Case Report

Spontaneous regression of divided nevus of the eyelid evaluated by dermoscopy leaving a hypopigmented lesion

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Abstract

Background: Divided nevus, also known as “kissing nevus,” is a rare form of congenital melanocytic nevus that occurs on opposing margins of upper and lower eyelids. A paucity of literature on this rare anomaly exists, with most being case reports and series. Moreover, regression of this lesion was rarely reported.

Case Illustration: We present a rare case of congenital divided nevus of the eyelid that regressed after eight years, confirmed with dermoscopy. A six-year-old boy presented to the Dharmais National Cancer Hospital with two pigmented macules on the upper and lower right eyelid since birth. A year ago, the lesions started gradually disappearing and were replaced by a hypopigmented area. We evaluated the clinical and dermoscopic findings for two consecutive years. The dermoscopy showed pseudopigmentation networks, surrounded by a hypopigmented area resembling a halo. The pigmented lesions cleared with no residual lesions.

Discussion: The dermoscopic findings of the patient resemble a solar lentigo characterized by pseudopigmentation networks, a feature caused by the relatively flattened rete ridge on the face. The hypopigmented area reflects a regression process, like the halo nevus, and is accompanied by leukotrichia of the eyelashes, a feature usually found in patients with vitiligo. Regression of the divided nevus is related to an autoimmune process. A similar mechanism was also found in vitiligo. Since no atypical findings were present in this patient, we recommend only observation.

Conclusion: Divided nevus is a rare case. We present a case of congenital divided nevus of the eyelid that regressed spontaneously. Clinical and dermoscopic findings of hypopigmented regression area were similar with vitiligo, which might share similar pathological mechanisms.

Keywords: divided nevus, eyelid, regression, dermoscopy, vitiligo

Background

Divided nevus, also known as “kissing nevus,” is a rare clinical variant of congenital melanocytic nevus that involves areas of the body that undergo embryonic cleavage. Divided nevus can occur on the upper and lower eyelids of one eye, which is called “panda” nevus. The two nevi form a large one when the eyelid is closed.¹² The eyelids are formed between weeks 5 and 6 of embryo development, fuse around week 9 or 10, and reopen during the sixth or seventh month in utero. Hence, the divided nevus is formed before the seventh month, but after week 9 or 10. This kind of lesions was originally described in 1908, and only a few cases have been reported since then.²

Cases of divided nevus of the eyelid usually prompt the patient or family to seek medical treatment, such as surgical or laser removal. In cases of congenital nevus, the spontaneous regression is not prevalent. Leukoderma acquisitum centrifugum consists of halo depigmentation around a nevus, a process referring to its regression. The halo nevus is more
frequent in patients with acquired nevi, particularly in childhood and adolescence. Although not numerous, cases of halo nevus have been reported in congenital melanocytic nevi (CMN). The association of halo nevus with vitiligo is still unclear.3,4 Here, we present a patient with congenital divided nevus of the eyelid which has spontaneously regressed after seven years, mimicking a vitiligo lesion, and it was evaluated using dermoscopy.

Case Illustration

A six-year-old boy presented to our clinic with a history of two pigmented macules on his upper and lower right eyelids that slowly faded since several months ago. At birth, his mother noticed slight erythematous discoloration on the lower lid. In six years, the two macules became more hyperpigmented and obvious on the upper and lower lids, forming a large one when he closed his right eye. The size and extent of the lesion increased in proportion to the child’s growth (Figure 1). The macules became partially hypopigmented when he was six years old.

There was no similar history of illness in the family. The patient did not use topical medications or laser or have surgery to remove the moles. The patient’s mother worried about the gradual change of the lesions that became more hypopigmented over the last year. The clinical and dermoscopic images of the lesions were obtained within two-year follow-up. In the first visit in June 2018, below the right eye, hypopigmented macules with a pigmented area in the lower quadrant of the hypopigmented lesion were present. Some eyelashes were depigmented (leukotrichia). At the initial visit, a dermoscopic examination of the brown pigmented lesion showed pseudopigment networks or reticular pattern surrounded by a peripheral hypopigmented area resembling a halo.

We evaluated the lesions every six months and found that the pigmented area gradually disappeared and changed into a hypopigmented lesion (Figure 2). Leukotrichia of the eyelashes was still present. The dermoscopic examination also showed the disappearance of the networks, leaving a depigmented area, inverse networks, and several vascular patterns. We concluded that the melanocytic lesions had spontaneously regressed.

We observed the hypopigmented lesion and instructed the patient to use topical betamethasone valerate ointment. Histopathological examination of the lesion was being considered while monitoring the response of the topical steroid. For publication purposes, an informed consent was obtained from the parents.

Figure 1. Divided nevus of eyelid, not much change on the extent of the lesions. (A) Age of one week, (B) 2-month-old, (C) Age 2-year-old. Courtesy of patient’s parents, reproduced with permission
Figure 2. Clinical (left) and dermoscopic (right) evaluation of the lesions. Pictures taken in (A-B) June 2018 (six years old), (C-D) December 2018 (six years old), (E-F) July 2019 (seven years old), and (G-H) December 2019 (seven years old).

Discussion

CMN results from post zygotic mutations of proteins involved in the mitogen-activated protein kinase (MAPK) pathway within the embryonic melanocyte. These primarily include mutations of NRAS, resulting in abnormal accumulation of melanocytic cells along the migration pathways during normal development. This mutation is evident in large and giant CMNs, whereas small- and medium-sized lesions have been reported to have NRAS or BRAF mutations. Mutation in congenital divided nevus occurred when the nevus cells migrated to the eyelid in time after the fusion of eyelid by week 9 or 10, but before the eyelid separated on weeks 28–30.2,5,6

Dermoscopy has been extremely useful in diagnosing cutaneous pigmented lesions; it assists long-term follow-up and prevents unnecessary biopsies and surgeries. A case report from Spain showed dermoscopic features of a divided nevus on the penis. Both macules revealed melanocytic lesions in a compound.
in the periphery, there was a fine pigment network and multiple sized darkened globules in the center. Another case report shows dermoscopic findings of globular and globular-reticular composite (reticular network at the periphery and a variable number of globules in the central area) patterns, which are consistent with four previously reported pediatric cases. 

The dermoscopic features of eyelid divided nevus are also show the same with other melanocytic nevi. A study on 13 patients with eyelid divided nevus showed that the predominant structural patterns, identified before regression, were globular, reticular, homogeneous, parallel furrow, or mixed. Moreover, the dermoscopic features of the lesion on regression were described, including depigmentation and loss of structure and the presence of a greyish-whitish veil, greyish pepper-like granules, and vascular structures. 

The dermoscopic findings of the melanocytic lesion in our patient appeared as pseudonetwork patterns. The pigment network is usually absent on the face because of the relatively flattened rete ridges and is replaced by a pseudonetwork. The pigments were surrounding the “holes” that represent adnexal openings histologically. In our patient, there were aggregates of pigments that did not regularly distribute, a feature that can also be seen in solar lentigo. However, this feature then disappeared in the follow-up. The inverse networks and several vascular patterns appeared afterwards, indicating a regression process.

In a study on 217 pigmented lesions, including melanoma and benign lesions, described various features of regression. The features included atypical network, inverse network, atypical vascular pattern, irregular streaks, pink areas, and hypopigmented areas. These features were evident in both the melanoma and nevi, while blue-white veil, blue-gray areas, white scar-like areas, peppering, blue-gray globules, and regression >50% were statistically significant for melanoma lesions.

In the first visit, we observed that the melanocytic lesion was surrounded by a peripheral hypopigmented area resembling a halo. Given these findings, we concluded that the nevus was undergoing spontaneous regression, which may be related to an autoimmune process. Several publications have also described the regression of divided nevus. A case of a congenital divided nevus of the eyelid followed by gradual depigmentation at the age of 13 was reported from Spain. The depigmented area increased in size and a slight lightening occurred in the middle of the nevus. The patient was diagnosed with halo nevus on a congenital nevus. However, at the age of 15, he also had similar depigmentation in the contralateral periocular region, accompanied by whitening of the eyelashes of both eyes. He underwent skin biopsy of two lesions. The nevus specimen showed a congenital melanocytic nevus, and the depigmented region around the nevus showed unaltered skin with residual skin pigmentation but no inflammatory component. The nevus remained stable, with no clear signs of regression. Whether the lesions of both eyes are of the same entity or represent a halo nevus and a vitiligo was still debatable. 

The spontaneous regression has also been described in almost all types of cancers and occurs frequently in both the benign and malignant pigmented lesions on the skin, where the depigmentation is more visible. The halo nevus features have traditionally been thought to typify the regressing lesion. The underlying mechanism of regression was considered immune responses, apoptosis, inhibition of angiogenesis, terminal differentiation, and genomic instability. An immune mechanism seems to be the most consistently associated with melanocytic tumor regression.

Histologically, melanocytic nevus undergoing spontaneous regression showed the replacement of tumor cells with a fibrous stroma having varying degrees of inflammation, new blood vessel formation, and various numbers of melanophages. This process was considered related to the destruction of melanocytic nevus cells or cessation of pigment production. Melanocytic nevus cells express major histocompatibility complex class I (MHC class I) antigens, which allow recognition as a target for cytotoxic T cells. 

Although not numerous, cases of halo nevi have been reported in congenital melanocytic nevi. In addition, halo nevus is also frequently associated with the occurrence of vitiligo. Multiple halo nevi, the presence of Koebner phenomenon, and a family history of vitiligo are possibly adding to the risk factors for developing vitiligo in patients with halo nevi. These two phenomena can be seen in the same patient at the same time or different times. Whether the halo nevus and vitiligo share the same phenomenon or different processes remains unknown.

There are several explanations on an association between halo nevus and vitiligo. They both share
the same histological features, including infiltration of cytotoxic T cells (CD8) outnumbering T helper cells (CD4), absence of melanocytes, and scattered melanophages. Although various theories have been suggested, the precise etiology of both entities is unknown. In halo nevus, an immunologic mechanism has been proposed. Some studies show specific antibodies against nevus and melanoma cells. In a study reporting antinevus antibodies were also detected in both the halo nevus and vitiligo lesions using immunofluorescence. Both humoral and cellular immunity may be involved in the reactions against nevus cells and in the formation of the halo.

Various theories on the etiopathogenesis of vitiligo have been investigated; some of them involve neurotoxic agents, autoimmunity process, and damage of melanin. The immunologic process, as in the case of halo nevus, has also been proposed. The final result of both conditions is the regression or disappearance of melanocytes. The latest studies on vitiligo indicate that cytotoxicity is responsible for this destruction.

In our patient, the depigmented area appeared around the nevus described as a halo nevus, but the presence of leucotrichia imposes the question of whether it is merely a regression process of a nevus or an autoimmunity process of vitiligo. Unfortunately, we have not done the skin biopsy examination. We decided to observe the lesion while doing the routine follow-up using dermoscopy alone. We gave the patient topical steroid for treatment of vitiligo.

Another differential diagnosis that should be well excluded in the case of regression is melanoma showing halo-like regression. Clinically, the halo surrounding a regressive melanoma is usually more asymmetrical, and, in most cases, the central lesion is more irregular in shape, borders, and coloration. In addition, melanoma with halo-like regression may display a dermoscopic multicompontent pattern (i.e., simultaneous presence of atypical pigment network, blue-white veil, irregular dots/globules, and regression structures), a feature which we did not see in this patient.

The evolution of congenital melanocytic nevus is difficult to predict. It could regress with or without developing a halo nevus or vitiligo, and on the contrary, it may remain stable and exhibit repigmentation of the halo nevus area. Follow-up is essential. Histopathological examination and immunofluorescence antibody detection are the best options to confirm the pathological mechanism.

Conclusion

We present a case of spontaneous regression of a congenital divided nevus of the eyelid. The dermoscopic finding revealed a pseudopigment network surrounded by a hypopigmented area resembling a halo. The presence of a hypopigmented lesion and leukotrichia suggest developing vitiligo, which share possible similar mechanisms with the regression process of melanocytic nevi. Since there are no atypical findings in this patient, we suggest that only observation is needed.

References


