Pathological assessment of tumor biopsy specimen and surgical sentinel lymph node dissection in patients with melanoma

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Abstract

Introduction: Actual trends of cutaneous malignant melanoma show a faster increase then other forms of cancer. Early detection and diagnosis, and accurate pathologic interpretation of the biopsy specimen is extremely important for the treatment and prognosis of clinically localized melanoma. The surgical approach to cutaneous melanoma patients with clinically uninvolved regional lymph nodes remains controversial. Materials and Methods: A retrospective study of melanoma cases was conducted in the "Casa Austria" Department of Plastic and Reconstructive Surgery, Emergency County Hospital, Timisoara, Romania. We have analyzed the medical records of 21 patients that underwent surgical treatment for different stages of melanoma in the period 2008–2012. For histopathological diagnosis of melanoma and the sentinel lymph node(s) status, tissular fragments were routinely processed. For the difficult cases, additional immunohistochemical investigation was done. Results: A positive family history was noted in two cases. The presence of different sizes and localization of pigmented nevi was found in 38% of the cases. Different types of melanoma like superficial spreading melanoma, nodular melanoma or lentigo malignant melanoma and acral lentiginous melanoma was described. The surgical treatment consisted in all cases in wide excision of the primary tumor with respect to safe oncological limits with the prophylactic dissection of sentinel lymph node after lymphoscintigraphy examination. A positive biopsy of the sentinel lymph node was noted in 4.9% of the cases. Conclusions: The surgical treatment combining the wide excision of the primary tumor with respect to safe oncological limits with the prophylactic dissection of sentinel lymph node after lymphoscintigraphy examination had the confirmation done by the pathologic interpretation of the biopsy specimen showing that all the patients had a Breslow index more than 1.5 mm.

Keywords: melanoma, Breslow index, immunohistochemical investigation, sentinel lymph node.

5 Introduction

Contemporary epidemiological trends of cutaneous malignant melanoma show a faster increase then other forms of cancer. The annual increase in incidence rate varies between populations, but in general has the order of 3–7% per year for fair-skinned Caucasian population [1, 2]. Trends in rates differ between regions. The highest rates are found in northern European countries (Denmark, Norway and Sweden) and western European countries (France, the Netherlands and the United Kingdom), particularly among people aged less than 55 years, with an incidence of 6–9 per 100 000 for males and 8–16 per 100 000 for females. Austria and Switzerland have among the highest rates for both sexes: around six per 100 000 for men and around 10 per 100 000 for women. In contrast, in southern and Eastern Europe, the rates are generally increasing in all age groups [3, 4]. The lowest incidence is found in southern Europe (Greece, Italy, Portugal and Spain) with rates of 2–4 per 100 000 for both men and women. In Eastern Europe, the rates vary from low (less than two per 100 000 in Bulgaria, Latvia and Romania) to intermediate (up to six per 100 000 in Lithuania and Slovenia) [5, 6].

Early detection and diagnosis is a critical factor that probably accounts even for increase in overall survival rates. Accurate pathologic interpretation of the biopsy specimen is extremely important for the treatment and prognosis of clinically localized melanoma. Breslow’s thickness is predicting for recurrence in patients with primary cutaneous melanoma. Clark’s level is a prognostic factor taking into account the anatomic levels of invasion to the various dermal layers of the skin [7].

The surgical approach to cutaneous melanoma patients with clinically uninvolved regional lymph nodes remains controversial [8]. Some authors indicate wide excision of the primary tumor with elective lymph node dissection (ELND) [9–11]. Wide excision means removal of tumor and/or biopsy site with a predetermined (usually measured) margin of normal skin and subcutaneous tissue down to the level of muscle. The extent of excision for invasive melanomas is based primarily upon tumor thickness and varies between 0.5 mm up to 3–5 cm.

A reconstructive procedure such as a flap or graft is usually favored over possibly inadequate excision margins. Very narrow margins of excision, such as frozen-section guided margins or Mohs’ micrographic surgical excision technique are controversial and have not been studied in prospective randomized trials.

Other authors recommend excision of the primary site alone and therapeutic lymph node dissection (TLND) only when clinical nodal disease is present [9, 10].
Materials and Methods

A retrospective study of melanoma cases was conducted in the “Casa Austria” Department of Plastic and Reconstructive Surgery, Emergency County Hospital, Timișoara, Romania. We have analyzed the medical records of 21 patients that underwent surgical treatment for different stages of melanoma in the period 2008–2012. General information has been noted for each patient: age, gender, occupation, family history, UV exposure, artificial tanning, presence of pigmented nevi. Clinical findings such as anatomic site, pathological interpretation of the biopsy specimen and the type of surgical treatment have been reviewed.

We have used the staging system recommended by the American Joint Commission on Cancer [11].

For histopathological diagnosis of melanoma and the sentinel lymph node(s) status, the tissular fragments were routinely processed (fixation in 10% buffered formalin and paraffin embedding).

For the difficult cases, which required additional immunohistochemical investigation, we used prediluted antibodies anti-HMB45, anti-Melan A, anti-S100 protein, with Ultra/EnVision system, 3,3’-diaminobenzidine (DAB) as chromogen and counterstaining with Mayer’s Hematoxylin.

Results

The average age of the group was 58.3 years with large age limits (between 26 and 93 years). Gender distribution of the group showed 38.1% males and 61.9% females.

In general, primary lesions occur in decreasing order in the lower extremities, then upper extremities and in the trunk. Artificial tanning was noted only in two cases, while different times of UV exposure were characteristic for the whole group. A positive family history was noted in two cases. The presence of different sizes and localization of pigmented nevi was found in 38% of the cases.

In all cases, the pathology report contains a description of the tumor site, Breslow’s thickness, Clark’s level of invasion, presence of ulceration, dimensions, and margins. Different types of melanoma like superficial spreading melanoma, nodular melanoma or lentigo malignant melanoma and acral lentiginous melanoma was described (Figures 1–6).

According to the growth phase, three cases showed a radial growth pattern, meaning in a single plane of skin layer and four of them vertical growth, or deeper, into the tissues. Ulceration was present in six cases, what is thought to reflect rapid tumor growth, leading to the death of cells in the center of the melanoma. The rest of them have shown the tendency to growth phase.

Figure 1 – Malignant melanoma in the radial growth phase: aspects of melanoma in situ. HE staining, ×40.

Figure 2 – Vertical growth phase melanoma. HE staining, ×40.

Figure 3 – Nodular achromic ulcerated melanoma. HE staining, ×40.

Figure 4 – Nodular achromic ulcerated melanoma. HE staining, ×100.
The surgical treatment consisted in all cases in wide excision of the primary tumor with respect to the safe oncological limits and prophylactic dissection of sentinel lymph node after lymphoscintigraphy examination. The histopathological biopsy specimen confirmation showed that all the patients had a Breslow index more than 1.5 mm. A positive biopsy of the sentinel lymph node was noted in two cases. When necessary, an adjuvant therapy was prescribed by the oncologist.

Discussion

The incidence of melanoma is correlated with the amount of average annual UV radiation [4]. Moreover, the anatomic areas where melanoma develops seems to be somewhat related to the average amount of UV exposure for those sites [3]. It tends to be found more frequently on the legs in women and more commonly on the back in men where more episodic UV exposure may occur [10].

In our study, primary lesions occur in descending order in the lower extremities, then upper extremities and in the trunk. Artificial tanning was noted only in two cases, while different times of UV episodic exposure were characteristic for the whole group. A positive family history was noted in two cases and the presence of different sizes and sites of pigmented nevi was found in 38% of the cases.

A study of 571 first-time melanoma patients compared with 913 healthy controls found a significantly elevated odds ratio of 1.8 between indoor tanning and melanoma [12].

There are evidences that have demonstrated that dysplastic nevi are reported in up to 34% to 56% of melanoma cases [13] and their presence may confer up to a 10-fold increase in melanoma risk [14].

In our study, the presence of different sizes and localization of pigmented nevi was found in 38% of the cases.

The risk of melanoma increases with age and the risk is greater in males. An inability to tan is associated with increased melanoma risk. It is agreed that the MC1R gene is consistently a major determinant of pigment. The human MC1R coding region is highly polymorphic, with at least 30 allelic variants, most of which are associated with red hair. The “red-head” phenotype is defined not only by hair color but also by fair skin, inability to tan, a propensity to freckle, and high levels of pheomelanin [15].

A number of investigators have reported that melanomas are more prevalent in the wealthier socio-economic levels [16]. This may be attributable to the greater opportunity for recreational sun exposure and sunny holidays in the winter months.

The surgical approach in melanoma patients with no clinical nodal disease, the technique of lymphatic mapping and sentinel lymph node biopsy (SNB) was introduced as a minimally invasive method for detection of microscopic regional lymph node metastases in the early 1990s [17]. The sentinel node has been shown to be a sensitive indicator of metastatic melanoma in regional nodes [18, 19]. Morton et al. first reported the details of the SLN technique using intradermal blue dye injection around the primary site and reported that the SLN identification rate was 82% among 237 patients [17], which was considered a high identification rate at that time. The rate of interval SLN identification is reported to be approximately 5% to 10%, and the rate of microscopic metastasis in the interval nodes is approximately the same as that in the SLN in the regional nodal basins [20].

In our study, the surgical treatment combined in all cases the wide excision of the primary tumor with respect to safe oncological limits with the prophylactic dissection of sentinel lymph node after lymphoscintigraphy examination. A positive biopsy of the sentinel lymph node was noted in 4.9% of the cases. We consider that this approach is taking into consideration the predictive value of a negative SNB of patients with significantly lower risk of recurrence than would be predicted by tumor characteristics alone. Second, SNB identifies with minimal side morbidity high-risk patients who may benefit from additional oncological therapy (adjuvant interferon). Also, the psychological benefit for the patient whose SNB result is negative for metastases is significant.

Conclusions

In our study, the primary lesions occurred in descendent order in the lower extremities, upper extremities and then in the trunk. Among comorbid factors, different sizes
and sites of pigmented nevi were found in 38% of the cases. Artificial tanning and family history were inconsistent. In all the cases, the surgical treatment consisted in wide excision of the primary tumor with safe oncological limits and prophylactic dissection of the sentinel lymph node after lymphoscintigraphy characterisation. Different types of melanoma histology with different pattern of the growth phase were described. The biopsy of the sentinel lymph node was positive in 4.9% of all cases. We consider types of melanoma histology with different pattern of the limits and prophylactic dissection of the sentinel lymph nodes as a key point in the management of stage I malignant melanoma: wide excision of the primary tumor with safe oncological margins. In all the cases, the surgical treatment consisted in wide excision of the primary tumor with safe oncological margins and could help in selection of the patients who may benefit from an additional oncological therapy and thereafter to improve their life expectancy and quality of life.

References

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