Partially Regressive Melanoma Without Metastasis: Case Report

Keywords

Regressive melanoma, late regression, superficial spreading melanoma, Clark Nevi Syndrome, case report.

Abstract

Replacing the tumor volume with an eventual fibrotic tissue, the histologic phenomenon of regression has been described to target cutaneous melanoma sometimes partially and less often completely. Regressive melanomas have been a source of debate in figuring out whether this correlates to a positive or a less favorable patient outcome. Our case from Syria presents a contribution to a good prognostic indication of regression in a patient with superficial spreading melanoma and dysplastic nevi syndrome of Clark.

Introduction

Derived from the melanocytes residing in the basal layer of the epidermis, cutaneous melanoma is the most aggressive skin cancer and the sixth most common malignancy in the United States. Several risk factors play a role in the development of melanoma like ultraviolet radiation, sunburns in childhood or adolescence, number of congenital and acquired nevi and having a family history of melanoma (1). Dysplastic nevi are also of great importance due to their association with an increased risk for melanoma (2).

Regression of melanoma is mainly a histologic phenomenon characterized by the partial or complete substitution of the tumor tissue by fibrotic tissue as a result of an inflammatory process triggered by the host immune system. Around 10 – 35% of all melanoma cases may regress partially while complete regression is only seen rarely (3).

Controversial findings have been discovered regarding the relationship between regressive melanomas and cancer prognosis. While generally connected with poor prognosis, we hereby present a case of a partially regressive melanoma in a patient with dysplastic nevi without distant metastasis for one year following diagnosis and tumor resection.

Case presentation

A 42-year-old male without significant medical history presented to the dermatology clinic with a dark lesion on his trunk recently showing changes in appearance.

Physical examination revealed an asymmetric, elliptical, partially depigmented black skin plaque, measuring 2x2 cm in major diameter. The lesion located on the abdomen has a flat fibrotic pink center and black to brown raised upper borders with black dots. No ulceration, bleeding or lymphadenopathy were detected (Fig 1).

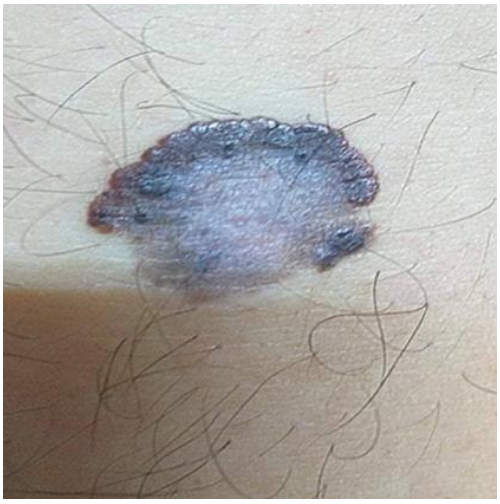

Fig 1: Partially regressive Melanoma: an asymmetric, elliptical, partially depigmented black skin plaque, measuring 2x2 cm located on the abdomen

According to the patient, the lesion has been stable for more than 15 years ago showing even black color and flat appearance. One year prior to this visit, the patient noticed the color fading out in some parts.

Dermoscopy examination disclosed white and blue areas in most of the lesion's space in addition to several black dots noticed in the periphery of the lesion.

An excisional biopsy of the lesion and with the use of hematoxylin and eosin staining revealed the presence of residual proliferation of atypical melanocytes showing large vesicular nucleoli and abundant clear cytoplasm with brown pigment. The abnormal cells are arranged in lentiginous fashion with nests on the dermal-epidermal junction and focal invasion of the dermis. The pigmented area is due to the presence of melanin-bearing macrophages. Areas of fibrosis is seen with clear deposition of collagen fibers and a mild lymphocytic infiltrate. Immunohistochemistry confirmed the presence of $CD3^+$ infiltrate. The tumor measures 5 mm in greatest dimension and 0.80 mm in depth using Breslow's thickness (the length from the granulosum stratum of epidermis to the deepest margin of the tumor). (Fig 2).

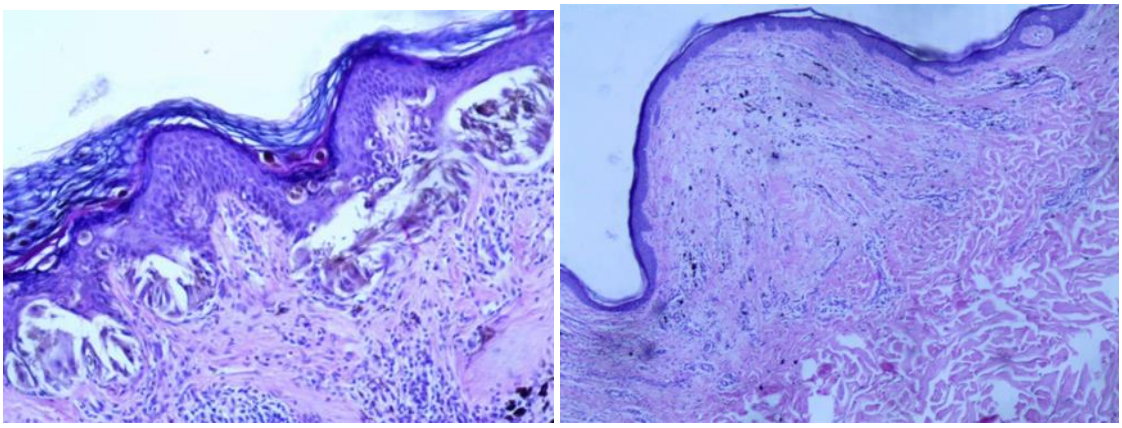

Fig 2: Partially regressive Melanoma: a hematoxylin and eosin staining of the excisional biopsy of the lesion.

These histologic findings are consistent with the diagnosis of a partially regressed superficial spreading melanoma on a previous dysplastic melanocytic nevus. The pathologist confirmed the regression to be in a late stage involving around 60% of the horizontal width of the whole tumor.

Further examination of the patient's body revealed multiple melanocytic nevi manifesting as macular lesions with un-defined borders and variegated color and diameter. This finding is compatible with Clark Nevi Syndrome present on the trunk and extremities (fig 3).

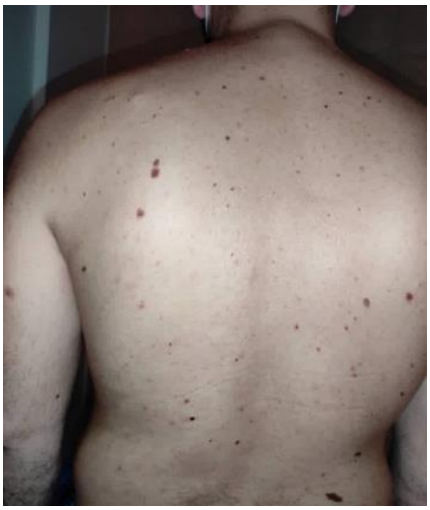

Fig 3: Clark nevi syndrome on trunk.

The patient has type II skin phenotype, red hair and blue eyes with a history of sunburns and excessive UV exposure.

Whole body Computed Tomography (CT) with contrast material was performed at the time of diagnosis, six months and one year later revealed no lymphatic or visceral metastases.

The patient did not give consent to proceed with sentinel lymph node biopsy and preferred to go for the surgical resection which was done successfully with free surgical borders and 1 cm safety margins.

Discussion

Regression of melanoma is an immunologically mediated phenomenon histologically described as a variable decrease in the number of cancerous melanoma cells accompanied by the presence of a host immune response consisting of inflammatory lymphocytic infiltrate, melanophages, dilation of blood vessels, dermal fibrosis, and epidermal attenuation (4).

Regression could happen spontaneously or in response to treatment. Spontaneous regression is defined as partial or complete disappearance of a tumor in the absence of therapeutic interventions. Clinically, regression may manifest with hyperpigmentation, followed by hypopigmentation of part or the entire lesion, resulting in blue, pink, white, or gray areas (4).

The mechanism of regression occurs in 35% of skin melanomas. Few cases of fully regressive melanomas are described in the literature (1). Melanoma regression tends to be seen in adult or elderly patients and is extremely rare in young people (5).

Classified into stages, histologic changes usually start with a mononuclear inflammatory cell infiltrate composed predominantly of mature lymphocytes followed by an intermediate stage consisting of near absence of melanocytes in a portion of the melanoma, along with scattered melanophages, fibroblastic proliferation, mild collagen deposition, and increasing vascularity within superficial dermis. Finally, the late stage is identified by complete absence of melanocytes, clear fibrosis in papillary dermis, variable numbers of melanophages and usually a few inflammatory cells. (4).

Furthermore, when assessing a regressive tumor, it is essential to determine the horizontal extent of regression which is usually classified as focal (≤50%), intermediate (50 to ≤ 75%) or extensive (>75%) as well as the maximum thickness of regression-associated dermal fibrosis and inflammatory infiltrate (similar to measuring Breslow thickness) (6).

In terms of prognosis, worldwide studies have shown controversial findings. Many studies have concluded to link between regression and the presence of lymph node invasion and metastases (1) while others have reported cases without metastases (3). our case adds up to the pool of cases where no distant metastasis was detected by means of radiological diagnostics at the time of diagnosis and one year after. Unfortunately, we couldn't perform the sentinel node biopsy respecting our patient's will.

Breslow thickness has been a contributing prognostic factor, but it is still debatable, as some authors suggest that the initial thickness of the melanoma in the area of regression might have been superior to that of the remaining tumor. Moreover, studies refer to the occurrence of regression only in thin melanomas less than 1 mm (5).

Conclusion

As it affects many solid tumors, regression in cutaneous melanoma refers to an inflammatory process triggered by the host immune system which leads to the replacement of tumor tissue with an inflammatory infiltrate and eventually a fibrotic structure. While the global studies have discovered different findings, our case adds another proof that regression could be connected to good patient prognosis as no metastasis has been identified for one year following the diagnosis.

In the absence of clear criteria for histologic regression, it is recommended that all pathologists assess regression in an objective manner and include regression-associated parameters (extent and depth) in their report to help in better understanding of regression dynamics.

Compliance with Ethics Guidelines. The patient gave written informed consent for publication of her case details and images.

Data availability. The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Figure legend

Fig 1: Partially regressive Melanoma: an asymmetric, elliptical, partially depigmented black skin plaque, measuring 2x2 cm located on the abdomen

Fig 2: Partially regressive Melanoma: a hematoxylin and eosin staining of the excisional biopsy of the lesion.

Fig 3: Clark nevi syndrome on trunk.

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