Two cases of hereditary benign telangiectasia in Turkey: sporadic occurrence with punctate telangiectasias surrounded by anemic halos

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Hereditary benign telangiectasia (HBT) is a very uncommon, genetically inherited, benign skin disorder, identified by widespread cutaneous telangiectasias. Herein, we present two sporadic cases of HBT that were admitted to the dermatology clinic for multiple punctate telangiectasias surrounded by anemic halos, favoring sun-exposed areas. These cases had no mucosal or visceral involvement and exhibited no family history of the disorder. The phenotypes of HBT are clinically and genetically heterogeneous. More clinical experience and genetic analyses are needed to understand the basis for the genetic heterogeneity and to determine genotype-phenotype correlations. We aimed to emphasize the hereditary and clinical heterogeneity of HBT by presenting two cases of HBT with punctate telangiectasias surrounded by anemic halos, with a sporadic occurrence.

Key words: hereditary benign telangiectasia, anemic halo, sporadic occurrence.

Ryan and Wells[1] first described hereditary benign telangiectasia (HBT) and defined the characteristic features of the disease as a new clinical entity in 1971. HBT is a very uncommon, genetically inherited, benign skin disorder, identified by widespread various cutaneous telangiectasias, appearing generally in childhood without any associated systemic involvement or bleeding diathesis[1-3]. Herein, we present two sporadic *cases* of HBT that were admitted to the dermatology clinic for multiple punctate telangiectasias surrounded by anemic halos. These telangiectasias favored sun-exposed areas, with no visceral involvement and no family history.

Case Reports

Case 1

A 13-year-old girl was admitted to the dermatology outpatient clinic with asymptomatic multiple scattered red dots on her lips, face and the backs of her hands and forearms. The lesions had first appeared on the lips and perioral area at the age of seven years, and had increased in number and spread to the dorsal aspect of the hands and forearms gradually over time. There was no evidence for connective tissue disorders, and the patient was questioned about the presence of the Raynaud phenomenon, photosensitivity, arthritis/arthralgia, sicca syndrome and oral ulcers. She had no history of hemorrhagic episodes, epistaxis or bleeding from the mouth or gastrointestinal tract. Additionally, the patient had no previous history of any systemic disease or medication use. None of her family members (maternal and paternal grandfather, grandmother, parents, two sisters and elder brother) had any history of similar lesions or hemorrhagic episodes.

Upon dermatological examination, excessive blanching and punctate, erythematous telangiectatic vessels, surrounded by anemic halos, were seen on her lips, perioral area, ears, face and the dorsal surfaces of her hands and forearms (Fig. 1). There were no telangiectatic lesions on her trunk or legs. Upon further inspection, there was

no evidence of conjunctival, nasal, oral or genital mucosal telangiectasia. Histological examination of the telangiectatic lesion on her right forearm showed a normal epidermis with dilatation of the small vessels within the upper dermis (Fig. 2). Hematological and biochemical investigations, including complete blood count, platelet count, blood coagulation time, renal and liver function tests, serum estrogen and progesterone levels, thyroid function tests, anti-nuclear antibody, anti-double-stranded DNA and peripheral blood smear, were within normal limits, and the occult blood test on the stool was negative. In the ophthalmological and ear-nose-throat examinations, neither telangiectasia nor hematic dots were detected. From the clinical and histological findings, we made a diagnosis of HBT without family history. She was informed that the condition causes only cosmetic disability, and we suggested pulsed dye laser therapy.

Case 2

A 16-year-old girl was referred to us for painless, nonpruritic, numerous telangiectasias on her face and the backs of her hands and forearms. She had had these lesions since she was 10 years old, and the number of lesions had gradually increased. There was no history of bleeding problems, such as hemoptysis, epistaxis, gingival bleeding or hemorrhage from the mouth or gastrointestinal tract, and there was no similar history in her family. The patient was otherwise in good health, with no systemic disorders or medication use.

Upon examination, multiple erythematous fine telangiectatic vessels, surrounded by anemic halos, were seen on the patient's lips, face and the dorsal aspect of the hands and forearms, although there were no rashes on her mucous membranes or the rest of her body (Fig. 3). Histological sections obtained from the lesion on her left forearm showed dilated capillaries and venules within the upper dermis. Laboratory analyses were unremarkable, and the ophthalmological and ear-nose-throat examinations were normal. A diagnosis of HBT was made, and for treatment we recommended pulsed dye laser therapy, which the patient refused.

Discussion

Telangiectasia is a permanent abnormal dilatation of preexisting blood vessels in the subpapillary plexus of the papillary dermis[4]. HBT is a benign condition classified within the primary telangiectatic disorders. Affected individuals present with multiple, widespread cutaneous telangiectasias in various patterns, such as punctate, plaque-like, mottled, spider-like, radiating, arborizing or diffuse blush. The lesions may be limited to the light-exposed areas or scattered all over the body[2,5,6]. Punctate telangiectasia surrounded by white anemic halos is a rarely seen clinical presentation of HBT. Since its first description in 1971, there have been only a few case reports of HBT with punctate telangiectasia surrounded by anemic halos in the literature[2,6-8]. Ujiie et al.[7] suggested that the clinical appearance should be recognized as a distinctive and significant finding for the diagnosis of HBT.

The diagnosis of HBT is based on clinical examination. Differentiation of this benign entity from other primary telangiectatic disorders, and, in particular, distinguishing it from hereditary hemorrhagic telangiectasia (HHT), is important[2]. HHT is a genetic blood vessel disorder characterized by easily bleeding telangiectases on skin and mucosal surfaces that are associated with the presence of arteriovenous malformations in multiple organ systems. Nosebleeds are almost always the first prominent symptom; telangiectasias and visceral organ involvement then occur. Mucocutaneous telangiectasias, which are most often situated on the lips, tongue, nasal mucosa, palate and buccal mucosa, conjunctiva and ears, increase in size and number with age. Arteriovenous malformations may affect the lungs, brain and gastrointestinal tract and may entail potentially life-threatening manifestations such as gastrointestinal hemorrhage, pulmonary hemorrhage or stroke.[9] In most cases, the two disorders are easily distinguishable because of the absence of hemorrhagic diathesis, mucosal involvement and other systemic lesions in HBT. But cases with mucosal telangiectasias should be under follow-up for detection of the development of HHT, which has a broad range of different clinical organ manifestations. Generalized essential telangiectasia, which is more common among adult women without a family history, mainly occurring in the lower extremities and showing progression over time, is easily differentiated from HBT by the clinical

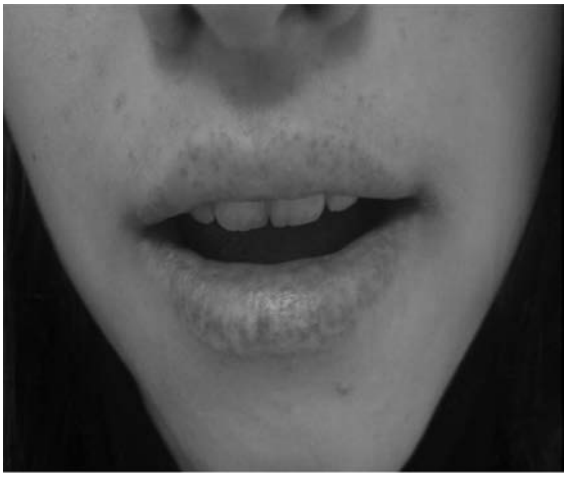

Fig. 1. Punctate telangiectases on the lips.

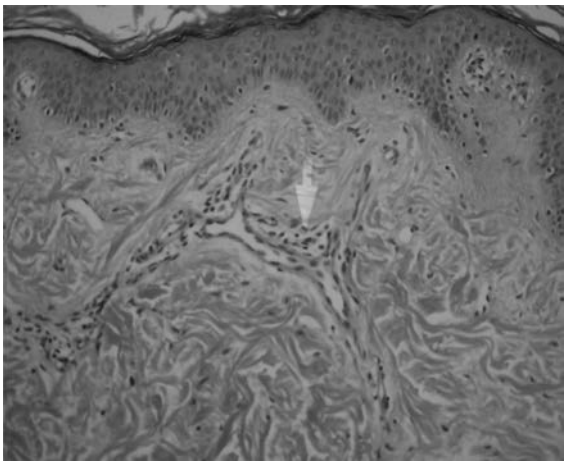

Fig. 2. Dilatation of the small vessels within the upper dermis (haematoxylin and eosin staining; original magnification X 4)

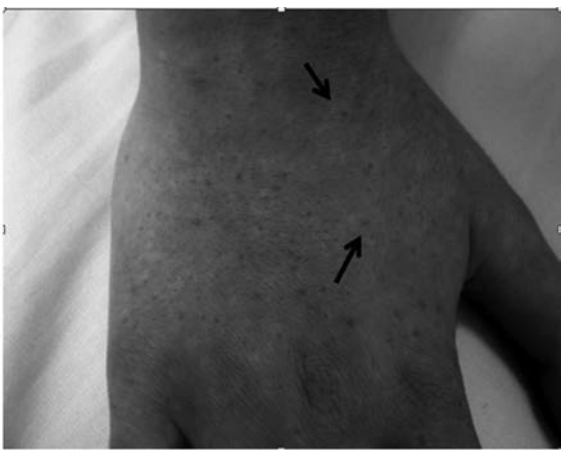

Fig. 3. Punctate, erythematous telangiectatic vessels surrounded by anaemic halos on the dorsal surfaces of the hands

features[10]. Port-wine stains, nevus flammeus, angioma serpiginosum, unilateral nevoid telangiectasia and telangiectasia macularis eruptiva perstans should also be kept in mind as differential diagnoses of HBT[2,11,12].

In this paper, we described two girls with numerous telangiectasias, restricted to sun-exposed areas, distributed over the face and dorsal aspects of the hands and forearms. Both girls were in good health, with no bleeding problems or mucosal or systemic involvement. When the disorders above were considered, and based on the clinical and histological findings, HBT was determined to be the best diagnosis for the punctate telangiectasias surrounded by white anemic vasoconstricted halos, with a sporadic occurrence.

The precise etiology of HBT remains unknown, and the condition is presently considered to be inherited in an autosomal dominant pattern[1,2,5,6,13]. Several familial cases of HBT have been reported, showing inheritance in an autosomally dominant fashion[5,6,13]. However, in 2006, HBT without a family history was described by Nakajima et al.[11] for the first time. The patient was a 22-month-old girl with scattered erythematous telangiectasias and telangiectatic patches of varying sizes, distributed mainly on light-exposed sites, including the face, forearms and upper body. In 2011, Cai et al.[12] reported the case of a 39-year-old woman in China with telangiectasias and telangiectatic erythema, especially on light-exposed sites, which was diagnosed as HBT.

A genetic analysis of a large family, by Brancati et al.[13], included 13 members over three generations with the diagnosis of autosomally dominant HBT, with the telangiectasias distributed in various locations. The researchers suggested a locus in the 7-Mb region of chromosome 5q14 as the possible cause of the disease. The linked interval was identical to the capillary malformation (CMC1) gene. In 2007, Molho-Pessach et al.[5] presented a four-generation pedigree, including 23 members, with HBT lesions distributed over sun-exposed areas, displaying autosomally dominant inheritance, possibly with incomplete penetrance. They conducted a genetic analysis to determine whether photodistributed HBT is linked to the same CMC1 locus described by Brancati et al.[13] However, they did not find a linkage

between the CMC1 locus and photodistributed HBT, and suggested that photodistributed HBT is not related pathogenically to capillary malformations or to nonphotodistributed HBT, and that it deserves to be recognized as a separate disorder.[5]

There are diverse clinical appearances of HBT, but the distinction between photodistributed and nonphotodistributed HBT has not been made. When we conducted an overview of the literature, considering the suggestion asserting that photodistributed HBT was a separate entity, we saw clinical heterogeneity. Lesions, varying from point-like telangiectasias to erythematous patches of various diameters, were seen in cases with both photodistributed and nonphotodistributed HBT[1,2,5-8,11-13]. Lesions of the anemic halo punctate telangiectasia variant appeared mainly on the face, upper extremities and upper trunk, and all of these cases (except ours) had a family history[2,7,8]. However, in the two previously reported cases of HBT without a family history, and the sporadic cases presented herein, the telangiectasias were mainly distributed in light-exposed areas[11,12]. There are many familial cases of HBT presenting with photodistributed lesions[5].

In conclusion, the phenotypes of HBT are clinically and genetically heterogeneous. More clinical experience and genetic analyses are needed to understand the basis for the genetic heterogeneity and to determine genotype-phenotype correlations. We aimed to emphasize the hereditary and clinical heterogeneity of HBT by presenting cases of HBT with punctate telangiectasias surrounded by anemic halos, with a sporadic occurrence.

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