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Misdiagnosis of Melanoma: A 7 Year Single-Center Analysis

Slavomir Urbancek^{1*}, Petra Fedorcova¹, Jela Tomkova¹ and Roman Sutka²

¹Department of Dermatology and Venerology, FNsP F.D. Roosevelta, Banská Bystrica, Slovak Republic

²Department of Dermatology, University Hospital, Martin, Slovak Republic

*Corresponding author: Slavomir Urbancek, Department of Dermatology and Venerology, FNsP F.D. Roosevelta, Banská Bystrica, Slovak Republic, Tel: +421 48 441 21 31; Fax: +421 48 4130302; E-mail: surbancek@nspbb.sk

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Abstract

Background: Despite implementation of dermoscopy, the accuracy of diagnosing melanoma remains a challenge. The aim of this study was to retrospectively analyze cases of histologically confirmed melanoma, which were incorrectly diagnosed during initial evaluation.

Methods: A retrospective analysis of histologically diagnosed melanomas referred to the F.D. Roosevelt Hospital between 2008 and 2014, in which the initial diagnosis was incorrect. We evaluated their histological characteristics, localization of the lesion as well as the specialty of the physician who made the incorrect diagnosis.

Results: From a total of 936 histologicaly confirmed melanomas, 150 (16%) were diagnosed incorrectly. Of those, 26 (17.3%) were melanoma *in situ*. The average value of the Clark's level of true melanomas was 3.49, with an average Breslow thickness of 3.09 mm. Sixty of the melanomas developed on the trunk and 55 on the extremities. Incorrectly diagnosed lesions included nevi in 80 cases, basal-cell carcinoma in 32, non-specific tumor in 16, pyogenic granuloma in 5, squamous-cell carcinoma in 5, haemangioma in 5, seborrheic keratosis in 4 cases, and histiocytoma, keratoacanthoma and cornu cutaneum each in 1 case. The diagnosis of melanoma was missed by a dermatologistin 85 cases, by a surgeon in 38 cases, and by a general practitioner in 2 cases. In the remaining 25 cases we were unable to identify the specialty of the physician who made the wrong diagnosis.

Conclusion: This analysis revealed a high proportion of melanomas that were missed during initial evaluation. The outcome of this study points to the need for better education in the field of diagnostics of melanocytic lesions for dermatologists, surgeons and primary care physicians. In addition, there is a need for periodic evaluation of diagnostic accuracy of dermatology centers using various tools (e.g. Melanoma Diagnostic Index). Continually increasing awareness of malignant melanoma in the general public is also very important.

Keywords: Malignant melanoma; Misdiagnosed melanoma; Diagnostic accuracy

Introduction

Malignant melanoma is a skin tumor derived from melanocytes. Due to its ability of hematogenous and lymphatic dissemination, it belongs in the category of the most malignant tumors. It is also the cause of the highest number of deaths from skin cancer [1].

The course of the disease is affected by the maturity of the tumor at the time of diagnosis and tendency of the tumor to rapidly form metastases. Prognosis is better in patients where melanomas develop on the extremities, and worse in patients with melanoma developing on the skin of the neck, head and upper back [2].

According to the World Health Organization (WHO), 48,000 people die due to malignant melanoma each year. Over the course of the last 30 years, the number of cases of skin cancer has increased four times. It is most frequently diagnosed in people of middle age, but a growing trend is observed in the age group 25-30 years (published on the web site of the Public Health Authority of the Slovak Republic) [3].

In most cases, skin metastases are initially spread by the lymphatic system, forming satellite metastases or transient metastases between the primary tumor and the regional lymph node. Lymph node metastases can affect one or more of the nodes, and later, nodes may form aggregates. Hematogenous dissemination usually occurs later, generally during the 3rd stage of the disease. The most frequently affected organs are the lungs, liver, heart, brain, skin or bone [2].

Even though awareness of malignant melanoma among both the layman and medical professional community is rising, there are still a relatively high number of cases when diagnosis of the malignant melanoma is delayed, or the disease is misdiagnosed. Due to its wide range of clinical presentations, melanoma often resembles various benign-looking melanocytic and non-melanocytic lesions. Despite constantly improving diagnostic modalities, including dermoscopy, accurate diagnosis of melanoma remains a clinical challenge.

At present, there is very little available literature dealing with the issue of errors in the diagnosis of malignant melanoma. For this reason, we performed a retrospective analysis of histologically diagnosed melanomas referred to the Department of Dermatology and Venerology F.D. Roosevelt Hospital between 2008 and 2014, in which the initial diagnosis was incorrect.

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Material and Methods

Between January 2008 and December 2014 a total of 936 patients referred to our Department for evaluation were histologically diagnosed with malignant melanoma. Of the total, 456 were males and 480 were females. The numbers of patients for each year is summarized in the Table 1. The average age was 60 years, with the youngest being 19 and the oldest being 93 years old. Patients who were initially diagnosed with dysplastic nevus, and received a subsequent histological diagnosis of melanoma *in situ*, were not included in the correctly diagnosed group.

We analyzed the spectrum of lesions that were incorrectly diagnosed during the initial evaluation, their most frequent localization, histological characteristics, as well as the specialty of the physician who made the incorrect diagnosis.

Year	Males	Females	M+F	Average age
2008	65	72	137	62
2009	74	76	150	59
2010	58	59	117	61
2011	55	62	117	66
2012	77	77	154	58
2013	71	77	148	58
2014	56	57	113	63
Total	456	480	936	60

Table 1: Demographics.

Results

Of the total number of referred patients, 150 (16%) were diagnosed incorrectly. The wrong diagnosis was made in 66 males (44%) and 84 females (56%) (Figure 1). The number of patients with an incorrectly established diagnosis was highest during the last three years of the study period (Table 1).



The most frequent misdiagnoses included pigmented nevus in 70 cases (46.7%) and basal-cell carcinoma in 32 cases (21.3%). The third most frequent diagnosis represented unspecified tumors in 16 cases (10.7%), followed by dysplastic nevus in 9 cases (6%). Five cases (3.3%)

per group were misdiagnosed as squamous-cell carcinoma, pyogenic granuloma and hemangioma, 4 cases (2.6%) as seborrheic verruca and 1 case (0.6%) per group as verrucous nevus, histiocytoma and cornu cutaneum (Table 2). Examples of misdiagnosed melanomas are displayed on Figures 2 and 3.



Figure 2: Example of misdiagnosed melanoma (Clark IV, Breslow 2,7 mm) considered as haemangioma.

Dg	n			
Naevus	70			
BCC	32			
Tumor without specification	16			
Pyogenic granuloma	5			
SCC	5			
Haemangioma	5			
Seborrheic keratosis	4			
Cornu cutaneum	1			
Keratoacanthoma	1			
Histiocytoma	1			

Table 2: Misdiagnoses (N=150).



Figure 3: Example of misdiagnosed melanoma (Clark IVb, Breslow 8 mm) considered as verrucous naevus.

Of the incorrectly diagnosed lesions, 63 (42%) were located on the trunk, 30 (20%) on the upper limbs, and 28 (18.7%) on the head. In 25 cases (16.7%), the lesions were located on the lower limbs. In 3 cases (2%) melanoma occurred on the neck and in 1 case (0.7%) on the perineum.

Of the incorrectly diagnosed melanomas, 26 were histologically confirmed to be melanoma *in situ*. Other malignant melanomas were expressed by Clark's level and Breslow scale, with true melanomas having an average Clark's level of 3.49, and an average Breslow thickness of 3.09 mm.

Metastases were present at the time of diagnosis or in the follow-up period in 20 patients (13.3%). No information about the presence of metastases was available at the time of analysis in 4 patients who were diagnosed in 2014. Metastases were present at the time of diagnosis in 6 patients.

Of the total number of melanomas diagnosed incorrectly, a false negative diagnosis was made in 85 cases by a dermatologist, in 38 cases by a surgeon, and in two cases by a general practitioner. For 25 patients it was not possible to determine the specialty of the doctor who initially diagnosed the melanoma incorrectly (Table 3). Of the total number of patients included in this study, dermatologists diagnosed malignant melanoma in 871 patients, which is to say that a false negative diagnosis by a dermatologist was made in 9.8% of all examined patients referred over a 7 year period. The percentage of incorrectly established diagnosis by the surgeon, general practitioner or other physician specialties was impossible to determine, as all

Speciality	Number of misdg
Dermatologist	85
Surgical excision without previous dermatology exam	38
GP	2
Not identify	25

 Table 3: Speciality of physician making incorrect (false negative)
 diagnosis (N=150).

Discussion

There are only few papers evaluating the accuracy of diagnostics of melanomas.

In a study performed at The John Hopkins University School of Medicine from 1925 to 1955, McMullan and Hubener described 87 cases of histologically confirmed malignant melanoma, of which only 44 cases were diagnosed clinically. Similar studies, documenting a high percentage of melanomas diagnosed histologically which were not identified on clinical examination, have emerged in the following years [4].

In 1990 Grin et al., retrospectively analyzed the diagnostic accuracy during three periods, 1955-1963, 1964–1973 and 1974-1982 [5]. Their analysis revealed a trend showing gradual improvement in the accuracy of diagnosing malignant melanoma. This improvement however did not reach statistical significance. Gradually improving awareness of malignant melanoma among patients also likely contributed to this improvement due to early visits by patients with a suspicious lesion to a dermatologist. In this work, Grin presents, for the first time, the term of index of suspicion, which tells how often the diagnosis of melanoma is established clinically compared to how often the diagnosis is established histologically. In other words, how often melanoma is underdiagnosed or overestimated.

As pointed out in a study by Esdaile et al., physicians should be aware that the ratio between benign and malignant lesions is low, as is the ratio between invasive malignant melanoma and melanoma *in situ* [9]. These two ratios should be used in combination as an indicator of diagnostic accuracy in detecting melanoma. In addition, it is important to raise awareness of malignant melanoma and methods for preventing lesion formation among the general public.

Accuracy in the diagnosis of malignant melanoma, connected with the specialty of the doctor who established the diagnosis, was addressed by Osborne et al., in 2003 [6]. These authors compared the rate of false negative diagnoses of cutaneous melanoma between general dermatologists, plastic surgeons and clinics for pigmented lesions. Seven hundred thirty one cases were evaluated for the number of false negative diagnosis made (i.e., the cases when the false negative diagnosis was determined in relation to a histological positive finding of malignant melanoma). The rate of false negative diagnosis was the lowest at the clinic for pigmented lesions (10%), followed by general dermatologists (29%), plastic surgeons (19%), other specialists (55%), and general practitioners (54%). It has been previously documented that the prognosis of melanomas located on the head, neck and upper torso is worse than that of melanomas localized elsewhere on the body [7]. Based on our results, a similar conclusion can be made, with the highest rate of metastases in misdiagnosed melanomas occurring in the same locations.

According to Strmenova, in 80% of patients the malignant melanoma metastasis will develop within three years after the primary lesion was removed [2]. Therefore, in patients who were included in the study over the course of the last three years, it was not possible to precisely evaluate the progress of the disease.

Our analysis revealed a high number of cases of incorrectly diagnosed malignant melanoma. Most of which had significant Breslow levels. A high number of melanomas were removed without prior dermoscopy. This likely represents a significant area for improvement. Rosendahl et al., documented that dermoscopy improves diagnostic accuracy in the case of non-melanocytic lesions and the use of simple evaluation algorithms can improve the diagnostic accuracy for malignant melanoma and non-melanoma skin cancer [8].

The outcome of this analysis points to the need for better education in the field of oncodermatology for dermatologists, surgeons and primary care physicians, who are often the first contact physicians for patients with suspicious pigmented lesions. It is also important to introduce regular assessments of diagnostic accuracy of malignant melanoma by various dermatological and oncological facilities as well as the introduction of various evaluation criteria (e.g. Melanoma Diagnostic index).

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