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CASE REPORT

Generalized Vitiligo After Stem Cell Transplantation: A Case Report

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Abstract: Graft versus host disease (GVHD) is a complex immune-mediated pathophysiological process, which is caused by allogenic immune reactions between donors and recipients. No matter ac-ute or chronic GVHD, skin involvement is the most common, severe skin damage can lead to permanent disfigurement, which seriously affects the long-term quality of life of patients. We herein report a patient with generalized vitiligo after allogeneic peripheral hematopoietic stem cell transplantation (allo-HSCT) for aplastic anemia.

Keywords: graft versus host disease, vitiligo, aplastic anemia, allogeneic peripheral hematopoietic stem cell transplantation

Introduction

In vivo, GVHD is a transitional reaction in which donor-derived immune-active cells mediated attack host cells and organs.[1,2] Previous reports have documented the occurrence of localized or generalized pigment loss following transplantation, followed by the development of mossy-like skin rashes that merge into patches.[3,4] The patient experienced two separate episodes of acute GVHD after receiving an allogenic peripheral hematopoietic stem cell transplant for severe aplastic anemia. These episodes were characterized by successive systemic light red and brown rashes. After shedding, it evolved into the vitiligo-like chronic GVHD, which is rarely reported in both domestic and international publications. This report aims to draw the attention of dermatological clinicians to this possibility and early intervention, and treatment.

Case Presentation

A 13-year-old female child came to our hospital with "white spots scattered all over the body for 2 years". The patient was diagnosed with "severe aplastic anemia" at another hospital three years ago. During this period, the patient was treated with repeated red blood cells and platelets transfusion. In April 2019, an unrelated, blood group incompatible, HLA10/10 homozygous, and allo-HSCT was performed following the planned pretreatment regimen (FLU+CTX+A1G). On the 22 postoperative day, the child's extremities gradually started to show signs of pale red rash on the extremities, accompanied by multiple scattered watery pustules up to 7–8 cm in diameter. Then, the patient developed extensive desquamation. In the second month after surgery, the patient developed intermittent high fever (38°C to 39.5°C) without obvious inducement, along with a broad brown florid rash, desquamation, which was later diagnosed as "acute graft-versus-host disease, EBV infection, and cytomegalovirus infection". In the eighth month after surgery, white spots began to appear on the patient's hands, which gradually increased and became larger. The white spots further enlarged in size and spread to the entire body. Due to the improvement in bone marrow biopsy results 15 months after surgery, medications such as cyclosporin, Mycophenolate Mofetil, and hormone were discontinued. At 20 months after surgery, phalangeal joint size showed systemic scattered color recovery, which connected into flake-like, with a gradually larger area. The patient came to our hospital for a diagnosis and was diagnosed with vitiligo-like GVHD. Auxiliary examinations: skin CT (neck): which was considered

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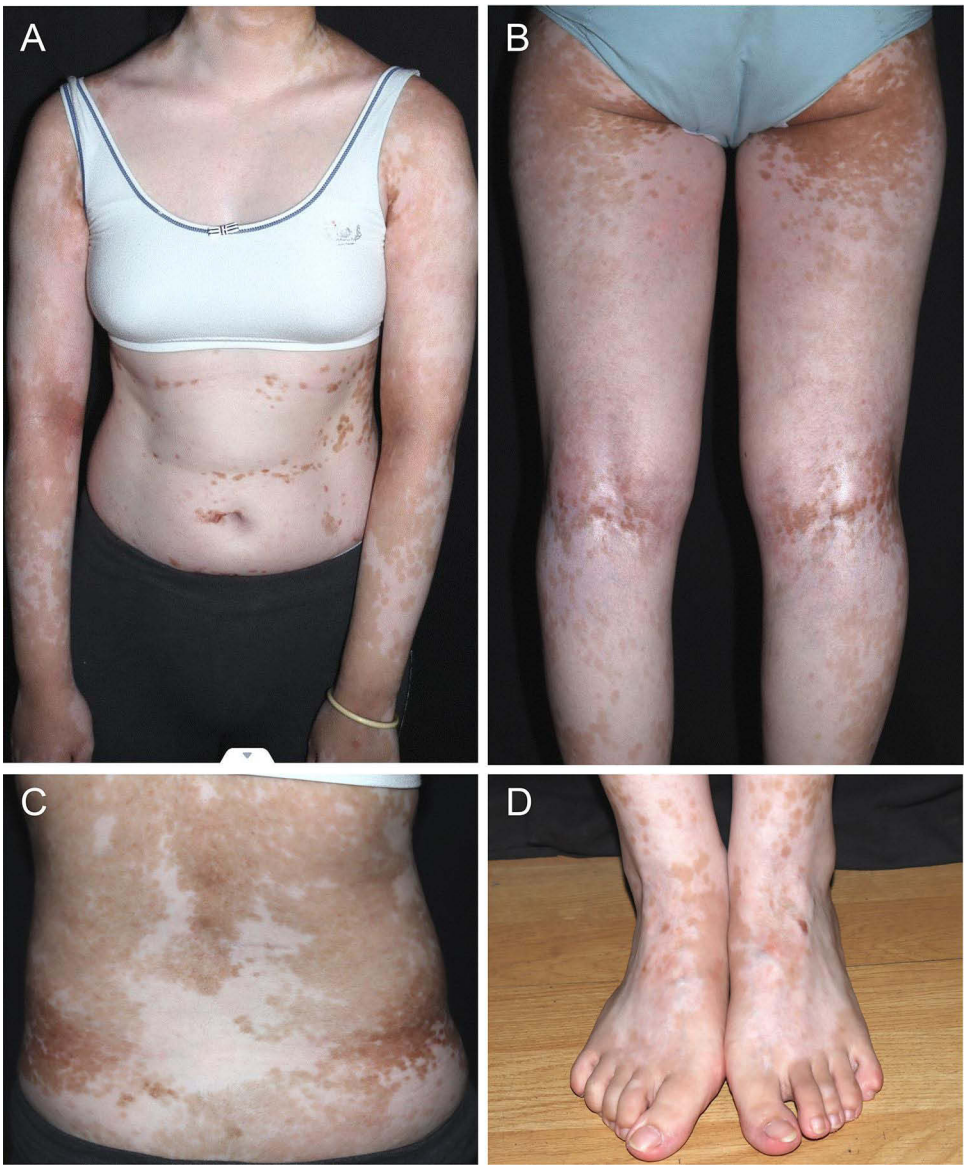

Figure 1 (**A**–**D**) Spot or patchy hyperpigmentation after generalized depigmentation.

progressive vitiligo. Laboratory tests revealed Hematology parameters: Lymphocyte subsets: CD45+: 6200 (1200–3700), CD3+: 4210 (690–2540), CD19+: 1494 (90–560), CD8+: 1556 (190–1140), CD4+: 2306 (410–1440), B lymphocytes: 24.1% (5–20%), NK: 6.4%(7–40%), with no other obvious abnormalities observed. Physical examination at the Dermatology Department suggested that the entire body had well-defined depigmented plaques in various areas were observed in the whole body, and it took up about 64% of the body's surface area. (Figure 1). In the treatment, Compound Betamethasone Injection is administered via intramuscular injection to control the progression of the disease. Additionally, Large topical application of Halometasone/Triclosan Cream once daily, 0.1% Tacrolimus Ointment twice daily, and systemic NB-UVB phototherapy once a week are implemented to manage the condition. The patient pays clinical follow-up visits currently.

Discussion

The main mechanism of GVHD, an unfavorable type IV delayed-type hypersensitivity secondary to allogenic peripheral hematopoietic stem cell transplant (allo-HSCT). Excessive pretreatments and blood transfusion of the patients before allo-HSCT increased the risk of sensitization to minor histocompatibility antigen (MIHA) in the blood donor, thus

leading to a higher risk of GVHD.[5] According to laboratory analyses of lymphocyte subpopulations, the proportions of CD3+ and CD8+T Lymphocytes increased, while those of CD4+T lymphocytes, B lymphocytes, and CD4+/CD8+ ratio decreased, revealing the immune dysfunction of the patient. Meanwhile, A clear diagnosis of progressive vitiligo in combination with auxiliary examinations. High levels of CD8+ cytotoxic T cells were detected in the peripheral blood of progressive vitiligo patients, which have cytotoxic and skin-homing abilities and may form a local immune microenvironment and migrate towards the skin tissue mediated under the mediation of chemokines and were localized within melanocytes at the dermal-epidermal junction.[6] Besides, they specifically killed melanocytes through perforin and granzyme-B.[7,8] Due to the repeated attacks of GVHD, the repeated inflammatory reactions induced persistent immune dysfunction of B cells and T cells, leading to gradual destruction, aging, acute apoptosis, and necrosis of melanocytes. These pathological changes exceeded the compensatory capacity of the body, leading to the systemic progression of skin color evolution from light red to brown to white. With the subsequent withdrawal of drugs like immunosuppressants, the immune system was restored, and the existing melanin stem cells in the hair follicles proliferated and migrated, gradually resulting in the occurrence of spontaneous color recovery.[9,10]

Conclusion

Early recognition, intervention, and treatment are essential to avoid further development of skin reactions. Considering that the patient developed systemic skin decoloration, it is crucial to prevent color recovery when necessary, maintain permanent decoloration, and identify the disease's progression mechanism, which requires further investigation.

Abbreviations

GVHD, graft versus host disease; allo-HSCT, allogeneic peripheral hematopoietic stem cell transplantation.

Consent Statement

The patient's guardian provided informed consent to publish their case details and any accompanying images. Institutional approval is not required for this case study.

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Disclosure

The authors have no conflicts of interest to declare.

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