Successful Repigmentation of Vitiligo after Allogeneic Bone Marrow Transplantation for Hodgkin's Lymphoma by Autologous Noncultured Melanocyte-keratinocyte Transplantation

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Abstract

The treatment of vitiligo is derisory since the pathogenesis of vitiligo is not clear at present. Most conservative treatments are difficult to approach satisfactory therapy. So transplantation is the only way left when the disease becomes insensitive to those conservative treatments. Here we describe an 18-year-old patient who developed vitiligo, which was triggered by graft-versus-host disease after a allogeneic bone marrow transplantation for the treatment of Hodgkin's lymphoma from his sister. In the following treatment to vitiligo, the patient successfully performed the transplantation of autologous uncultured melanocyte on the premise of poor reaction to other conservative methods. We infer that transplantation can be a treatment of the vitiligo after allogeneic bone marrow transplantation.

Key Words: *Allogeneic bone marrow transplantation, transplantation, vitiligo*

What was known?
There were 19 vitiligo patients who have been reported after autologous bone marrow transplantation.

Introduction

Allogeneic bone marrow transplantation (BMT) is widely used in the treatment of various hematologic disorders, such as leukemia and aplastic anemia, and the major complication of BMT is graft-versus-host disease (GVHD). Vitiligo is not the common but can occur as a complication of GVHD. We discuss whether autologous melanocyte transplantation is an appropriate way as a treatment of the vitiligo after allogeneic BMT. In this report we describe a patient with Hodgkin's lymphoma who developed universal vitiligo after allogeneic BMT from his sister. He underwent four times melanocyte-keratinocyte transplantation (MKT) for the treatment of vitiligo; all treated depigmented patches had a significant repigmentation.

Case Report

An 18-year-old patient was diagnosed with Epstein-Barr virus-related Hodgkin-like lymphoma in 2003, and antivirotic had been used to control his lymphoma, but the treatment was ineffective. Then in March 2009, he received the histocompatibility leukocyte antigen (HLA)-matched allogeneic BMT from his sister. Cyclosporine and methotrexate were used as a prophylaxis strategy to prevent GVHD for 6 months after the allogeneic BMT. During the 6-month recovering period, the patient developed a small erythematous rash, which was consistent with the clinical features of graft-versus-host disease (GVHD) of the skin. No external agents were used and the rash dissipated in a short period of time. Small depigmented macules started to appear on his cheek 11 months after allogeneic BMT in February 2010, and followed by rapid progression to the whole body from the face to hands within 1 month. The patient had no psychological factors that may be associated with vitiligo.

Dermatologic physical examination: More than 50% of body surface were involved except feet. We indicated it to be a typical universal vitiligo by the reason that the depigmentation macules had a chalky white appearance under Wood's light.[1] Moreover, leukotrichia appeared at the same time associated with his vitiligo, affecting back and arms [Figure 1].

The depigmentation macules did not expanded any more after he received whole-body NB-UVB therapy twice a week for 2 months. Simultaneously, following the doctor's advice, 0.1% tacrolimus was used and Traditional Chinese Medicine was orally taken. The patient underwent the therapies mentioned above for 8 months in total, but with poor repigmentation. Then he discontinued medical

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therapies and performed non-cultured MKT on January 17, 2011, including left forehead and temple [Figure 2]. Almost complete repigmentation was shown after 8 months since the first transplantation [Figure 3a]. Then he received MKT on his right face on September 29, 2011. And 8 months after the second MKT, well repigmentation of his face were observed [Figure 3b]. 28 months after the first-time transplantation, all of the transplanted areas had almost completely repigmented and the color of the repigmented area matched with the normal surrounding skin excellently [Figure 3c]. Then the patient underwent the third and the fourth MKT procedure on the right and the left side of his neck respectively on May 28, 2012 and January 22, 2013 [Figure 4a]. Significant improvement was shown in the area around the left side of his neck while there's also a majority repigmentation on the right side [Figure 4b and c]. No hyperpigmentation, scar, infection and any other adverse effects on both recipient and donor sites by now were noticed.

Discussion

Vitiligo is a most common depigmentation disorder and affects 0.5-2.0% of the world population. The etiology of vitiligo remains obscure, the most prevalent hypothesis today considers vitiligo as an autoimmune disease and focuses on a melanocyte-specific cytotoxic T-cell immune reaction in the destruction of melanocytes. Vitiligo is very uncommon after BMT.[2] Sanli *et al*.[3] supported that there perhaps be four explanations for the development of vitiligo after BMT, such as the destruction of melanocytes stimulated by pretransplantation chemotherapy and radiotherapy, chronic GVHD, infusion of a larger number of lymphocytes and adoptive passive transfer from the donor to the recipient. In the case of our patient, vitiligo might be a result of an immune response directed against the melanocyte destruction initiated by GVHD. There are reported cases about allogeneic posted-BMT vitiligo. But most of the pre-BMT[4,5] diagnosis were chronic myelogenous leukemia, none of them were diagnosed with Hodgkin's lymphoma as our report. In terms of treatment during those cases, just partial of them accepted therapies, but none of them performed with transplantation.

In the BMT context, the extensive and relentless vitiligo progression indicated an aggressive alloimmune process,[6] so the destruction of melanocyte is alloimmune in nature. There was no report to make discriminate of melanocyte destruction between alloimmune and autoimmune, but Au *et al*.[6] proposed the success of melanocyte autografts for autoimmune vitiligo could be used in an alloimmune setting. Therefore, we came up with the idea of vitiligo melanocyte transplantation while other treatment was invalid for the patient.

Melanocyte grafting technique include cultured autologous melanocyte suspension transplantation and

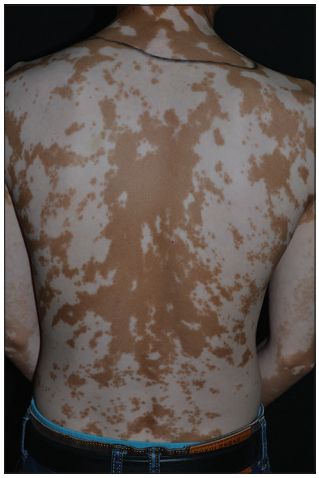

Figure 1: The patient with extensive vitiligo of the back and arms

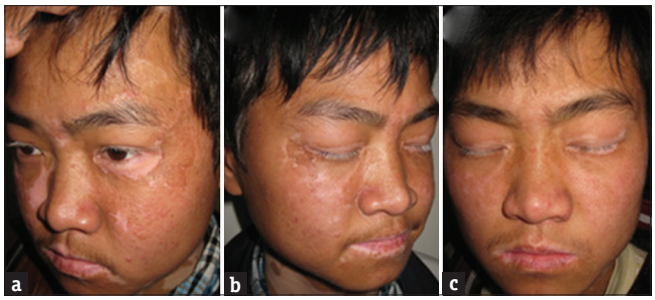

Figure 3: Repigmentation of vitiligo by MKT on his face. (a) 8 months after the first transplantation, 100% repigmentation was achieved. (b) 8 months after the second transplantation, 98% repigmentation was obtained. (c) 28 months after the first time transplantation, significant repigmentation obtained and normal skin achieved

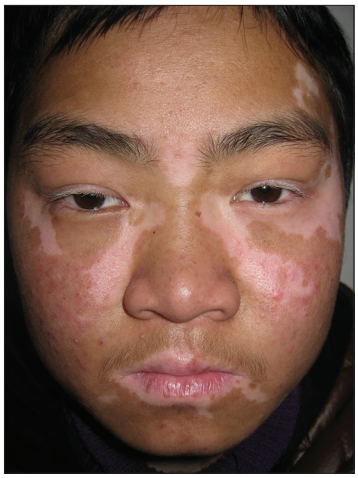

Figure 2: Leukasmus involving the face symmetrical, around the nose, eyes and mouth

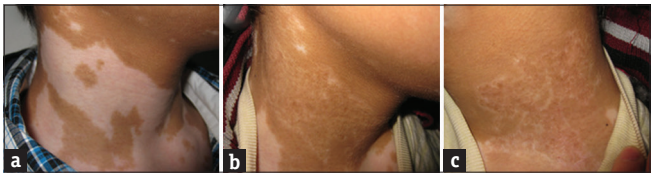

Figure 4: MKT performed on his neck. (a) Lesions before the surgery. (b) 12 months after the surgery of right neck showing nearly 100% repigmentation. (c) 4 months after the surgery of left neck showing 95% repigmentation

autologous noncultured melanocyte-keratinocyte.[7,8] In our report, the patient obtained universal vitiligo after allogeneic bone marrow transplantation for Hodgkin's lymphoma. In the condition of vitiligo failed to respond to non-surgical treatment, the patient underwent four times of MKT during 2 years. The largest area of treated lesions was 50 cm^2; repigmentation rate achieved more than 95% after each transplantation without any adverse effects or Koebner's phenomenon. The pattern of the repigmentation was uniform in the first three times MKT but diffuse in the last one; whatever, more follow-up time is needed in the future. After 2 years of follow-up, graft sites still repigmented obviously, and the color was similar to the surrounding normal skin which illustrated MKT can treat allogeneic vitiligo successfully. This is the first time to report about treating vitiligo after allogeneic bone marrow transplantation by MKT.

We suggest that autotransplantation especially autologous grafting with noncultured melanocyte is simple, safe, and inexpensive for remedying the loss of melanocyte after BMT in the case of depigmented macules is stable. But whether the melanocyte transplantation used in alloimmune vitiligo is effective as in autoimmune, we need more follow-ups.

What is new?
This is the first time to report about treating vitiligo after allogeneic bone marrow transplantation for Hodgkin's lymphoma by non-cultured melanocyte-keratinocyte transplantation without Koebner's phenomenon and adverse effects but all successful. It probably suggests that therapy of transplantation can be used in the treatment of vitiligo after allogeneic bone marrow transplantation.

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