ORIGINAL ARTICLE

Subsequent vitiligo after hematopoietic stem cell transplantation: A nationwide population-based cohort study from Korea

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Background: Subsequent vitiligo after hematopoietic stem cell transplantation (HSCT) has been described sporadically in case series.

Objective: To investigate the incidence and risk factors of subsequent vitiligo after HSCT.

Methods: A nationwide, population-based cohort study was performed using the Korean National Health Insurance Claims Database from 2009 to 2013. All HSCT recipients who had undergone HSCT between 2010 and 2011 and not treatment for vitiligo in 2009 (to exclude preexisting active vitiligo) were included in the HSCT recipient group, and an age- and sex-matched control group without HSCT was also established.

Results: A total of 2747 HSCT recipients and 8241 controls were enrolled. Newly acquired vitiligo occurred in 1.06% of HSCT recipients between 2010 and 2013, and there was a significant increase (OR 3.130, 95% CI 1.859-5.271) in cases of vitiligo in HSCT recipients compared with controls (0.34%). Allogeneic HSCT (OR 5.593, 95% CI 1.628-19.213) and bone marrow-sourced stem cells (as compared with peripheral blood-sourced stem cells; OR 2.492, 95% CI 1.114-5.576) were independently associated with the development of vitiligo after HSCT.

Limitations: Medical record review was not available.

Conclusion: Vitiligo developed at a significantly increased rate after HSCT compared with controls. Allogeneic HSCT and bone marrow—sourced stem cells were independent risk factors. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.08.064.)

Key words: hematopoietic stem cell transplantation; incidence; leukemia; nationwide population study; vitiligo.

Vitiligo is a common skin disease characterized by depigmentation of the skin resulting from selective destruction of melanocytes and affects around 1% of the population worldwide.[1] Although autoimmune factors, genetic susceptibility, oxidative stress, and cell detachment abnormalities have been suggested as etiologies,[2] the exact pathogenesis of vitiligo has not been established. Many studies have demonstrated associations between vitiligo and other systemic autoimmune diseases, including autoimmune thyroid disorders, rheumatoid arthritis, adult-onset diabetes mellitus, pernicious anemia, and systemic lupus erythematosus.[1]

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Drs Bae and Choi contributed equally to this work.

Conflicts of interest: None declared.

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The development of de novo vitiligo has often been observed in association with the treatments of malignant diseases, including immunotherapy in melanoma,[3,4] and radiation therapy for the treatment of breast cancer[5-7] and buccal mucosa cancer.[8] This phenomenon can be attributed to immunologic disturbances during cancer treatment and radiation-induced injury to melanocytes. Although subsequent vitiligo after hematopoietic stem cell transplantation (HSCT) for the treatment of leukemia has also been described in sporadic reports,[9-18] this phenomenon is not clearly understood.

We conducted a nationwide population-based retrospective cohort study using the National Health Insurance (NHI) Claims Database in South Korea. The Korean NHI covers about 98% of the 51 million populations of South Korea and is a compulsory social insurance system.[19] This study was performed to investigate the incidence rate and risk factors of subsequent vitiligo after HSCT.

CAPSULE SUMMARY

- Sporadic reports describe the development of vitiligo after hematopoietic stem cell transplantation (HSCT).
- The risk of newly acquired vitiligo in HSCT recipients is significantly increased compared with controls.
- Allogeneic HSCT and bone marrow–derived stem cells are independent risk factors for development of vitiligo after HSCT.

MATERIALS AND METHODS

Study design and database

This nationwide, population-based, retrospective cohort study used the Korean NHI Claims Database (diagnoses according to the International Classification of Disease, Tenth Revision [ICD-10] code), which contains all claims data provided by the Korea NHI program and the Korean Medical Aid program from 2009 until 2013. This study was approved by the Ethics Committee of Uijeongbu St Mary's Hospital, the Catholic University of Korea (UC16RISE0007) and was conducted according to the principles of the Declaration of Helsinki.

Study population

We enrolled all patients who had undergone HSCT between January 2010 and December 2011 and had not visited a physician with a diagnosis of vitiligo in 2009 to exclude preexisting active vitiligo (HSCT group). The control group was drawn from all individuals who had undergone hemorrhoidectomy or appendectomy in the same time period and had not visited a physician with a diagnosis of vitiligo in 2009, and three controls were randomly selected for each HSCT patient after frequency matching for age and sex to the HSCT group (control group).

Outcome of interest

The outcome of interest was newly acquired vitiligo. In the HSCT group, patients with newly acquired vitiligo were defined as those who had a documented principle diagnosis of vitiligo (ICD-10, L80) after HSCT between January 2010 and December 2013. Patients who had provided medical service under the diagnosis of vitiligo in 2009 were excluded in this study. If a patient with preexisting stable vitiligo had been provided a medical service under the principle diagnosis of vitiligo after one year of absence of clinic visits in 2009, then the patient was considered having newly acquired vitiligo after enrollment. In the control group, patients with newly acquired vitiligo were defined by the same criteria.

Covariates

To investigate the risk factors for acquiring vitiligo after HSCT, we established covariates in the HSCT group. Patients were categorized based on sex and age group (pediatric <20 years old; adults ≥20 years old). The indications for HSCT were categorized as 1) bone marrow failure disorders, including myelodysplastic syndrome and aplastic anemia, 2) leukemia, and 3) others, including lymphoma and multiple myeloma. The methods for HSCT were classified as allograft and autograft, and the stem cell sources were classified as bone marrow, peripheral blood, and cord blood.

Statistical analysis

We examined the risk of subsequent vitiligo after HSCT using multivariable logistic regression model with adjustments for age and sex. Sensitivity analysis was performed with adjustments for age, sex, and insurance level. Additional analyses were performed to determine the independent risk factors for the development of subsequent vitiligo among HSCT patients. Data were analyzed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Characteristics of the study population

We identified 2747 HSCT patients who had undergone HSCT between January 2010 and December 2011. The age- and sex-matched control group included 8241 individuals. The demographic