



Probability of Chagas Reactivation Following Hematopoietic Stem Cell Transplantation (HSCT) on Maintenance Lenalidomide - Are there Guidelines for Active Surveillance?

Mridula Krishnan^{1*}, Andrea Zimmer², Sarah Holstein¹ and Matthew Lunning¹

¹Department of Hematology and Oncology, University of Nebraska Medical Center, USA

²Department of Infectious Disease, University of Nebraska Medical Center, USA

Abstract

Chagas Disease (CD) is an endemic disease in developing countries caused by *Trypanosome cruzi* (*T.cruzi*), which has been shown to have a chronic asymptomatic phase. However, immunosuppressed patients, particularly transplant recipients (both bone marrow and solid transplant), are at a risk of reactivation of CD which can be fatal. Our primary focus involves bone marrow transplant recipients with chronic CD. There is a lack of guidelines for surveillance of these patients. We sought guidance from the Center for Disease Control (CDC) for active surveillance. We present a case of a Hispanic female with chronic CD who was on maintenance Lenalidomide following autologous hematopoietic stem cell transplant for multiple myeloma.

Introduction

Chagas Disease (CD) is caused by *Trypanosome cruzi* (*T.cruzi*), which is endemic to South and Central America and Mexico [1]. Symptoms of acute infection are often non-specific, but if left untreated, it progresses into a chronic phase. 20% to 30% of patients with chronic CD will develop cardiac or gastrointestinal involvement [1]. Transplant recipients, are at an increased risk of reactivation of a latent infection. The incidence of reactivation of CD has been estimated to be 17% and 40% following autologous and allogenic HSCT respectively [2].

Case Presentation

A 41-year-old Hispanic female was found to have a jaw mass. An excisional biopsy, revealed a plasmacytoma. Urine Protein Electrophoresis (UPEP) demonstrated 23 mg/day of protein. Free light chain assay showed elevated Kappa light chains (57.5 mg/dl) and lambda light chains (22.5 mg/dl) with a ratio of 2.56. Bone marrow biopsy showed 98% plasma cells consistent with kappa associated oligo secretory multiple myeloma. Magnetic Resonance Imaging (MRI) showed a right ilium plasmacytoma. She was started on lenalidomide, bortezomib and dexamethasone induction therapy. She achieved a complete response after six cycles which was suggested by the resolution of the plasmacytoma and also repeats bone marrow biopsy with no residual plasma cells. Given her nativity, she underwent screening for CD with *T.cruzi* enzyme strip assay which was found to be positive. Confirmatory testing with Enzyme Linked Immunosorbent Assay (ELISA) was positive. We contacted the CDC who recommended confirmatory testing to be performed including Indirect Fluorescent Antibody (IFA) and Enzyme Immuno Assay (EIA). These were positive, but Polymerase Chain Reaction (PCR) was negative. They recommended against treatment at this time. She underwent autologous HSCT. She underwent monthly surveillance with peripheral smears and PCR. She had a positive PCR twice; however this was followed up by negative peripheral smears and did not require treatment as she was asymptomatic. She was placed on maintenance lenalidomide at 3 months post-HSCT with continued surveillance for reactivation of CD.

Discussion

Lenalidomide maintenance therapy results in higher numbers of naive CD8+ T cells and memory T cells although, decreases the number of terminal effector T cells [1]. Both CD4+ and CD8+ T-cells have been shown to be important for the generation of protective immunity against

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*Correspondence:

Mridula Krishnan, Department of Hematology and Oncology, University of Nebraska Medical Center, Nebraska, USA, Tel: 402-161-1664; E-mail: mridula.krishnan@unmc.edu

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Table 1: CD reactivation following autologous and allogenic HSCT.

Author	Patient description	Pre-transplant evaluation and follow up	Pertinent details of the case	Outcome
Altclas et al., [3]	27-year-old male from Argentina	i) Positive pre-allogenic transplant serology ii) Post-transplant PCR's and blood cultures at suggested intervals for surveillance of reactivation	On day + 101, <i>T.cruzi</i> was detected in peripheral blood	Completed therapy for <i>T.cruzi</i> for 7 weeks with good response
Angheben et al., [4]	9-year-old female from Italy	No donor information about Chagas testing	Developed fever, pancytopenia and elevated liver enzymes 46 days following allogenic HSCT for ALL (which was performed in Argentina)	Succumbed to <i>T.cruzi</i> infection
Guiang et al., [5]	54-year-old female from El Salvador	Pre-transplant evaluation showed <i>T.cruzi</i> ELISA repeatedly positive -> additional serologic testing with positive antibodies to <i>T.cruzi</i> . Followed up post-transplant with weekly PCR testing	Underwent Autologous HSCT as salvage therapy for Multiple Myeloma (MM). PCR was positive (on weekly PCR testing) 15 days following transplant	Completed therapy for <i>T.cruzi</i> infection for 60 days with no complications

T. cruzi infection. We enlist a few case reports of CD reactivation following autologous and allogenic HSCT in Table 1. Our patient was diagnosed with Chronic CD as a part of her initial pre-transplant evaluation. It was hypothesized that she was probably infected as a child or a young adult in Central America. Establishing a definitive diagnosis of CD requires two or more positive serological assays or one positive assay with positive parasitological testing. PCR is the most sensitive method for detection of reactivation [2]. For our patient, the CDC recommended PCR testing weekly for 2 to 3 months followed by biweekly testing for one month followed by monthly PCR for a few months [6]. If serology was negative, parasitological testing was carried out [7]. Serologic testing of donors and recipients from endemic areas is indicated during pre-autologous transplant evaluation. Close surveillance is indicated in recipients with chronic CD. Prophylaxis can be used among seropositive recipients, but this is not a strong recommendation [3]. Also, to note at the time this article was written, the two recommended agents to treat CD, benznidazole and nifurtimox, are only available in the U.S. through the CDC. Our patient is greater than two-year post-HSCT on maintenance with lenalidomide. She has had consistently negative PCR testing for CD. At one-year post-HSCT, it was decided to stop testing for Chagas unless she was symptomatic and required further evaluation [8-10].

Conclusion

Our case report outlines proposed monitoring for reactivation in patients with chronic CD following HSCT. This is important especially in non-endemic areas with a low suspicion for CD, as a delay in the diagnosis of disease reactivation could lead to increased fatality among autologous HSCT recipients. There is a lack of established guidelines on screening for reactivation of CD for those on immunomodulating agents after autologous HSCT and requires further studies.

References

- McDaniel JM, Pinilla-Ibarz J, Epling-Burnette PK. Molecular action of lenalidomide in lymphocytes and hematologic malignancies. *Adv Hematol*. 2012;2012:513702.
- De Faria JB, Alves G. Transmission of Chagas' disease through cadaveric renal transplantation. *Transplantation*. 1993;56(3):746-7.
- Altclas J, Sinagra A, Jaimovich G, Salgueira C, Luna C, Requejo A, et al. Reactivation of chronic Chagas' disease following allogeneic bone marrow transplantation and successful pre-emptive therapy with benznidazole. *Transpl Infect Dis*. 1999;1(2):135-7.
- Angheben A, Giaconi E, Menconi M, Casazza G, Najajreh M, Anselmi M, et al. Reactivation of Chagas disease after a bone marrow transplant in Italy: first case report. *Blood Transfus*. 2012;10(4):542-4.
- Guiang KM, Cantey P, Montgomery SP, Ailawadhi S, Qvarnstrom Y, Price T, et al. Reactivation of Chagas disease in a bone marrow transplant patient: case report and review of screening and management. *Transpl Infect Dis*. 2013;15(6):E264-7.
- Altclas J, Sinagra A, Dictar M, Luna C, Verón MT, De Rissio AM, et al. Chagas disease in bone marrow transplantation: an approach to preemptive therapy. *Bone Marrow Transplant*. 2005;36(2):123-9.
- Dykewicz CA. Summary of the guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. *Clin Infect Dis*. 2001;33(2):139-44.
- Fernandes CD, Tiecher FM, Balbinot MM, Liarte DB, Scholl D, Steindel M, et al. Efficacy of benznidazol treatment for asymptomatic chagasic patients from state of Rio Grande do Sul evaluated during a three years follow-up. *Mem Inst Oswaldo Cruz*. 2009;104(1):27-32.
- Guidelines for Preventing Opportunistic Infections among Hematopoietic Stem Cell Transplant Recipients. *MMWR Recomm Rep*. 2000;49:1-125.
- Golgher D, Gazzinelli RT. Innate and acquired immunity in the pathogenesis of Chagas disease. *Autoimmunity*. 2004;37(5):399-409.