung biopsy, may be the primary diagnostic approach to exclude infection, as the patient mentioned that all his chest CT scans have had the same readings over the years.

5. Contributors

The authors wrote and edited the manuscript. The authors approved the final version of the manuscript and are responsible for all aspects of this study.

6. Competing Interests

The author declares no competing interests.

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REFERENCES

1. Bekele A, and Azoulay E. Critical care of the hematopoietic stem cell transplant recipient. Crit Care Clin. 2010;26(1):133-150. PubMed| Crossref
2. Shannon VR, Andersson BS, Lei X, et al. Utility of early versus late fiberoptic bronchoscopy in the evaluation of new pulmonary infiltrates following hematopoietic stem cell transplantation. Bone Marrow Transplant. 2010;45(4):647–655. PubMed| Crossref
3. Gratwohl A, Brand R, Frassoni F, et al. Cause of death after allogeneic haematopoietic stem cell transplantation (HSCT) in early leukaemias: An EBMT analysis of lethal infectious complications and changes over calendar time. Bone Marrow Transplant. 2005;36(9):757–769. PubMed| Crossref
4. Bjorklund A, Aschan J, Labopin M, et al. Risk factors for fatal infectious complications developing late after allogeneic stem cell transplantation. Bone Marrow Transplant. 2007;40(11):1055–1062. PubMed| Crossref
5. Puig N, De La Rubia J, Jarque I, et al. Characteristics of and risk factors for pneumonia in patients with hematological malignancies developing fever after autologous blood stem cell transplantation. Leuk Lymphoma. 2007;48(12):2367–2374. PubMed| Crossref
6. Marr KA, Carter RA, Crippa F, et al. Epidemiology and outcome of mould infections in hematopoietic stem cell transplant recipients. Clin Infect Dis. 2002;34:909–917. PubMed| Crossref
7. Park B, Pappas P, Wannemuehler K, et al. Invasive non-aspergillus mold infections in transplant recipients, United States, 2001–2006. Emerg Infect Dis. 2011;17(10):1855–1864. PubMed| Crossref

8. Xhaard A, Lanternier F, Porcher R, et al. Mucormycosis after allogeneic haematopoietic stem cell transplantation: A french multicentre cohort study (2003–2008). Clin Microbiol Infect. 2012;18:E396–400. PubMed| Crossref
9. Gooley TA, Chien JW, Pergam SA et al. Reduced mortality after allogeneic hematopoietic-cell transplantation. N Engl J Med. 2010;25(363):2091-2101. PubMed| Crossref
10. Kontoyiannis DP, Marr KA, Park BJ, et al. Prospective surveillance for invasive fungal infections in hematopoietic stem cell transplant recipients, 2001–2006: Overview of the Transplant-Associated Infection Surveillance Network (TRANSNET) Database. Clin Infect Dis. 2010;50:1091–100. PubMed| Crossref
11. Caillot D, Couaillier JF, Bernard A, et al. Increasing volume and changing characteristics of invasive pulmonary aspergillosis on sequential thoracic computed tomography scans in patients with neutropenia. J Clin Oncol. 2001;19(1):253–259. PubMed| Crossref
12. Legouge L, Caillot D, Chrétien M, et al. The reversed halo sign: Pathognomonic pattern of pulmonary mucormycosis in leukemic patients with neutropenia? Clin Infect Dis. 2014;58(5):672–678. PubMed| Crossref
13. Madtes DK. Pulmonary complications of stem cell and solid organ transplantation. In: Broaddus VC, editor. Murray and Nadel's textbook of respiratory medicine. 6. Philadelphia, PA: Saunders; 2016. pp. 1612–23.e8.
14. Nucci M., Anaissie EJ, Dignani MC, et al. In: Neoplastic diseases of the blood. Wiernik P, Goldman J, Dutcher J, Kyle R, editors. Springer; New York, NY: 2013. Prevention of infections in patients with hematological malignancies; pp. 1149–1164.
15. Cartron G, Dacheux L, Salles G, et al. Therapeutic activity of humanized anti-CD20 monoclonal antibody and polymorphism in IgG Fc receptor FcgammaRIIIa gene. Blood. 2002;99(3):754–758. PubMed| Crossref
16. Itala M, Helenius H, Nikoskelainen J, et al. Infections and serum IgG levels in patients with chronic lymphocytic leukemia. Eur J Haematol. 1992;48(5):266–270. PubMed| Crossref
17. Soubani AO, Miller KB, Hassoun PM. Pulmonary complications of bone marrow transplantation. Chest 1996;109:1066–1077. PubMed| Crossref
18. Heussel CP, Kauczor HU, Heussel G, et al. Early detection of pneumonia in febrile neutropenic patients: use of thin-section CT. AJR Am J Roentgenol 1997;169:1347–1353. PubMed| Crossref
19. Azoulay E, Mokart D, Rabbat A. Diagnostic bronchoscopy in hematology and oncology patients with acute respiratory failure: prospective multicenter data. Crit Care Med. 2008;36:100–107. PubMed| Crossref
20. Sullivan KM, Dykewicz CA, Longworth DL, et al. Preventing opportunistic infections after hematopoietic stem cell transplantation: the Centers for Disease Control and Prevention, Infectious Diseases Society of America, and American Society for Blood and Marrow Transplantation practice guidelines and beyond. Hematology (Am Soc Hematol Educ Program) 2001:392–421p.
21. Clark JG, Hansen JA, Hertz MI, et al. NHLBI workshop summary. Idiopathic pneumonia syndrome after bone marrow transplantation. Am Rev Respir Dis. 1993;147:1601–1606. PubMed| Crossref
22. Wick MR, Moore SB, Gastineau DA, et al. Immunologic, clinical, and pathologic aspects of human graft-versus-host disease. Mayo Clin Proc. 1983;58:603–612. PubMed

23. Kantrow SP, Hackman RC, Boeckh M, et al. Idiopathic pneumonia syndrome: Changing spectrum of lung injury after marrow transplantation. Transplantation. 1997;63:1079–1086. PubMed| Crossref
24. Irum K, Shah NN, Matthew U. Hematopoietic cell transplantation and cellular therapy", American Society of Hematology Self-Assessment Program. 2022.

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