

CLINICAL CASE

FAST-GROWING MALIGNANT MELANOMA

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Abstract

Melanoma is the most serious form of skin cancer; its incidence increases with age. Melanomas are malignant tumors that are derived from melanocytes. The most common site of involvement is represented by the skin. Melanomas are considered a major cause of premature death from cancer. Melanomas produce pigment in varying amounts and may elicit an immune response that will be reflected in the clinical appearance. Some melanomas may lack pigment. A small but significant number of melanomas are undiagnosable clinically. A history of change may be the only clue to the correct diagnosis. We present the case of a 45-year-old woman, presented to our service with a rapidly changing nevus that bled with minimal trauma, located on her back.

Keywords: malignant melanoma, skin cancer, melanocytes, BRAF-V600E, dabrafenib

Introduction

Melanoma is the most serious form of skin cancer; its incidence increases with age. Melanomas are malignant tumors that are derived from melanocytes. The most common site of involvement is represented by the skin, although occasionally primary melanoma may appear in other organs – eye, oral and nasal mucosa, vulvar and anorectal mucosa, other gastrointestinal mucosa and the central nervous system.

There are 5 stages: stage 0 is in situ (intraepithelial) melanoma, stages I and II are localized invasive cutaneous disease, stage III is regional nodal disease, and stage IV is distant metastatic disease.

Melanomas are considered a major cause of premature death from cancer. The risk factors include personal or family history of melanoma,

large numbers of naevi or dysplastic naevi, giant melanocytic congenital naevi, skin that easily sunburn, damaged skin because of the sun, history of non-melanoma skin cancer, and also the immunodeficiency [1].

The legs of women and the backs of men are the most common sites for malignant melanoma, despite these not being the sites of greatest sun exposure. If the tumor is detected early the survival can be improved [1].

Surgical treatment of malignant melanoma involves wide excision with safety circumferential margins of 3-5 cm with deep dissection up to the fascial level [2]. A Cochrane meta-model suggests that narrow excision with 1-2 cm limits could have oncological results similar to wide excision [3]. Regional lymphadenectomy should be considered in all patients with tumor size larger than 4mm. In patients without clinically detectable

adenopathy, to avoid lymphedema or other complications, the sentinel lymph node technique is the gold-standard in lymph node management [4].

Any malignancy will increase irregularly, and function abnormally. Malignant melanomas produce pigment in varying amounts and may elicit an immune response that will be reflected in the clinical appearance of the tumor. Some melanomas may lack the pigment. A small but a significant number of melanomas are undiagnosable clinically. A history of change of the tumor, may be the only clue to the correct diagnosis [5].

Case presentation

We present the case of a 45-year-old woman from the urban area, with grade II obesity, non-smoking, with HTA, presented to our service with a rapidly changing nevus that bled with minimal trauma, located on her back. She is a teacher with dark eyes and reported many years of sun exposure and occasionally sunburns. There was no personal history of previous skin cancer and no family history of melanoma known. Except the skin lesions, physical exam revealed no other abnormal findings. The laboratory tests were normal.

On clinical exam of the skin we found: macroscopically, the tumor formation had a diameter of about 2 cm, irregular edges, dark brown color, highlighted, with a small crust formed of fibrin located in the center, suggesting ulceration.



Figure 1 – The macroscopic view of the tumor

Dermatoscopy showed a multicomponent pattern with asymmetry in two axes, atypical pigment network, streaks, atypical dots and globules, blotches, blue-gray veil, regression structures, milky red areas, atypical vascular structure, multicomponent structure, and variety of colors.

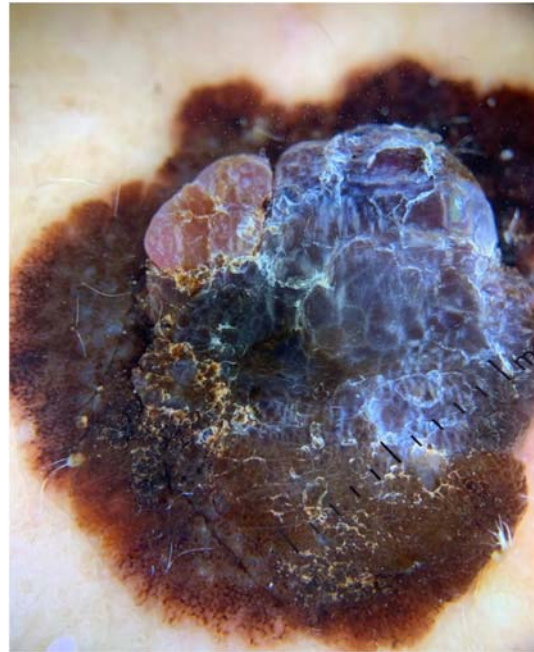


Figure 2 – Dermatoscopy view of the tumor with asymmetry, atypical pigment network, streaks, atypical dots and globules, blotches, blue-gray veil, regression structures, milky red areas, atypical vascular structure, multicomponent structure, and variety of colors

A rather rapid increase in size was noticed between May and September 2019, at which time the growth was excised. The lesion removed measured 2x2.5 cm and was surgical excised with 2 cm resection margins and deep to the muscle fascia.

Axillary and groin ultrasound was performed and did not detect any adenopathy.

Histopathology showed an ulcerated malignant melanoma Clark level IV, extensively on the surface, with vertical growth phase, characterized as lentigo malign type. The tumor extended into the superficial subcutaneous tissue. Breslow depth was 10.9 mm (pT4a). The cutaneous excision piece that includes a large melanocytic tumor proliferation, with radial growth phase consisting of confluent nests and atypical melanocytes disposed lentiginos, with pagetoid invasion of the epidermis, and vertical

growth phase, eccentric, exo-endophytic, plateau, nests and nodules of large, pleomorphic epithelioid cells, with invasion of the reticular dermis, level at which the tumor proliferation measures 10.9 mm thick. An index of mitotic activity of up to 4 mitoses per mm^2 is detected. A lymphohistiocytic infiltrate with intratumoral melanophage is present, lymphovascular invasion and perineural invasion were present. The lesion is an extensive melanoma in the surface, with the growth node vertically. Proliferation was completely excised, with lateral margins at least 5.6 mm and deep margins 11 mm apart.

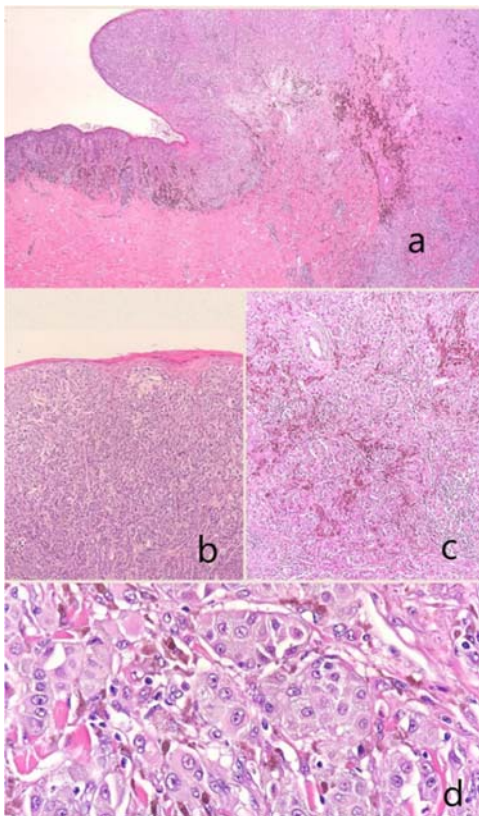


Figure 3 – Melanocytic tumor proliferation, with radial growth phase consisting of confluent nests and atypical melanocytes disposed lentiginos, with pagetoid invasion of the epidermis, and vertical growth phase, eccentric, exo-endophytic, plateau, nests and nodules of large, pleomorphic epithelioid cells, with invasion of the reticular dermis

Computed tomography showed that there were no secondary disseminations. Plastic surgery and oncology evaluations were recommended for sentinel lymph node biopsy before surgical re-excision of the scar by the

Plastic surgery Department. The lymphatic mapping by lymphoscintigraphy and intraoperative injection of radioisotope and blue dye to identify the lymph node immediately downstream from the primary tumor showed the sentinel lymph node status, that is considered the most important prognostic factor for disease-specific survival of patient. Histological examination of the sentinel lymph node has identified the absence of metastatic cells in the entire lymph node basin.

This patient's melanoma had a mutation in BRAF-V600E, and due to its aggressive nature, oncology evaluation recommended targeted therapy with dabrafenib as first-line systemic treatment. No side effects of therapy were observed until the moment.

Discussions

The five-year survival rate is over 90%. In the absence of any new significant chemotherapy, the improvement in survival has been attributed to public education that made possible an early diagnosis and an early excision. The re-excision after the sentinel lymph node biopsy, the elective lymph node dissection, the chemotherapy, the radiotherapy and the immunotherapy are considered to improve survival at one year but they have not been shown to improve five-year survival. The adjuvant therapy with interferon results in a significantly greater disease-free survival rate although it is also associated with a significant toxicity [3].

Regarding metastases, studies have shown that macroscopic locoregional lymph node metastasis reduces the survival at five-year to 43%. The patients who had just locoregional metastasis had a better survival rate than the patients with metastasis to viscera [4]. So, to rule out the presence of metastasis we should performed a meticulous anamnesis and physical exam, chest X-ray, liver function test, ultrasound, computerized tomography, magnetic resonance imaging and others tests if it is required.

In our case, her disease was locally aggressive with rapid development, but with no metastasis. This patient's tumor had a BRAF-mutation, which activates a mutant protein in the MAPK pathway that can be inhibited by the selective small-molecule kinase inhibitors vemurafenib

and dabrafenib. BRAF-targeted agents are typically recommended as initial therapy in those with aggressive and symptomatic disease based on the high rate of response to therapy and rapid onset of action [5, 6].

Thus, we can say that a malignant melanoma that has a very short duration of growth, as was the case with our patient, metastases may be missing due to timely presentation to the doctor. On the other hand, some melanomas that develop slowly over several months/years, delay the presentation to the specialist doctor, so the prognosis may be worse.

It is prudent to recommend melanoma patients avoid solarium (that predominantly emit UV-A) and take precautions to minimize solar UV exposure. When first-degree relatives of the melanoma patient attend for their skin check, they should also receive advice regarding both primary and secondary prevention of melanoma. In particular, they should be advised to avoid solarium and take precautions to minimize solar UV exposure.

Conclusion

This case highlights the need for complete surgical excision of a rapidly evolving tumor, followed by the histological examination of the biopsy piece in a specialized histopathological diagnostic service on the skin examination and the need to be diagnosed at an early stage where appropriate treatment can be done. The specificity of the case is the rapid evolutive nature, the histopathological diagnosis being malignant melanoma stage Clark IV, after only 6 months since the patient states that it appeared.

Since the survival and prognosis depends on early diagnosis, the need for a general public education and an increased doctors' awareness of the clinical picture of the disease is vital for the prevention and treatment of this deadly cancer.

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