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Halo Phenomenon with Regression of Acquired Melanocytic Nevi: A Case Report

Jaka Radoš[1], Zrinjka Paštar[1], Jasna Lipozenčić[1], Ivana Ilić[2], Daška Štulhofer Buzina[1]

[1]University Department of Dermatology and Venereology, [2]Department of Clinical Pathology, Zagreb University Hospital Center and School of Medicine, Zagreb, Croatia

Corresponding author:
Jaka Radoš, MD, MS
University Department of Dermatology and Venereology
Zagreb University Hospital Center Center and School of Medicine
Šalata 4
HR-10000 Zagreb
Croatia
sodarakaj@yahoo.com

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SUMMARY We report a case of halo-phenomenon in excisional biopsy of junctional nevi in a 19-year-old girl. The diagnosis was established histopathologically because of the lack of clinical halo and unspecific dermoscopic features. Clinicopathologic difficulties in establishing the diagnosis of these pigmented lesions, etiopathogenesis and differential diagnosis of halo nevi are emphasized. Dermatologists should be familiar with the possible changes in benign melanocytic nevi, halo reactions and possible complete regression of melanocytic nevi. Diagnostic difficulties are seen in the ultimate phase of regression when melanocytes are diminished or destroyed with immune reaction.

KEY WORDS: halo nevus, halo phenomenon, regression of nevi

INTRODUCTION

The halo nevus (HN) presents clinically as a pigmented melanocytic nevus surrounded by a hypopigmented border. Histologically, HNs demonstrate dense lymphocytic infiltrates that permeate a portion of or, sometimes, all the melanocytic lesion. The term “halo reaction” or halo phenomenon refers to the nevi that demonstrate dense lymphocytic infiltrates histologically, but lack halo clinically. In these cases, the diagnosis is established on the basis of histologic examination (1-4).

We present a case of halo phenomenon of acquired melanocytic nevi that was established by histopathology, since the clinical and dermoscopic diagnosis was equivocal.

CASE REPORT

A 19-year-old girl with skin type I presented with symptomless, sharply demarcated erythematous papules on the left breast that had appeared six years before. Clinically, there was an erythematous papule measuring 9x4 mm perimammillary; in the upper lateral quadrant of the left breast there was a papule measuring 4x3 mm (Fig. 1a,b). The halo was seen neither clinically nor with Wood lamp. Thorough inspection of the entire skin revealed no further abnormalities. Dermoscopy revealed erythematous homogeneous pattern and brown streaks distributed symmetrically at the periphery (Fig. 2). According to brown streaks seen on dermoscopy, this lesion could have been classified

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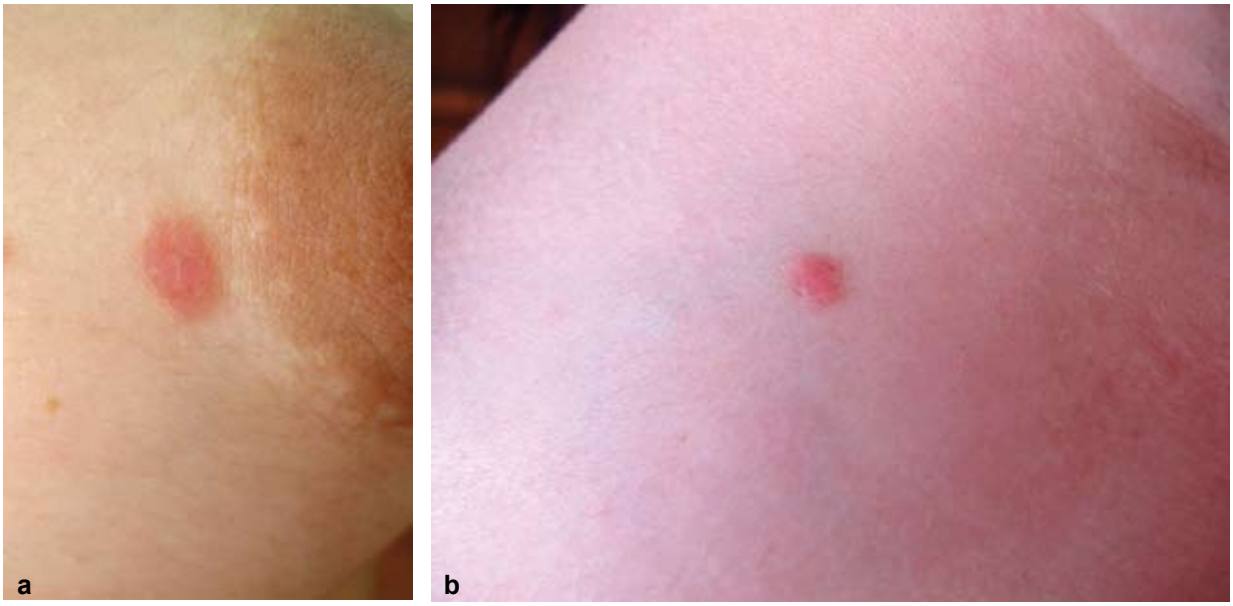

Figure 1a,b. Two symptomless erythematous papules on the left breast; a papule measuring 9x4mm in the perimammillary region and a papule measuring 4x3mm in the upper lateral quadrant of the left breast.

as melanocytic lesion and working diagnosis was Spitz nevus. However, differential diagnosis also included non-melanocytic lesions such as adnexal tumors. As the clinical and dermoscopic diagnoses were equivocal, the lesions were excised to make definitive diagnosis.

The patient's personal and family history for atopic dermatitis, vitiligo, thyroid disease, melanoma, and dysplastic nevus syndrome was negative. In the last two years, solarium was used 4 times a year; in childhood she experienced sunburns.

Histology of the lesion in the upper lateral quadrant revealed dense lichenoid infiltrates of mononuclears and fibroplasias in the upper dermis; rare nests were seen at the rim of the dermoepidermal junction (Fig. 3). Staining with HMB 45 was positive exclusively at the dermoepidermal junction (Fig. 4).

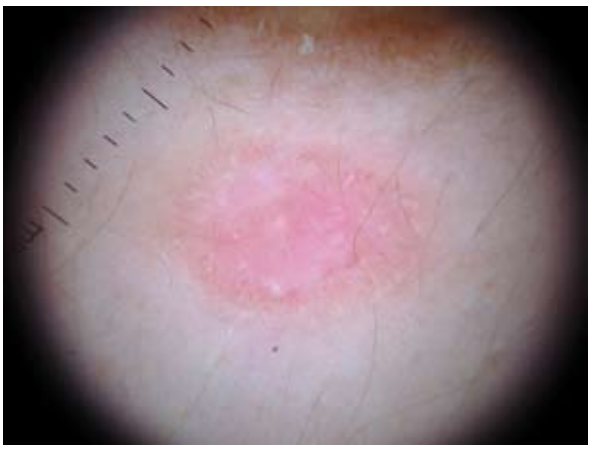

Figure 2. Dermoscopy findings: erythematous homogeneous pattern; brown streaks at the periphery (DermLite II PRO-HR, 3Gen, LLC; Sony DSC-P200; original magnification, X10).

In the perimammillary lesion there were single melanocytes and rare melanocytic nests at the dermoepidermal junction, with moderate lymphocyte and histiocyte infiltration. In both cases, histologic diagnosis was melanocytic junctional nevus with halo phenomenon.

DISCUSSION

HNs, also known as Sutton nevi or *leukoderma acquisitum centrifugum*, are defined as benign melanocytic nevi surrounded by a rim of depigmentation area measuring several millimeters and resembling a "halo". It is more common in children and younger adults, with an average age of onset at 15 years. In some patients there is a high number of HNs, their preferential site may be the trunk, and they may be grouped (1,2). The incidence of HNs in the population is around 1% (5).

There is no sex or racial predilection. Familial occurrence and association with atopic dermatitis, autoimmune disorders like vitiligo or Hashimoto thyroiditis have been described (1,2). Association with melanoma is rare (6).

During the period of several months or even years, HNs have a tendency to go through four

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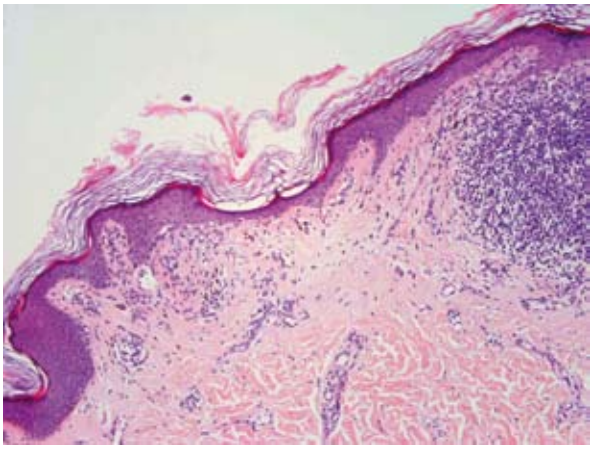

Figure 3. Histology of the lesion in the upper lateral quadrant: dense lichenoid infiltrates of mononuclears and fibroplasias in the upper dermis and rare nests in the periphery at the dermoepidermal junction (hematoxylin-eosin stain; original magnification, X25).

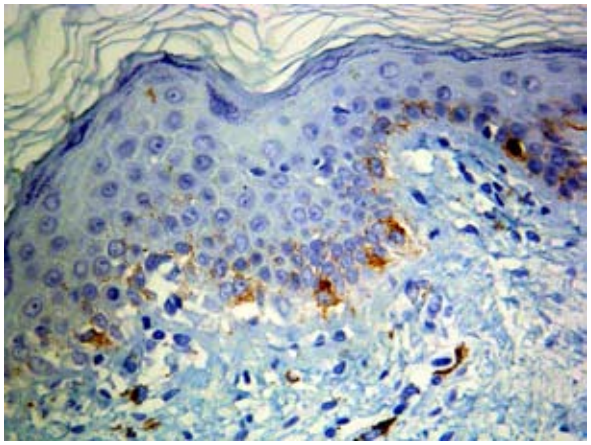

Figure 4. Staining with HMB 45 positive exclusively at the dermoepidermal junction (original magnification, X40).

clinical stages with subsequent progressive involution that ends in total regression of central nevus. Each pathologic stage is characterized by the cellular profile of the inflammatory cell infiltrate. In stage I or pre-regression stage, nests of nevus cells are surrounded by a moderate number of T-lymphocytes. In stage II or early regression stage, there are nests of nevus cells in close contact with an increased number of T-cells, and Langerhans' cells. Stage III or late regression is characterized by isolated nevomelanocytes with mild atypia scattered among the inflammatory infiltrate. Finally, in stage IV or complete regression stage, there are a moderate number of inflammatory cells with no nevus cells. Moreover, coexistence of different stages may be present in the same nevus (7,8).

The etiology of halo phenomenon is not known. Sometimes it follows sunburns, application of topical bleaching preparations, or it is idiopathic (1,2). Histologic changes can also be seen in UV exposed or traumatized nevi and higher metabolic activity as a result of trauma induced reparatory mechanisms has been postulated (9,10). These molecular alterations could be antigen structures that induce immune response (7,11,12). As previously mentioned, HNs can be associated with vitiligo and rarely with melanoma (6,13). Patients with halo nevi very often have circulating antibodies to cytoplasmic antigens in melanoma cells (7). These antibodies disappear upon excision or spontaneous resolution of the central lesion (1,2,7). Therefore, the possible connection between halo nevi and melanoma could be through atypical changes of melanocytes' nuclei that are usually found in halo nevi (11). These atypically changed nuclei can act as initial factors for immune mechanisms (7,11). Once the immune system has been stimulated, it recognizes simple antigens in malignant/atypical and also in normal cells. Therefore, the immune mechanism can cause halo phenomenon in cross reaction with normal nevi, which would explain multiple halo nevi in some individuals (7).

The pathogenesis has not yet been fully elucidated, as the impact and ratio of cellular *versus* humoral immunology is unknown. T-lymphocytes, especially cytotoxic T-lymphocytes, have significant impact in progressive destruction of nevus cells (7). This is confirmed by immunohistochemistry with abundance of antigen presenting cells in the regressing nevus and presence of T-lymphocytes at the site of depigmentation (8). The influence of circulating antibody as a secondary factor in immune elimination of nevus cells and associated vitiligo remains a possibility (7). The role of B-cells in the halo phenomenon is not known as some suggest that B-cells do not have a significant role, while others suggest that it may play a role in regression of HN (7,8,11,12).

However, as mentioned above, antibodies against the cytoplasm of melanoma cells that disappear with regression or surgical excision are produced in patients with halo nevi (7). This antibody production may occur after cell mediated lysis of the nevus cells with concomitant release of the nevocellular antigen that stimulates B-cells, or activated CD4 positive helper T-cells may stimulate B-cells *via* production and release of lymphokines to undergo differentiation with subsequent production of a specific antibody (7,8,11,12).

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Halo phenomenon is a histologic term and it is not only reserved for melanocytic lesions as it can be in association with neoplastic and inflammatory diseases, e.g., neurofibroma, histiocytoma, basalioma, seborrheic keratosis, sarcoidosis and psoriasis (1-4). The prototype of halo lesion is classic HN. HN is not a unique clinicopathologic entity. Lesions are classified on the nevomelanocytic basis according to conventional criteria into junctional, compound, intradermal and Spitz nevus (1-4). Therefore, any actual classification of nevi can be used as long as the "halo phenomenon" is emphasized. Microscopic criteria for halo phenomenon include obligatory lichenoid lymphohistiocytic infiltrates with diminishing or disappearance of melanin pigment in the periphery at the dermoepidermal junction (1-4).

The most important differential diagnosis of HN is melanoma. Typically, in regressing melanoma or dysplastic nevi there is mitotic activity, and nuclear and cytoplasmic pleomorphism that is not seen in HN. However, halo reaction can also cause increased cytologic atypia in lesional melanocytes and obscure the architectural features of the underlying nevus, making distinction between a benign melanocytic nevus and melanoma more difficult (4). Furthermore, the cellular infiltrate accompanying melanoma is usually more monomorphic and is often located at the base of the tumor rather than actively infiltrating it, except for those undergoing regression (1,2).

Another differential diagnosis includes Meyerson's nevus, in which there is an eczematous halo surrounding the nevus (14).

In nevus with halo phenomenon the number of nevus cells depends on the stage at which the biopsy is taken. Identification of residual nevus cells can be done by immunohistochemical staining with S100 protein in cases in which a dense inflammatory infiltrate tends to obscure the nature of the lesion (1-4).

Dermoscopy increases diagnostic accuracy of melanocytic lesion over clinical visual inspection, and therefore influences subsequent therapy. The most frequently observed pattern in HNs is globular and/or homogeneous pattern (15). On the contrary, dermoscopy of melanoma with halo reveals the multicomponent structure with asymmetry such as atypical pigment network, blue-white veil, irregular dots and globules, streaks, regression structures and colors that vary from white, brown to blue and black (15). In "featureless" melanomas such as amelanotic or hypomelanotic melanoma, which lack specific surface microscopic features (16), dermoscopy has great limitations and surgical excision of unspecific lesions is based on thorough history and clinical examination.

CONCLUSION

With this case, with no associated diseases with HNs except for the risk factor of UV exposure, we give an insight into the evolution of pigmented lesions and explanations for uncharacteristic clinical and dermoscopic features. In advanced stage of regression with almost complete loss of melanocytes, clinical and dermoscopic diagnosis of melanocytic lesions is impossible while histologic diagnosis is harder if melanocytes are completely missing.

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