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Skin, hair and nail findings in children with beta-thalassemia

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Abstract
Beta thalassemia is a disease that affects many organs and leads to mortality and morbidity. We also aimed to investigate the skin findings in children with beta-thalassemia major. Between April 2016 and September 2016, cross-sectionally 24 children with beta-thalassemia who were followed-up and transfused with blood at the Thalassemia Center of Muğla Sıtkı Koçman University were included in the study. The dermatological examinations of the patients were performed by two dermatologists. In addition to dermatological examinations, additional diseases, iron chelator agents and other treatments, hemoglobin, hematocrit, ferritin levels, accompanying skin, hair and nail findings were recorded. Seventeen of the 24 beta-thalassemia patients were male (70.8%), seven were female (29.2%) evaluated in our study. When we assessed the skin, hair and nail findings of patients; 62.5% of the patients had xerosis, 54.2% had pigmentation disorders, 33.3% had nevi, 33.3% had splenectomy scar, 25% had dermatoses, 16.7% nail involvement, 16.7% had pruritus, tinea versicolor in 8.3% and other skin findings in 37.5%. As a result, xerosis was detected as the most common skin finding in our study. The second most common disorders were pigmentation diseases. Ferritin levels were found to be significantly increased in patients with impaired pigmentation. Patients with thalassemia disease should be followed for xerosis and pigmentation diseases. Moisturizing creams and sunscreens should be recommended to patients by hematology and dermatology doctors. Our study is limited with few cases, and multi-centered studies are needed in the future.

Keywords: Beta thalassemia, dermatological diseases, skin

Introduction

Thalassemia syndromes are inherited disorders of alpha or beta globin biosynthesis. In beta thalassemia minor (TI) disease there is one defective beta-globin gene, and in beta-thalassemia major (TMJ) disease, there are two defective beta globin genes [1].

Clinical features of beta thalassemia vary between subgroups. Beta thalassemia minor is usually clinically asymptomatic, whereas infants with TMJ usually have anemia after three months [2]. It was seen growth retardation, ridging in the nasal root, prominence of maxillae, and Mongoloid facial appearance in patients without the appropriate transfusion. The dysfunctions of the organs are due to iron build-up and inadequate oxygenation, and the number of complications increases with age [2].

Growth retardation, hepatosplenomegaly, renal dysfunction, neurological/endocrine disorders, and skin pigmentation are observed in patients with beta-thalassemia [2,3,4]. As far as we know in the literature, there are few studies examining skin findings in adults with TMJ, while there is a study of skin findings in pediatric patients [5-7]. In our research; it is aimed to investigate skin, hair and nail findings in children with beta-thalassemia who have a blood transfusion and registered at the Thalassemia Center of Muğla Sıtkı Koçman University.

Material and Methods

Between April 2016 and September 2016, cross-sectionally 24 children with beta-thalassemia who were followed-up and transfused with blood at the Thalassemia Center of Muğla Sıtkı Koçman University were included in the study. The study was approved by the Muğla Sıtkı Koçman University Scientific Research and Publication Committee (Protocol No. 63). A written consent form was obtained from the participants included in the study. Two dermatologists performed the dermatological examination of the patients. The follow-up form to be used in the research was prepared by evaluating the literature on the topic [6,8-10]. The follow-up form included sociodemographic features of the participants, additional diseases, used iron

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chelator agents and other treatments, laboratory hemoglobin, hematocrit, ferritin results, skin, hair and nail findings. The data were obtained from patient follow-up forms and the hospital automation system.

SPSS for Windows 20 statistical program has been used for database creation and statistical analysis. A significance limit of $p < 0.05$ was considered by using the Verified Final Chi-Square Test, which was obtained by counting whether the level of risk encountered varied according to the independent variables.

Results

Seventeen of the 24 beta-thalassemia patients evaluated in our study were male (70.8%) and 7 were female (29.2%). One of the patients participating in the study had thalassemia intermedia, two had hemoglobinopathy, and twenty one had thalassemia major. The mean age of the patients was 10.44 ± 5.6 years. The duration of illness ranged from 1 to 15 years with a mean of 8.7 ± 5.1 years. Hemoglobin, hematocrit and ferritin levels of patients were 9.89±0.85, 30.54±2.79, 1367.60±1031.78 respectively. One patient had diabetes mellitus and 1 patient had asthma. Sixteen patients (66.7%) received deferasirox, 5 patients (20.8%) received deferiprone and 3 patients (12.5%) received deferoxamine (Table 1).

Table 1. Demographic and clinical findings of patients

Characteristic of participants	Patients (n:24)
Age(years) (mean±SD)	10.44 ± 5.6
Gender, Male n(%)	17 (70.8%)
Duration of illness (years)	8.7 ± 5.1
Hemoglobin (gr/dl)	9.89±0.85
Hemotocrit	30.54±2.79
Ferritin (ng/ml)	1367.60±1031.78
Diagnosis of patients	24(100%)
Thalassemia major	21(87.5%)
Hemoglobinopathy	2 (8.4%)
Thalassemia intermedia	1 (4.1%)
Comorbid disease	2 (8.4%)
Diabetes mellitus	1 (4.1%)
Asthma	1 (4.1%)
Chelator agents	24 (100%)
Deferasirox	16 (66.7%)
Deferiprone	5 (20.8%)
Deferoxamine	3 (12.5%)

When we evaluated the skin, hair and nail findings of patients, 62.5% of the patients had xerosis, 54.2% had pigmentation disorders, 33.3% had nevi, 33.3% had splenectomy scar, 25% had dermatoses, 16.7% had pruritus, nail involvement (onychodystrophy) in 16.7%, tinea versicolor in 8.3% and other skin findings in 37.5% (Table 2). In all patients, the scalp was considered normal.

When we look at the relationship between ferritin levels and skin findings in patients; ferritin levels were found to be high only in patients with pigmentation impairment and statistically significant ($p = 0.033$) (Table 3).

Table 2. Skin, hair and nail findings of patients

Pigmentation diseases	**13 (54.2%)**
Ephelides	5 (20.8%)
Idiopathic guttate hypomelanosis	1 (4.2%)
Pityriasis alba	6 (25%)
Cafe au lait	1 (4.2%)
Postinflammatory hyperpigmentation	5 (20.8%)
Nevi	**8 (33.3%)**
Melanocytic nevi	7 (29.2%)
Blue nevi	1 (4.2%)
Xerosis	**15 (62.5%)**
Dermatoses	**6 (25%)**
Keratosis pilaris	1 (4.2%)
Irritant contact dermatitis	3 (12.5%)
Chronic urticaria	2 (8.3%)
Nail findings (ingrown toenail,nail dystrophy,leukonychia)	**4 (16.7%)**
Hair findings	**0 (0%)**
Pruritus	**4 (16.7%)**
Scar (secondary to splenectomy)	**8 (33.3%)**
Infections (Tinea versicolor)	**2 (8.3%)**
Other skin findings (acne vulgaris, hyperhidrosis, atopic dermatitis, ichthyosis vulgaris, bullous pemphigoid)	**9 (37.5%)**

Table 3. The relationship between ferritin levels and pigmentation

		Ferritin <1000 (ng/mL)	Ferritin >1000 (ng/mL)
Pigmentation	Present	2	11
	Absent	7	4
	p value	0.033	

Discussion

Beta thalassemia is a primary endemic disease in the Mediterranean, the Middle East, and Southeast Asia, in contrast, which is rare in the European Union and North America. In beta thalassemia, significant functional and physiological abnormalities may occur in various organs due to severe anemia and severe hemosiderosis [11,12]. Growth retardation, hepato-splenomegaly, renal dysfunction, neurological/endocrine disorders, and skin pigmentation are increased in childhood [11,12]. There is one study of investigating in childhood. In this study, pruritus was the most common, followed by scarring and hyperpigmentation, respectively [5]. In our study, the most common skin findings were xerosis, pigmentation disorders and other skin diseases (acne vulgaris, hyperhidrosis, atopic dermatitis, ichthyosis vulgaris, bullous pemphigoid). No diseases were observed in hair. Nail dystrophy was the most common nail disease. In our study, ferritin levels were significantly elevated in patients with pigmentation impairment.

Xerosis is an essential psychosocial morbidity condition in which skin atrophy, erythema and pruritus are seen together due to changes in lipid ratios and a decrease in fluid retention [13]. In tissues with TMJ, deterioration of skin hydration and barrier function associated with iron deposition have been reported to increase the

risk of developing xerosis [5,8,13]. In our study, xerosis was the most common. Thalassemia is a chronic disease and we think that xerosis is the most common skin disorder due to the deterioration of the skin barrier due to recurrent blood transfusions.

As we know, pigmentation diseases such as melasma and post-inflammatory hyperpigmentation are common in dark-skinned patients. Thalassemia patients also appear darker due to hemosiderosis [6]. In our study, the second most common disorders were pigmentation disease.

One study investigated the association of skin findings with serum ferritin levels in patients with TMJ, and reported that high ferritin levels might be associated with skin findings in patients with TMJ who developed diffuse exanthematous skin findings [10]. Ferritin levels were significantly correlated with scar, hyperpigmentation, xerosis, and efelide in children with beta-thalassemia in Egypt [5]. In our study, the relationship between iron deposition and pigmentation was determined and no relation was found with other skin findings.

In the literature, skin findings of thalassemia patients due to applied iron chelator treatments have been reported [4,14]. In one case maculopapular eruption was seen, whereas in another case urticarial vasculitis was seen [4,14]. In our study, no drug eruption due to iron chelation therapy was detected. In another study, patients with deferoxamine had an increased risk of scarring, hyperpigmentation, xerosis, and efelide [5]. In our study, no relation was found between iron chelator and skin findings.

Pruritus is common in patients with TMJ. Also, few have researched skin manifestations in patients with TMj and studies carried out in Turkey and Egypt pruritus has been identified as the most frequent skin manifestations [5,6]. Because thalassemia is a chronic disease, requiring constant blood transfusions causes the skin to become dry, and itching is the result of dryness [5,6]. In our study, we found pruritus in one-sixth of the patients, and we attributed the low rate of pruritus to the duration of illness, the drugs used, and accompanying diseases such as xerosis.

Melanocytic nevi are seen in one in five of the individuals in the community. In our study, one-third of the patients had melanocytic nevi, and 4.2% of them had blue nevi. Melanocytic nevi were observed in half of the patients in the adult study [7]. We think that less melanocytic nevi are detected because our research is done in the childhood age group, duration of illness, ferritin levels are different.

Infection diseases are common due to recurrent blood transfusions in beta-thalassemia, which is a chronic disease [6]. In our study, tinea versicolor was detected as an infectious disease in 8.3% of the patients. Dogramaci et al. found tinea infection in 5% of adult thalassemia patients [6]. In a study of adult patients with thalassemia, one fourth of patients had an infectious disease [7].

In a study conducted in patients with adult thalassemia, nail disease was observed in one-third of the patients and nail dystrophy was the most common [7]. In pediatric thalassemia patients, we have not been able to find the study of hair and nail diseases in the literature. In our study, nail dystrophy was found in two patients, nail penetration in one patient and leukonychia in one patient.

Conclusion

In conclusion, in this study, skin findings in children with beta-thalassemia were examined and xerosis was detected as the most common skin finding. Ferritin levels were found to be significantly increased in patients with impaired pigmentation. It was thought that dermatologists with hematologists might be useful in the follow-up of patients with thalassemia major which is a chronic disease. Our study is limited with few cases and multi-centered studies are needed in the future.

Competing interests
The authors declare that they have no competing interest.

Financial Disclosure
The study was approved by Mugla Sıtkı Kocman University Scientific Research and Publication Committee (Protocol No. 63).

Ethical approval
Ethics committee approval was obtained.

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