Improving Melanoma Path Reports: the Importance of Histopathological Parameters in Diagnosis of Cutaneous Melanoma

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ABSTRACT

Background: Despite the fact that melanoma is an easy approachable tumor for diagnosis, the incidence of this skin cancer is still increasing. Histopathological assessment of melanocytic tumors is the gold standard in melanoma diagnosis and represents a problematic aspect of dermatology and pathology. Over the past decades many efforts have been made in determining histological characteristics influencing the prognosis and survival of patients with clinically localized primary melanoma. Some of these parameters also proved to be essential for tumor staging and choosing adequate clinical management.

Objective: We present a retrospective study of 21 melanoma cases with histopathological errors or incomplete path reports, with the intention to raise awareness about the importance of an accurate diagnosis for the management of these cases and for patient prognosis.

Methods: We retrospectively reviewed data from pathology reports and discharge medical records from 21 patients diagnosed with melanoma between 2006 and 2014 and treated in other hospitals that presented in our clinic for second opinion. All slides were reviewed by an authorized dermatopathologist and the new path report was compared with the other ones, presented by the patients.

Results: The majority of the path reports were incomplete, with absent (35.7\%) or wrong (35.7\%) tumor thickness, making impossible to stage the tumor. Absence of histopathological diagnosis was noticed in 3 cases and a wrong diagnosis was determined in 3 patients. Other missing parameters were ulceration status, mitotic rate, microsatellitosis and surgical margins evaluation. missing or incorrect determined in half of the cases.

Conclusions: This study presents the fact that there is a lack of relevant information in the path reports of melanoma cases, making impossible to stage and treat this patients, with adverse clinical impact. We want to emphasize the importance of a standardized histopathological evaluation of melanocytic tumors, consistent with the generally accepted standards, leading to improved healthcare quality and reduced medico legal risks associated with melanoma.
Increased attention to the essential elements for the diagnosis and treatment of melanoma can improve the care of most of these patients and improve prognosis and survival rates.

Keywords: melanoma, path report, error, prognostic factor, Breslow index

INTRODUCTION

The poor prognosis and limited treatment options for advanced cutaneous melanoma highlights the importance of early and correct diagnosis in order to increase quality of patient care and survival rates (1-4). Improving histopathological diagnosis accuracy in identification of melanomas is an ongoing effort. Many histological parameters have been described, with impact on patient prognosis and are currently introduced in every guideline for the diagnosis and treatment of melanoma (5-8). Recommended pathology data sets that include these parameters are currently included in many evidence-based protocols for the examination of melanoma specimens (9,10). In 2013, a comparison of the most important protocols, developed by the Royal College of Pathologists of Australasia, Royal College of Pathologists (United Kingdom) and College of American Pathologists, showed that some of these histological parameters are recommended but some are considered required (11,12). According to these guidelines diagnosis, macroscopic description of the tumor, Breslow thickness, ulceration status, mitotic rate, microsatellites, surgical margin involvement and AJCC/TNM staging are mandatory (10,13).

Tumor thickness is the most important prognostic factor in primary localized melanoma, reported by Breslow since 1970 (14). Patients with thin melanoma, < 1 mm tumor thickness, have a very good prognosis, with 5-year survival rate over 90%, while for Breslow index > 4 mm, the rates decrease to 50% (4,15). It represents a principal T stage parameter, essential for tumor staging and has replaced the Clark level of invasion in terms of patients outcome prediction (16). Surgical excision margins recommended in all guidelines for the diagnosis and treatment of melanoma are currently established according to the tumor thickness (7,17). It is a potentially relevant predictor of sentinel lymph node metastasis in both thin and thick invasive cutaneous melanomas (18). Depending on the value of this parameter, clinicians can decide whether to recommend the sentinel lymph node biopsy to a patient. SLNB is indicated for values between 1 and 4 mm, but also for patients with melanoma of 0.76-1 mm associated with young age, high mitotic rate and ulceration (19-21).

The mitotic rate is the second most powerful prognostic factor that replaced the Clark level of invasion for T1 staging in the 7th edition of American Joint Committee on Cancer (AJCC) Melanoma Staging, implemented in 2010 (22-25). The presence of tumor ulceration is associated with lower survival rates and a high risk of developing metastasis (9,26). Other histological parameters recommended to be included in the path reports are: Clark level of invasion (I-V), regression (present/absent), angiolymphatic invasion (present/absent/indeterminate), lymphocytic infiltrate (absent/present brisk/present non-brisk), radial versus vertical growth phase, perineural invasion (present/absent/indeterminate) (10).

MATERIAL AND METHODS

We conducted a retrospective study of 21 melanoma cases, diagnosed with different types of cutaneous melanoma and treated in other hospitals or private practices between 2006 and 2014. These patients presented in our clinic for second opinion and the incomplete or wrong path report made the therapeutic approach very difficult. The slides were reviewed by an authorized dermatopathologist and a complete path report, with all 13 histologic parameters recommended by the international protocols, was issued for each case. Findings were compared with the first path report, presented by patient. We evaluated variables such as histopathological subtypes, Breslow depth, mitotic rate, ulceration status, Clark level, peritumoral and intratumoral lymphocytic inflammatory infiltrate, perineural and angiolymphatic invasion, regression, microscopic satellitosis and surgical margins. Clinical variables were obtained from the patient’s medical records. A written informed consent was signed by every patient, allowing us to use the data for research purposes.
RESULTS

The study sample included 21 melanoma cases; 62% were women and 38%, men. The mean age was 49.28 years. The mean age of women was lower than that of men, 47.53 and 52.12 years, respectively. The age ranged from 25 to 93 years. There was a peak of incidence for those aged between 35 and 55 years (Table 1).

The histological subtypes of melanoma in the path reports from our pathologist showed the following frequencies: superficial spreading melanoma (SSM) (52.6%), lentigo malign melanoma (LMM) (5.3%), nodular (31.6%), acral (10.5%) (Table 2). In two cases this parameter was not assessed: for the patient with laser intervention of the primary tumor and for the patient diagnosed with melanoma instead of a nevus.

We divided the path report errors found in our study in 4 categories: absence of histological examination, wrong histological diagnosis, incomplete path reports and delayed diagnosis (Table 3). In the majority of cases a histopathological second opinion wasn’t indicated by the dermatologist or the plastic surgeon.

The histopathological diagnosis was absent in three cases. Two patients had laser intervention for melanocytic lesion without dermoscopic evaluation and biopsy. One presented subsequently a recurrent lesion confirmed histologically as lentigo malign melanoma and the other patient presented multiple cutaneous metastases. The third patient had metastatic melanoma, with a brain metastasis surgically removed, but the nodular melanoma of 3/4 cm on his left deltoide area wasn’t excised during this first hospitalization.

In the wrong diagnosis category we included 3 cases. One patient had a paranasal tumor removed and diagnosed as papilloma instead of melanoma and had three different histological diagnoses for the lymph node metastasis in three different clinics: poorly differentiated parotid carcinoma, papillary adeno-carcinoma and melanoma metastasis. The slides of the primary tumor were reviewed and the diagnosis was of nodular melanoma. The second wrong diagnosis was of a melanoma brain metastasis diagnosed as carcinoma metastasis. The third patient was histologically misdiagnosed with melanoma, instead of a benign nevus (confirmed by other two histopathologic examinations by different pathologists).

The majority of patients in the incomplete path reports subgroup had no determination of the Breslow index (35.7%) or it was erroneously assessed (35.7%), making impossible to stage the tumor and establish the treatment options and prognosis of these patients. In all of these cases the doctor didn’t ask or recommend for a second opinion of another pathologist, a fact that in some cases contributed to adverse clinical outcomes. For a young 30 years old female patient, with nodular melanoma and a tumor thickness of 4 mm, the histopathology report was delayed for 42 days. During this time she made several phone calls to the clinic, asking about the diagnosis, as she was very scared about it.

For this lot of patients, the information provided in the pathology reports was not in accordance with the recommendations from the international consensus for melanoma (Table 4).

OUTCOMES

We believe it is very important to continuously try to improve the diagnosis and management of cutaneous melanoma by any means. The fact that melanoma incidence is still increasing, the young age and advanced stages that patients are diagnosed in our country, are

<table>
<thead>
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<th>Gender</th>
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<th>Female</th>
<th>Total</th>
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<tr>
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<td>3</td>
<td>4</td>
</tr>
<tr>
<td>36-45</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>46-55</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
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<td>56-65</td>
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<td>2</td>
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<td>76-85</td>
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<tr>
<td>86-95</td>
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TABLE 1. Distribution of the patients by age range and gender.

<table>
<thead>
<tr>
<th>Histological subtype</th>
<th>Frequency</th>
<th>%</th>
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<tbody>
<tr>
<td>SSM</td>
<td>10</td>
<td>52.63</td>
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<tr>
<td>Nodular</td>
<td>6</td>
<td>31.58</td>
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<tr>
<td>Acral lentiginous</td>
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<td>10.53</td>
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<tr>
<td>LMM</td>
<td>1</td>
<td>5.26</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>100.0</td>
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TABLE 2. Distribution of subtypes of primary cutaneous melanoma.

<table>
<thead>
<tr>
<th>Path report error</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence of histopathologic exam</td>
<td>3</td>
</tr>
<tr>
<td>Wrong diagnosis</td>
<td>3</td>
</tr>
<tr>
<td>Incomplete reports</td>
<td>14</td>
</tr>
<tr>
<td>Delayed diagnosis</td>
<td>1</td>
</tr>
<tr>
<td>Second opinion not indicated</td>
<td>17</td>
</tr>
</tbody>
</table>

TABLE 3. Path report categories.
strong reasons for our viewpoints. In Romania, 25% of the patients present with stage III and IV disease. The difficulty that we encountered in managing these cases, the time lost for the patients, spent walking from one hospital or clinic to another and from one specialist to another, prompted us to present these errors. The number of cases we present in our study may seem small but they were selected only from one doctor’s records and only the cases with complete medical documents. So we believe that the number is much higher across the country. A recent study, published in February 2015, investigated the adherence to international guidelines for the pathology reporting of melanoma in several centers from Italy. Over 600 cases were included but the information was obtained from seven cancer registries. The authors recommend a better dissemination and adoption of a standardized reporting system (27). In our country the data reported by the eight regional registries established since 2007 (28) are incomplete, making it impossible to know the real impact and characteristics of this disease in the population, essential for prevention and control. Melanoma cases are not reported separately but together with other types of skin cancers and no information from pathology reports is included.

We continue with the presentation of two cases which exemplify our conclusions.

Case 1: A 25 year old male patient, presented to a plastic surgeon for a bleeding, ulcerated tumor, in the left pectoral area. Excisional biopsy was performed. The path report was incomplete: no histologic subtype, Breslow thickness or mitotic rate were reported. Also no information about angiolymphatic and neural invasion, inflammatory infiltrate, regression, growth phase and microscopic satellitosis were found in this report. The Clark level of invasion was II. Six days after receiving the diagnosis he presented it to a dermatologist but no second opinion for the histologic slide was recommended. The patient went by himself for a second opinion and the diagnosis was of ulcerated nodular melanoma, with 2.89 mm thickness, Clark level IV. He received adjuvant therapy with interferon.

Case 2: A 54 year old female patient was diagnosed with melanoma located in the parietal left area of the scalp. The tumor was excised with 1 cm surgical margins. The histopathological diagnosis was incomplete, with no histologic subtype, a Breslow index of 0.9 mm and a Clark level IV. A month later, a cutaneous metastasis appeared near the surgical scar. The diagnosis was confirmed after surgical removal. She received adjuvant therapy with interferon in low doses and chemotherapy with Dacarbazine. Our pathologist reviewed the primary tumor slides and the diagnosis was of invasive superficial spreading melanoma, ulcerated, with a 4.35 mm tumor thickness (not 0.9 mm). The patient continued the oncologic treatment.

**CONCLUSION**

Although we have a better understanding of the pathogenesis of melanoma and improved early diagnostic possibilities, the burden of disease and societal costs remain high. This article raises some current issues regarding melanoma diagnosis in our country in the 21\textsuperscript{st} century. Our study investigated the actual practice of melanoma diagnosis in Romania and presented the most frequent path report errors, with an influence on the patient outcome. A correct diagnosis starts from a complete and properly performed examination protocol. We want to emphasize the importance of a standardized histopathological evaluation of melanocytic tumors, consistent with the generally accepted standards, leading to improved healthcare quality and reduced medico legal risks associated with melanoma.
Conflict of interests: none declared.
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