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Review

»Halo Nevi« and UV Radiation

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A B S T R A C T

Halo nevi, also termed Sutton nevi, are defined as benign melanocytic nevi that are surrounded by an area of depigmentation resembling a halo. Halo nevi are common in children and young adults, with a mean age at onset of 15 years. The incidence in the population is estimated to be approximately 1%. Affected individuals frequently have multiple lesions which are usually localized on the back. A familial tendency for halo nevi has been reported. The etiology of halo nevi is unknown. It is an autoimmune response and T lymphocytes are considered to play a key role in the progressive destruction of nevus cells. Halo nevi may be associated with autoimmune disorders such as vitiligo, Hashimoto thyroiditis, alopecia areata, celiac disease, atopic dermatitis and others. It has been proved that halo nevi are detected after an intense sun exposure especially after sunburns. The etiology of halo nevi, association with malignant melanoma and the role of sun exposure in the development of halo nevi are discussed.

Key words: *halo nevi, UV radiation, malignant melanoma*

Introduction

Halo nevi (HN), also termed leukoderma acquisitum centrifugum or Sutton nevi, are defined as benign melanocytic nevi that are surrounded by an area of depigmentation resembling a halo[1,2]. This phenomenon often indicates the beginning of involution and subsequent regression of the melanocytic nevus, a process that extends over a period of several months or years[3]. The central nevus may persist unchanged or become less pigmented over time, but often the nevus involutes, leaving a localized area of depigmented skin[4,5]. The localized area of depigmentation may persist for months or years, or repigment totally[4,5].

HN is common in children and young adults, with a mean age at onset of 15 years[6]. The incidence in the population is estimated to be approximately 1%[6,7]. Affected individuals frequently have multiple lesions which are usually localized on the trunk and back. A familial tendency for halo nevi has been reported[8].

The most frequent association of HN is vitiligo, with vitiligo lesions appearing in nearby regions, as well as at other sites[9]. HN may also be associated with autoimmune disorders such as Hashimoto thyroiditis, alopecia areata, celiac disease, atopic dermatitis and others[10,11]. The association with malignant melanoma has been reported by a large number of authors[12].

The prototype of halo lesion is classic HN. The halo phenomenon may also be observed around other benign or malignant lesions, such as blue nevus, Spitz nevus, Mongolian spot, café au lait spot, neurofibroma, basal cell carcinoma, seborrhoeic keratosis, dermatofibroma and flat wart[13]. The halo phenomenon has been reported in association with malignant melanoma as well[13].

Halo Nevi, Etiology and UV Radiation

The etiology of the HN is unknown. It seems to occur either following exposure to UV radiation, especially after sunburns[13, 14] or most often idiopathically. Rarely, it may occur following application of topical bleaching preparations[13].

UV light exposure, measured as amount of UV radiation at the particular location or the amount of time spent in the sun and sunburns before the age of 20 have been associated with increased risk of melanoma, with the development of multiple melanocytic nevi and clinically atypical nevi[15–18]. Histological changes and higher metabolic activity can be seen in UV-exposed nevi as a result of trauma-induced reparatory mechanisms[19,20]. These molecular alterations could be antigen structures that induce immune response[20–22]. Once the immune system

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has been stimulated, it recognizes simple antigens in atypical and also in normal cells and that explains multiple halo nevi in some individuals[21,23].

The pathogenesis of the HN is also unclear. Histopathologically HN is characterized by progressive degeneration and disappearance of the melanocytes, with inflammatory infiltrate composed mainly of T lymphocytes, with prevalence of the cytotoxic CD 8+ subset[3]. These data prove involvement of T-cell-mediated immune response[21]. The influence of circulating antibodies as a secondary factor in immune elimination of nevus cells remains a possibility[21]. Patients with HN very often have circulating antibodies to cytoplasmic antigens in melanoma cells[21] that disappear after excision or spontaneous resolution of HN. These antibodies may occur after cell-mediated lysis of the nevus cells with release of the nevocellular antigen that stimulates B-cells. Furthermore, 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 antibodies[21–24].

Halo Nevi and Malignant Melanoma

There are many reports about the possible relationship between HN, vitiligo or vitiligo-like leukoderma on one hand and melanoma on the other[12,25–28]. Cutaneous depigmentation and hypopigmentation have been frequently reported during the course of malignant melanoma, such as regression of the primary malignant melanoma or its metastases, HN around melanocytic nevi and vitiligo appearing in nearby regions or at sites distant from malignant melanoma[12,25–28]. The halo phenomenon has also been reported in association with malignant melanoma and it is called halo melanoma[13,29].

The development of different types of hypomelanosis in association with malignant melanoma represents an immunologic reaction, cellular and humoral, to the antigens shared by normal melanocytes and melanoma cells[9,13,30,31]. Malignant melanoma is a tumor that can spontaneously regress and once the immune response is stimulated, it recognizes common antigens in the malignant cells and in the normal cells. The occurrence of depigmentation in melanoma patients is commonly believed to be a positive prognostic factor, suggesting the development of an antitumoral response[32–34]. However, larger studies are needed to clarify if different types of hypomelanosis represent a favourable sign in the course of malignant melanoma.

Approach to Patients with Halo Nevi

Approaches to the management of HN in children differ from approaches in adult patients. In children and young adults, HN are common, usually benign, symmetrical lesions and clinical observation over time is the best policy. It is important to examine not only HN but whole skin and visible mucus membranes. Multiple lesions in children are common, so all patients with HN should be examined with Wood's filter. Children's skin is pale and multiple lesions are not necessarily seen with naked eye. However, HN may be associated with other diseases, so in children with multiple HN we recommend to do complete blood count, antinuclear antibodies, screened for thyroiditis and celiac disease. There is no need for treatment in patients with solitary HN. Halo melanoma in a child is extremely unusual and should be considered suspicious only if the halo is asymmetrical, or if the central lesion is unusual[35]. *Lai et all* also suggest caution if the nevus is congenital[35]. The »ABCD« diagnostic criteria for melanoma are also applied to the central lesion of a halo melanoma[36]. These include asymmetry, border irregularity, colour variegation and diameter.

HN are uncommon in adults. A sudden onset of HN, vitiligo or leukoderma in adult patients can be a reason for paying more attention in the examination of other melanocytic lesions[25]. If there is any doubt, clinicians should perform an excision biopsy to obtain a histological diagnosis. Halo melanoma and melanoma are more common in adults than in children.

Conclusions

There are many reports about the possible relationship between HN, vitiligo and other forms of cutaneous depigmentation and malignant melanoma. It is now known that excessive exposure to sunlight early in life is an important determinant in the later development of malignant melanoma and such exposure may also be an initiating factor in the development of HN. It is important to emphasise that the majority of changes in pigmented skin lesions occur during childhood and adolescence, so sun protection must start from the first days of life[37].

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»HALO NEVUSI« I UV ZRAČENJE

S A Ž E T A K

Halo nevusi, poznati i kao Sutton nevusi, su benigne melanocitne lezije okružene zonom depigmentacije-haloom. Obično se javljaju u djetinjstvu i adolescenciji, najčešće oko 15. godine života. U općoj populaciji javljaju se s incidencijom od 1%. Lezije mogu biti pojedinačne ili multiple, najčešće lokalizirane na koži leđa. Opisana je i obiteljska pojava halo nevusa. Iako se radi o dobroćudnim promjenama potreban je oprez jer se halo nevusi mogu pojaviti udruženi s malignim melanomom češće nego što se prije mislilo te mogu predstavljati imunološki odgovor na melanom. Etiopatogeneza halo nevusa je nepoznata. Dokazano je da se radi o autoimuno pokrenutom odgovoru te da T limfociti imaju glavnu ulogu u razaranju nevus stanica. Česta je udruženost halo nevusa s drugim bolestima najčešće autoimunim bolestima kao vitiligo, Hashimotov tiroiditis, alopecija areata, celijakija, atopijski dermatitis i druge. Potvrđena je pojava halo nevusa nakon intenzivnog izlaganja UV zračenju, osobito nakon sunčanih opeklina. Prikazana je etiopatogeneza halo nevusa, udruženost halo nevusa i malignog melanoma te utjecaj UV zračenja na nastanak halo nevusa.