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An unusual case of cutaneous desmoplastic melanoma

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Abstract

Desmoplastic malignant melanoma (DMM) is an extremely rare subtype, encompassing up to 1% of all melanoma cases, worldwide. DMM features a prolonged clinical course and a variable clinical picture, which usually delays the exact diagnosis. The main differentiation from common malignant melanoma includes local recurrence rate, lymph node and distant organs involvement. DMM is further histologically divided into two subtypes – pure DMM and mixed / partial/ combined DMM. The division is important part of the diagnostic verification since these variants demonstrate different biological behavior and prognosis. Herein, a clinical case of a clinically atypical, pure desmoplastic malignant melanoma, occurring in a relatively young patient, is presented. A comprehensive overview highlights the most important DMM epidemiological, clinical and histological characteristics.

Key words:
desmoplastic melanoma, pure and mixed types

Introduction

Desmoplastic malignant melanoma (DMM) is an uncommon histological variant of malignant melanoma that affects up to 1% of all cases (1). It is a diagnostically challenging disease due to the non-specific clinical appearance, encompassing a spectrum of atypical variants. The low incidence rate further complicates the accumulation of sufficient scientific data (2).

To date, DMM is referred to as a subtype of melanoma with a more benign clinical behavior, a lower incidence of lymph node involvement, and short- and long-distance metastases (2). The delay of diagnosis, however, makes the 5-year survival rate similar to that in patients with common malignant melanoma (CMM) (1). The precise histology verification requires further differentiation

into pure and mixed/partial/combined DMM subtype (3). Recent studies report important differences in these two variants. Pure DMM has a higher rate of local recurrences, while mixed DMM shows a prognostic profile that is closer to CMM, featuring higher rate of lymph node metastases and systemic involvement. Yet, more clinical, histological and molecular biology studies are needed to further enlighten these observations.

Herein, a clinical case of an atypical hyperpigmented pure subtype of DMM in a relatively young male with no previously known genetic predisposition of malignant melanoma, is presented.

Case report

A 40-year-old Caucasian man came to our Depatment with complaints of a growing tumor formation on the scalp for around 4 years. The lesion grew over time slowly without any subjective symptoms. The patient was disturbed only by the lesion's size and black color. He denied any erosions or bleeding at the site. His general health condition was perfect. There was no accompanying disease or any concomitant medication. His personal and family history was devoted from any neoplastic disease.

Physical examination revealed a solitary dome-shaped, well-defined hyperpigmented nodule with a diameter of 2 cm, localized on the left parietal area of the scalp. There was no evidence of erosion or ulceration. A 2-mm halo of erythema was surrounding the central hyperpigmented zone within the margins of the nodule (Figure 1).

Fig.1 A dome-shaped hyper-pigmented nodule on the left temporal zone of the sclap

Laboratory examination revealed no changes in the complete and differential blood counts, biochemistry and urinalysis. The clinical differential diagnosis included a large list of benign and malignant skin formations including haemangioma, naevus Spitz, malignant melanoma, etc.

Patient underwent surgery with total deep excision within 1cm/d. The histological examination showed superficial epithelial necrosis, overlying a deep dermal infiltrate expanding to the subcutis, presented by elongated, spindle-shaped atypical melanocytes with severe pleiomorphism and numerous mitosis that were placed in a prominent fibrotic stroma (Fig.2).

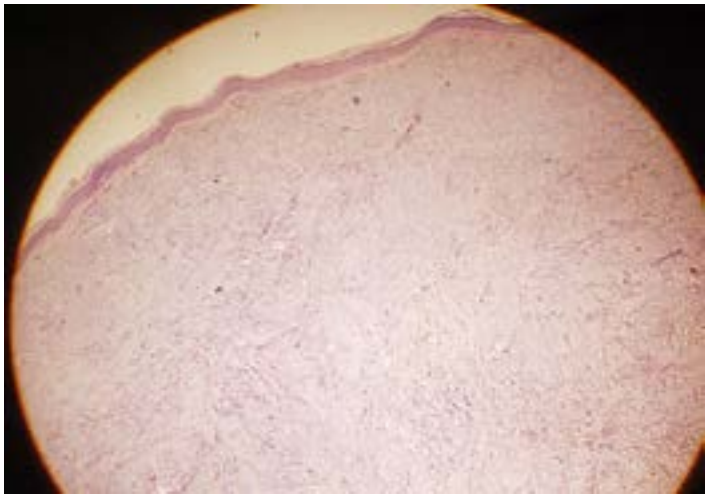

Fig.2 A diffuse dermal infiltrate of elongated, spindle-shaped atypical melanocytes in a desmoplastic stroma (H&E, x 20).

Immunohistochemical analysis showed strongly positive melanoma stains, vimentin (Fig.3) and CD117 in the spindle-shaped cells.

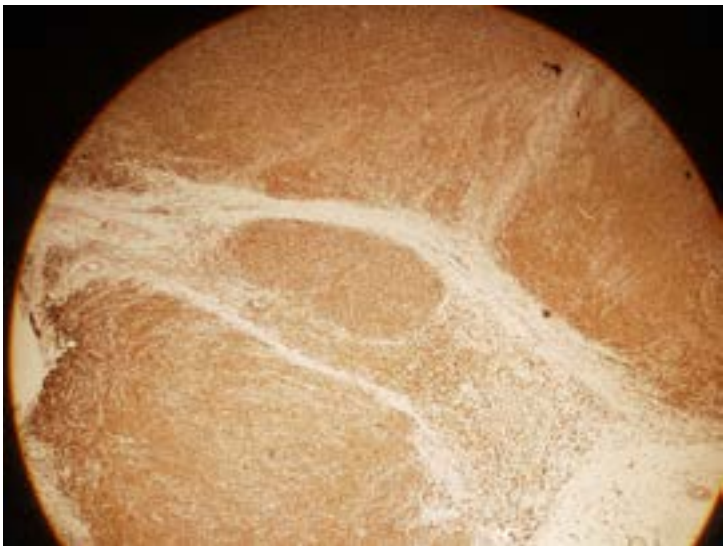

Fig. 3 Strongly positive vimentin stain (x 20).

The proliferating activity verified by Ki-67 was more than 60%. There was perineural invasion. Breslow thickness was more than 6 mm. Based on these findings; the patient was diagnosed with desmoplastic malignant melanoma and underwent wide margin re-excision within 2cm in order to avoid local recurrence. He was referred for oncology clinic for further staging and therapy.

Discussion

DMM is a rare histological form of spindle-cell melanoma, first described in 1971 by Conley et al. (4). DMM overall incidence is around 1% of all melanoma types (1,2, 5). It is more frequently observed in elderly men in their seventh decade, which is a decade over CMM cases. The male preponderance is twice higher (1, 3, 5).

DMM has variable clinical presentation. The most frequent location is the head and neck region (50%), followed by the extremities (20-25%) and the trunk (20-25%) (3). It is especially found in the scalp area and becomes visible at later stages as the lesion grows in size (2).This predilection site suggests that skin cells' DNA damage from excessive ultraviolet light may be the primarily etiological factor for this MM subtype (6).

DMM usually presents as an indurated slowly spreading plaque or nodule, lacking the typical melanoma-associated characteristics (7). The lesions are most often hypopigmented and well-defined (1). There is no ulceration or bleeding at the site. No subjective symptoms occur, which add to the patient's neglect and the delay of the clinical diagnosis (7).

DMM's histological picture reveals strands of elongated fusiform, spindle-shaped cells surrounded by variably pronounced stroma, composed of mature collagen bundles (5, 8).The desmoplastic cells resemble fibroblasts. Therefore, this type of malignant melanoma is considered a fibrosing variant of spindle cell melanoma. Other features include presence of multinucleate cells and foci of neural transformation and neurotropism (8).

DMM is further divided into "pure" variant, which consists of at least 90% desmoplastic cells, and a "combined" or "partial" subtype that is mixed with non-desmoplastic features (3, 8).This division serve as an important prognostic factor as it has influence on the tumor's biological behavior (3, 5).

DMM have lower incidence of ulceration and mitotic rate compared to CMM (9) as well as higher frequency of regression (2). Usually, regression is associated with a better outcome, corresponding to the ability of the immune system to fight the tumor (10). Ulceration and mitoses are considered poor prognostic factors, referring to an aggressive course, high invasive potential and ability to recur locally and disseminate with short- and long-distance metastases (9). This raises the suggestion that DM has a more benign biological course and a better survival rate compared to CMM. However, the statistical analysis shows similar 5-year survival rate (75%), which is probably a result of the delay of the DMM diagnosis (2). Remarkably, the mean Breslow thickness at the time of the diagnosis is more than 4mm (1), which is 4 times greater than the mean diagnostic CMM Breslow thickiness (3).

Recent studies suggest that the rate of DMM local recurrence is higher, compared to other MM subtypes (1, 5). The reported incidence of local recurrence for DM is 11-40% and the overall rate for all MM subtypes with Breslow > 4mm is 7.6% (1). Another histological

factor associated with higher local recurrence's rate is the presence of neurotropism in the initial lesion (20% versus 6.8% for non-neurotropic lesions) (5, 7).

Important survival prognostic factors are the presence of micro- and macro-metastases in the lymph nodes and other organs. Patients with DMM has lower risk of lymph node involvement (overall rate of 0-17%), compared to those with CMM with similar thickness (25% or greater) (1, 3). Systemic metastasis occur in 7% to 44% of DMM cases. The lungs, the liver and the bones are most commonly affected (5).

The two DMM histological subtypes feature some significant differences. Some studies found the median Breslow thickness of pure DM to be greater than that of mixed DMM (3). Meanwhile, patients with pure DMM have lower risk of lymph nodes metastases (2.2%), compared to patients with mixed DMM (15.8%), and with non-DMM (17.5%) (3,11). There are other reports with similar results: for example, a study found 11% frequency of regional lymph node involvement for patients with mixed DMM versus 1% for patients with pure DMM (12). Furthermore, patients with mixed DM were found to have significantly higher risk for death and metastases compared to those with pure DM (8, 3). Mixed DM cases have a three-time higher mortality rate than the pure DM (3, 13). On the other hand, studies show greater rate of local recurrence for patients with pure DMM. Maurichi et al. reported incidence of 40% local recurrence in pure DM cases compared to 18% for those with mixed DMM (1, 14).

Despite the emphasized epidemiological and clinical differences, staging criteria and therapy methods for DMM do not differ from those in other types of MM (1, 15). The higher local recurrence rate, however, suggests wider surgical excision of a minimum of 2-cm for all pure DM lesions, which is statistically associated with improved outcome (1). A four-time lower DMM local recurrence rate is associated with adjuvant radiation therapy, which is nowadays routinely indicated in its treatment protocols (16-18).

A recent retrospective study of 60 patients showed a potential higher responsiveness of DMM to checkpoint inhibitors (PD-1 or PD-L1 blockade therapy) compared to other types of MM (19,20). The used drugs were: pembrolizumab (75%), nivolumab (13%), nivolumab or pembrolizumab, combined with iplimumab (5%) and BMS-936559 (an anti-PD-L1 antibody) (5%). According to the report, tumor formations shrank in 70% and the lesion was no longer detectable in one-third of all patients (32%) (19, 20).

Conclusions

DMM is a rare subtype of malignant melanoma, histologically sub-differentiated into pure and combined forms. DMM follows distinct clinical behavior and is generally considered to have better prognosis than CMM. Controversial statistic data accumulates worldwide, probably due to the low incidence and indolent clinical appearance of a painless, slowly growing formation, which usually delays the diagnosis. The main histological DMM subtypes show different biological course and prognosis; hence, the poor scientific data gives no enough credentials for building precise diagnostic and management guidelines.

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