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ORIGINAL ARTICLE

Risk factors and treatment responses in patients with vitiligo in Japan—A retrospective large-scale study

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Abstract Vitiligo is a refractory skin disease. To investigate the risk factors and treatment responses of patients with vitiligo in Japan, we recorded and analyzed the details of 713 vitiligo patients (comorbidity, treatment responses, family history, age, and sex) who visited the dermatology clinic of the Nagoya City University Hospital, Nagoya, Japan between January 2004 and August 2010 (mean age, 35.2 years; 302 men, 411 women) using logistic regression analysis. The results are expressed as odds ratios (OR) with 95% confidence interval (CI). Patients were diagnosed with vitiligo [$n = 644$; 338 generalized type (47.4%), 170 segmental type (23.8%), and 136 localized type (19.1%)], nevus depigmentosus ($n = 53$, 7.4%), halo nevus ($n = 14$, 2.0%), and hypomelanosis of Ito ($n = 2$, 0.3%). For generalized and localized types, none of the analyzed factors were statistically significant. For the segmental type, antinuclear antibody (OR = 1.005; 95% CI, 1.00–1.01; $p < 0.05$) and onset age < 14 years were the significant factors in patients between 15 years and 29 years (OR = 0.246; 95% CI, 0.113–0.538; $p < 0.001$), 30–54 years (OR = 0.0419; 95% CI, 0.0133–0.132; $p < 0.001$), and >55 years (OR = 0.0171; 95% CI, 0.00333–0.0879; $p < 0.001$). The treatment response rates for narrow-band UV-B, topical vitamin D_3, and punch graft (1 mm minigraft) were, respectively, as follows: (1) generalized type: 46.3%, 21.1%, and 38.9%; (2) segmental type: 20.3%, 29.0%, and 77.3%; and (3) localized type: 29.2%, 54.8%, and 73.3%. We report the comorbidities and efficacy rates of these treatments. The response data for these treatments, in particular, would be of assistance to the previous explanations, because there were only a few reports

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on the response data for these treatments. The appropriate treatment should be selected depending on the type of vitiligo.

Introduction

Vitiligo is a refractory skin disease in which risk factors and treatment modalities are not yet established. There are three clinical types of vitiligo: (1) generalized type, which spreads widely over the body; (2) segmental type, which spreads along the course of a nerve; and (3) localized type, which is unclassifiable and can develop into either generalized or segmental type in the future [1]. The efficacy of treatment was different for each type [2]. Some large-scale studies were conducted in Brazilian and Chinese populations [3,4]. In these studies, the risk factors of vitiligo included thyroid dysfunction and type 1 diabetes mellitus. In Japan, Narita et al [5] reported on the comorbidities and family history 133 vitiligo patients. Zaima and Koga [1], meanwhile, conducted a long-term follow-up of about 44 localized vitiligo cases. In this study, the data of >700 patients were collected and analyzed, although there was no such large-scale study in Japan. To investigate the risk factors and treatment responses of patients with vitiligo in Japan, we analyzed the data of vitiligo patients who visited our dermatology clinic (Nagoya City University Hospital, Nagoya, Japan).

Patients and methods

A total of 713 patients of Japanese origin with a chief complaint of depigmentation (mean age, 35.2 years; 302 men, 411 women) were recruited for the study. Of these, 69 patients were excluded because they were diagnosed to have other depigmented diseases [nevus depigmentosus ($n = 53$, 7.4%), halo nevus ($n = 14$, 2.0%), and hypomelanosis of Ito ($n = 2$, 0.3%)]. Therefore, we analyzed the details of 644 vitiligo patients [generalized type, 338 (47.4%); segmental type, 170 (23.8%); localized type, 136 (19.1%)], including their background, comorbidities, treatment responses, family history, age, and sex (Table1). Furthermore, multivariable logistic regression analysis comparing segmental vitiligo against other types was performed. As an evaluation for narrow-band UV-B therapy and topical vitamin D_3 therapy, when the pigmentation was found in the treatment area, the case was evaluated as effective; if not, the case was considered not effective. The accumulative dose of narrow-band UV-B was between 5.5 J/cm^2 and 25 J/cm^2. The 1-mm minigraft therapy was one of the surgical treatment options for vitiligo. The skin donor site was the abdomen, and full-thickness grafts were obtained using a 1-mm punch (Kai Industry, Seki, Japan) following the administration of local anesthesia or full anesthesia. Using the 1-mm punch, holes were made in the vitiligo lesions with 3–5 mm between them. After hemostasis, the grafts were implanted into the holes. Overall, 3–200 grafts were done for each case. In the 1-mm minigraft therapy, when the stable pigmentation was found around the transplanted point, that case was evaluated as effective; if not, that case was evaluated as not effective. We determined the effect of topical therapy after 6 months and that of narrow-band UV-B after 30 irradiations. The effect of 1-mm minigraft therapy was determined after 1 month. A total of 323 cases (head and neck, 148 cases; body, 144 cases; extremities, 31 cases) treated using at least one of these methods were analyzed based on their location. All treatment methods were explained to the patients, who then made their own choice. Patients who had vitiligos with large surface areas tended to select narrow-band UV-B. By contrast, patients with small vitiligo lesions tended to choose topical therapy. Surgical treatment was mostly selected by patients who were unresponsive to less invasive therapies. Statistical analyses were performed using the Pharmaco Analyst II software (Human Life, Tokyo, Japan) and Excel (Microsoft, Redmond, WA, USA).

Results

Table 2 shows the comorbidities of each type of vitiligo. Overall, 7.69% of patients with generalized-type vitiligos experienced complications (i.e., thyroid dysfunction), as compared to only 0.59% for those with the segmental type ($p < 0.01$, Chi-square test). Furthermore, 3.55% of patients with generalized-type vitiligos were complicated with carcinoma, as compared to only 0.59% for those with the

Table 1 Patients' profile.[a]

Type (cases)	Men/women (cases)	Age of onset (y)	Disease duration (y)
Generalized (338)	154/184	38.45 ± 22.38	7.080 ± 9.996
Segmental (170)	77/95	11.09 ± 12.03	3.360 ± 6.243
Localized (136)	50/84	32.71 ± 24.53	3.836 ± 8.078

[a] A total of 644 vitiligo patients who visited Nagoya City University hospital between April 2004 and August 2010 were analyzed in this study. There was a significant difference between generalized type and segmental type.