

CASE STUDIES

Development of systemic lupus erythematosus after hematopoietic stem cell transplant: A case report

Collins M¹, Kaur M², Patnaik A^{3*}, Roppelt H⁴

¹ Rheumatology Fellow, North Shore-Long Island Jewish Health System, New York, USA

² Faculty, Department of Rheumatology, Wheaton Franciscan Medical Group, Wisconsin, USA

^{3*} Assistant Professor of Medicine, Division of Rheumatology, SUNY, Stony Brook, NY, USA

⁴ Associate Professor of Medicine, Interim Chief and Program Director, Division of Rheumatology, SUNY, Stony Brook, NY, USA

Abstract

Development of autoimmunity after hematopoietic stem cell transplantation (SCT) is poorly understood. Autoimmunity has been known to manifest as graft-versus-host disease (GVHD) after a transplant. But recent literature evidence indicates an increase in documented rheumatic diseases without GVHD association. We report here a case of systemic lupus erythematosus (SLE) after an umbilical cord stem cell transplant (SCT).

Introduction

Stem cell transplantation (SCT) is used to treat various hematopoietic malignancies and autoimmune diseases. Organ-specific autoimmune diseases are reportedly more common than systemic diseases following transplantation.^{1,2} These systemic illnesses tend to be related to graft versus-host disease (GVHD).^{1, 3, 4, 6} We present here a case that developed SLE post-SCT with no evidence of GVHD.

Case report

A 43-year-old African American female was diagnosed with acute myeloid leukemia M5a, translocation (9, 11) involving band 11q23, and negative for FLT-3 (receptor tyrosine kinase with important roles in hematopoietic stem cell survival). The patient was initially induced with standard 7+3 chemotherapy. Bone marrow biopsy conducted two weeks post induction showed good cytoinduction and negative for t (9, 11) translocation. Reinduction was not indicated since she was considered to be in complete remission. However, on repeat bone marrow biopsy, her blasts remained at 5% and she was considered to be at intermediate risk for poor prognosis based on risk stratification. The consolidation chemotherapy given was high dose cytosine arabinoside (HIDAC) 3 gram/m² q12 hours (days 1, 3, 5), which was complicated by *Staphylococcus Aureus* bacteremia and *Aspergillus* pneumonia. Subsequent bone marrow biopsies continued to show 5% blasts and the patient

was referred for a stem cell transplant based on the aforementioned risk stratification. She was scheduled to receive the transplant from a double umbilical cord donor. The patient was bridged from consolidation therapy to transplant induction therapy with decitabine (regimen 20mg/m² for 5 days). After transplantation, she was treated with post-transplant medications including valtrex, tacrolimus, voriconazole, and dapsone.

Serology testing conducted three months post-transplant, confirmed that the patient had cytomegalovirus (CMV) viremia and was treated with valganciclovir. She developed scattered erythematous raised lesions on her upper extremities and a bilateral periorbital rash after seven months. Result of a punch biopsy was negative for GVHD and tacrolimus was tapered thereafter. Nine months post-transplant, the patient was diagnosed with deep vein thrombosis of the left internal jugular vein secondary to possible anti-phospholipid antibody (APA) syndrome. The patient was initiated on anticoagulation. She continued to develop several problems that required multiple hospitalizations such as diarrhea, diffuse arthralgias, myalgias, joint stiffness and swelling, and paresthesias involving the hands and feet. An endoscopy and colonoscopy was performed subsequently. The colonic biopsy showed no gland necrosis or immunoblast reaction. No apoptotic cells were identified in the glands, although cellular debris was seen in some of them.

The small intestinal biopsy showed no lymphocytic infiltration, damage to the epithelial cells or glandular hyperplasia. The gastric biopsy results demonstrated moderate inflammation and mild glandular injury, but no apoptosis suggestive of GVHD. Serology was negative for celiac disease. A rheumatologic work-up revealed: positive ANA titer of 1:2560, homogenous pattern, positive anti-Smith, anti-RNP (47), anti-ds DNA (>286), anticardiolipin antibody IgG (22) and IgM (65) and B-2-glycoprotein IgM (30), with an elevated ESR (99) and CRP (5). Rheumatoid factor, anti-CCP, lupus anticoagulant, hepatitis panel, anti-Ro, and anti-La were negative. The diagnosis of SLE was made on the basis of clinical and serological criteria (polyarthritis, malar rash, +ANA, +dsDNA, +APS antibodies). The patient was subsequently maintained on prednisone and plaquenil.

Discussion

The incidence of autoimmunity following SCT is around 2-5%, but the exact etiology and pathophysiology remain unclear.^{1, 2, 3} Possible explanations include: transfer of autoantibodies from donor to recipient, T-cell memory driven development of autoimmunity as a result of homeostatic expansion, epitope-specific antibody production, and altered immunity associated with GVHD.^{4, 7, 8} This may differ among umbilical cord transplants, since these cells are considered immature/naïve.⁵ Use of immunosuppressants prior to SCT has been associated with the development of secondary autoimmunity.⁵ Lymphodepletion post-transplant is an additional independent risk factor.⁶

The present case study underscores the increased risk for developing unexpected consequences following SCT. Further studies evaluating the effect of age, type of induction of chemotherapy, and the course of the disease on SCT-related autoimmunity in comparison to SLE patients without a history of stem cell transplantation are highly significant. The diagnosis of SLE should be considered in patients presenting with suspicious clinical features post SCT and the disease should be promptly differentiated from GVHD based on tissue biopsy and diagnostic serology.

Conclusion

The pathogenesis of developing SLE after a SCT is complex and not clearly understood. The chances to overlook or delay the diagnosis of SLE in post-transplant patients are high. Hence high index of suspicion for SLE is necessary if any signs/symptoms are present. Moreover, it is important to exclude infectious etiologies

and obtain early tissue biopsy to differentiate SLE from GVHD. Early diagnosis will help in preventing treatment delay and irreversible disease complications.

Competing interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Citation

Collins M, Kaur M, Patnaik A, Roppelt H. Development of systemic lupus erythematosus after hematopoietic stem cell transplant: A case report. *IJRCl*. 2014;2(1):CS3.

Received: 30 March 2014, **Accepted:** 23 May 2014, **Published:** 9 September 2014

*Correspondence: Dr. Asha Patnaik, Division of Rheumatology, Department of Internal Medicine, State University of New York, Stony Brook, New York, USA.

asha.patnaik@stonybrookmedicine.edu

References

1. Hequet O, Salles G, Ketterer N, Espinouse D, Dumontet C, Thieblemont C, et al. Autoimmune thrombocytopenic purpura after autologous stem cell transplantation. *Bone Marrow Transplant*. 2003 Jun 23;32(1):89–95.
2. O'Brien TA, Eastlund T, Peters C, Neglia JP, Defor T, Ramsay NKC, et al. Autoimmune haemolytic anaemia complicating haematopoietic cell transplantation in paediatric patients: high incidence and significant mortality in unrelated donor transplants for non-malignant diseases. *Br J Haematol*. 2004 Oct;127(1):67–75.
3. Lambertenghi-Deliliers GL, Annaloro C, Della Volpe A, Oriani A, Pozzoli E, Soligo D. Multiple autoimmune events after autologous bone marrow transplantation. *Bone Marrow Transplant*. 1997 Apr;19(7):745–7.
4. Hartert A, Willenbacher W, Günzelmann S, Roemer E, Basara N, Fauser AA, et al. Successful treatment of thrombocytopenia and hemolytic anemia with IVIG in a patient with lupus-like syndrome after mismatched related PBSCT. *Bone Marrow Transplant*. 2001 Feb;27(3):337–40.
5. Daikeler T, Tyndall A. Autoimmunity following hematopoietic stem cell transplantation. *Best Practice and Research Clinical Hematology*, 2007; vol.2, No 2.pp348-360
6. Daikeler T, Tyndall A. Autoimmunity following haematopoietic stem-cell transplantation. *Best Pract Res Clin Haematol*. 2007 Jun;20(2):349–60.
7. Gluckman E, Ruggeri A, Volt F, Cunha R, Boudjedir K, Rocha V. Milestones in umbilical cord blood transplantation. *Br J Haematol*. 2011 Aug;154(4):441–7.
8. Page KM, Mendizabal AM, Prasad VK, Martin PL, Parikh S, Wood S, et al. Posttransplant autoimmune hemolytic anemia and other autoimmune cytopenias are increased in very young infants undergoing unrelated donor umbilical cord blood transplantation. *Biol Blood Marrow Transplant*. 2008 Oct;14(10):1108–17.
9. Loh Y, Oyama Y, Statkute L, Quigley K, Yaung K, Gonda E, et al. Development of a secondary autoimmune disorder after hematopoietic stem cell transplantation for autoimmune diseases: role of conditioning regimen used. *Blood*. 2007 Mar 15;109(6):2643–2548.