

SURGICAL TREATMENT OF CUTANEOUS MELANOMA- TO DO AND NOT TO DO

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Abstract: Cutaneous melanoma is an aggressive tumour, responsible for over 9000 deaths in 2015. It is the second most diagnosed cancer among young patients, under 30 years old. Despite the significant progress made in the diagnosis and treatment of melanoma in the last decade, the incidence is still increasing. For this reason, early diagnosis and prompt treatment of the primary tumour remains the best strategy for improving patient survival. For Romania, we add another important reason, that of limited therapeutic options for advanced melanoma. Until November 2015, Dacarbazine was the only chemotherapeutic agent available in our country for patients with metastatic melanoma, despite its reduced efficacy. In this article, surgical treatment of primary and secondary melanoma is revised and a few melanoma cases are presented, special situations that can occur in current practice, in order to raise awareness and minimize errors in the therapeutic approach of melanoma.

The public health problem of cutaneous melanoma is a difficult one in our country. Lack of a national registry of melanoma impairs us to know the true impact of this disease in the population. In Romania, more than 25% of patients are diagnosed in advanced stages, III and IV AJCC.(1) The prognosis of these patients is poor, with long term survival of stage IV melanoma patients < 10 %.(2,3) Until November 2015, therapeutic options in these stages were limited to chemotherapy with Dacarbazine, the only agent reimbursed by the public health system in our country. Studies have reported a response rate between 6 and 20% for the monotherapy with Dacarbazine and less than 2% of patients survive 6 years.(4,5) The new reimbursed agent Dabrafenib, an inhibitor of BRAF V600 E mutation, is not an option for patients with BRAF negative melanomas.(6) All these have a great impact on the prognosis and survival of melanoma patients and secondarily on the healthcare system.

Primary tumour treatment. The only effective treatment for primary melanoma, potentially curative, is surgical excision. It has remained essentially unchanged during the past decades, except for modification of the safety margins. Recommendations are now uniform in all international guidelines for the diagnosis and treatment of melanoma, after they were established in a large series of trials performed by the World Health Organization (WHO) Melanoma Group, the French Melanoma Cooperative Group, United Kingdom Melanoma Study Group etc.(7-11) International protocols recommend performing an initial excision biopsy with narrow surgical margin (0.5 or 1 cm) and a final surgical excision of the biopsy site, performed within 4-6 weeks after diagnosis, according to the Breslow index reported by the pathologist (table no. 1).(12-15) If poor compliance of the patient is suspected, safety margins of 2 cm are recommended for the initial excision. Incisional biopsy is rarely indicated because the specimen can influence the histopathological evaluation and the tumour thickness can be incorrectly assessed. It is acceptable when excisional biopsy cannot be performed, low suspicion of

melanoma, large lesions on the face or acral area or in case of mucosal lesions.(16-18) Current guidelines recommend a 5 mm safety margins for in situ melanoma but Kunishige suggested in 2012 a 9 mm standard surgical margins.(19,20)

Table no. 1. Excision margins recommended for primary melanoma according to AJCC guideline

| Tumour thickness (Breslow index) | Excision margins (cm) |
|----------------------------------|-----------------------|
| In situ | 0,5 -0,9 |
| ≤ 1mm | 1 |
| 1,01 mm- 2 mm | 1-2 |
| >2 mm | 2 |

Regional lymph nodes micrometastases treatment. Sentinel lymph node biopsy (SLNB) is indicated, according to American Joint Committee on Cancer (AJCC) 2009 guideline, for patients with Breslow index >1 mm and for high risk patients with tumour thickness between 0,75-1 mm associated with a mitotic rate $\geq 1/\text{mm}^2$, ulceration, angiolymphatic invasion or satellitosis on histopathological evaluation or age < 40 years old. It is also indicated when tumour thickness is not determinable, after shave-biopsy.(12,21) Although the procedure is included nowadays in all international guidelines for the management of melanoma, there are still controversial opinions regarding treatment decision because no overall survival benefits were demonstrated for patients who were submitted to this procedure, according to Multicenter Selective Lymphadenectomy Trial (MSLT-1) results in 2014.(22,23) But it is an essential tool for tumour staging that may provide a better estimate of prognosis, and effective regional control, the micrometastasis status being introduced in AJCC staging system.(12,24)

The 2009 AJCC guideline states that a SLN is considered positive by detection of tumour cells by hematoxylin-eosin staining or by immunohistochemistry. Even a single tumour cell represents a positive SLN and is classified as stage III A AJCC (N1a or N2a) or III B when the primary tumor is ulcerated.(12,25) Differentiating melanoma cells from nevus cells in lymph nodes can be challenging, HMB-45 being a more

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accurate marker for the micrometastases.

Complete lymph node dissection (CLND) is recommended for positive SLN patients in the 2009 AJCC.(12) In 2015, the intermediate results of the Dermatologic Cooperative Oncology Group (DeCOG) trial comparing CLND versus observation stated no significant differences on relapse-free survival, disease free survival and melanoma free survival after 3 years.(26) The final results, after 6 years, as well as the results of the MSLT-2 trial are expected to bring new information regarding the benefits of this procedure.

Distant metastases treatment. Melanoma has an aggressive behaviour, with the potential of rapid development of distant metastasis via lymphatic and hematologic dissemination.

Surgical removal is indicated for lymph node macrometastases, including the surrounding lymph node region. In case of more extensive disease, postoperative radiotherapy can help obtaining local disease control. Complete surgical removal is the therapy of choice for single parenchymal metastases and cutaneous metastasis.(27,28)

For brain metastasis, surgical resection and stereotactic radiosurgery are standard treatment options that provide local control.(29)

Table no. 2. Example of clinical cases- not to do

| | |
|----------|---|
| C Case 1 | 30 year-old female patient, surgical excision of 2 melanocytic lesions sent to the histopathology lab in the same container although one was suspected of melanoma, histopathologically confirmed; the second lesion was a benign nevus; reexcision was necessary so it was performed for the both lesions because the location of the melanoma was uncertain |
| C Case 2 | 19 year-old female patient, surgical excision of 3 nevi located in the same anatomic region, without specification of the position from each other, one of the histopathological result was melanoma with Breslow index 0.4 and a reexcision was performed for all three tumour sites |
| C Case 3 | 74 year-old male patient, laser intervention for a melanocytic lesion on the scalp without a biopsy for the histopathological examination, no dermoscopic evaluation, one year later multiple cutaneous melanoma metastases on the scalp, confirmed histopathologically. |

Conclusions:

Melanoma affects many young people and for this reason melanocytic lesions should be treated with great awareness, a biopsy and histopathological examination being mandatory. Lack of a national guideline, complete and periodically revised, causes an uneven approach of melanoma in different centers around the country and for this reason we recommend adherence to international guidelines. With the present cases we raise some current issues regarding diagnosis and therapy of melanocytic tumours.

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