



Evaluation of Prognostic Factors in our Malignant Melanoma Cases

Malign Melanom Olgularımızda Prognostik Faktörlerin Değerlendirilmesi

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Abstract

Introduction: Melanomas are neoplasms that usually develop on the skin with a high prevalence and a mortality rate that is increasing year by year. Studies reflecting the data of this neoplasm, which has a very high mortality rate in our country, are still limited today. Our aim in our study was to retrospectively evaluate the skin melanoma cases treated in our hospital and to compare them with other studies.

Material and Method: The clinical and histopathological features of 57 patients diagnosed with skin melanoma in the pathology clinic of our hospital between 2010 and 2019 were examined.

Results: The mean age (1956) of patients was 63.18±16.54 years. The lesions were located in the head and neck in 21 patients (36.8%), in the lower extremities in 16 patients (28.1%), in the upper extremities in 11 patients (19.3%) and in the trunk in 9 patients (15.8%). Metastasis developed in 9 (15.8%) patients during a minimum 1-year and maximum 10-year follow-up of our cases. In the present study, 40 patients (70.2%) were diagnosed with nodular melanoma, 8 (14%) with superficial melanoma, 2 (3.5%) with lentigo and 7 (12.3%) with acral melanoma.

Discussion and Conclusion: As a result, most of our melanoma cases appeared as nodular type in the head and neck region due to sun exposure. Our study showed that these patients applied to the health institution in the late stage. In melanoma, early diagnosis seriously affects the prognosis.

Keywords: Skin; melanoma; histopathology; prognosis.

Özet

Amaç: Melanom her yıl insidansı artarak giden mortalitesi oldukça yüksek ve genellikle deriden gelişen neoplazmdır. Mortalitesi oldukça yüksek olan bu neoplazma ait ülkemiz verilerin yansıtan çalışmalar günümüzde hala sınırlıdır. Biz de hastanemizde tedavi edilen deri melanom olgularını retrospektif olarak değerlendirdik ve diğer çalışmalarla karşılaştırmayı planladık.

Gereç ve Yöntem: 2010-2019 yılları arasında hastanemiz patoloji kliniğinde deri melanoma tanısı almış 57 hastanın klinik ve histopatolojik özellikleri incelendi.

Bulgular: Hastaların ortalama yaşı (1956) 63.18±16.54'dür. Lokalizasyona göre 21 hastamız (%36.8) baş boyun, 16 hastamız (%28.1) alt ekstremitte, 11 hastamız (%19.3) üst ekstremitte, 9 hastamız (%15.8) gövde yerleşimlidir. Olgularımızın minimum 1 yıllık ve maksimum 10 yıllık takiplerinde 9 (%15.8) hastada metastaz gelişti. Çalışmamızda ki 40 hasta (%70.2) nodüler melanoma, 8 hasta (%14) süperfiyal, 2 hasta (%3.5) Lentigo, 7 hasta (%12.3) akrall melanom tanısı almıştır.

Tartışma ve Sonuç: Sonuç olarak, melanomalı olgularımızın çoğunluğu güneş maruziyetine bağlı olarak baş-boyun bölgesinde ve nodüler tip olarak karşımıza çıkmıştır. Çalışmamız, bu hastaların geç evrede sağlık kuruluşuna başvurduğunu gösterdi. Melanom'da ise erken tanı prognozu ciddi olarak etkilemektedir.

Anahtar Kelimeler: Deri; melanom; histopatoloji; prognoz.

Introduction

Melanoma is an aggressive tumor with increasing incidence and mortality (1). Although less common among cutaneous malignancies than Basal cell carcinoma and Squamous cell carcinoma, melanomas are the most common cause of mortality (2). According World Health Organization (WHO) figures, 265,000 new cases of melanoma were diagnosed worldwide in 2018, and 60,000 deaths were recorded (2,3). The incidence of melanoma varies between ethnic

groups (as well as the affected anatomical regions), being lower among the dark-skinned populations (African, Native American, Asian and Hispanic) than light-skinned populations (4). An annual incidence increase of 2–7% has been reported in light-skinned populations (5). The clinical and histopathological features that affect the prognosis of patients with melanoma have been studied for over 40 years, with the first multivariable analysis of prognostic factors being published in 1978 (6,7). Tumor thickness (thicker lesions are associated with worse prognosis),

presence of ulceration upon histopathological examination, high mitotic rate, anatomical site (body and/or facial lesions have a worse prognosis than lesions in the extremities), male gender and age (older patients have a worse prognosis) are well-known factors leading to a poor prognosis for primary invasive melanoma survival (6). The present study investigates the effects of melanoma on survival among cases treated in a single center, and the effects of such prognostic factors as age, gender, clinical stage, invasive depth, histology and anatomical region.

Material and Method

Fifty-seven patients who were diagnosed with melanoma in the pathology laboratory of our hospital between January 1, 2010 and December 31, 2019, whose pathological archive materials and

clinical information were accessed, were included in the study. Cases for which archival material was inaccessible were not included in the study follow-up. Data on the clinical findings, age and gender of the cases were obtained from the hospital information management system, and the cases were reevaluated with a histopathological assessment that included an evaluation of the histological type (superficial, nodular, acral, lentigo), ulceration, peritumoral inflammatory response, metastasis, Breslow thickness (mm) and Clark's level (Table 1, Figure 1). Life expectancy was determined from the medical records of the hospital and the patients we contacted personally. The affected anatomical regions were classified as head and neck, lower extremity, upper extremity, trunk and unknown localization.

Table 1: Breslow Thickness and Clark's Level

Level	Breslow Thickness	Clark's Level
Level 1	<0.75 mm	Melanoma in situ
Level 2	1.76-1.5 mm	Invasion of the papillary dermis
Level 3	1.51-4 mm	Filling but confined to the papillary dermis
Level 4	>4mm	Invasion of the reticular dermis
Level 5	-	Invasion of the subcutaneous fat

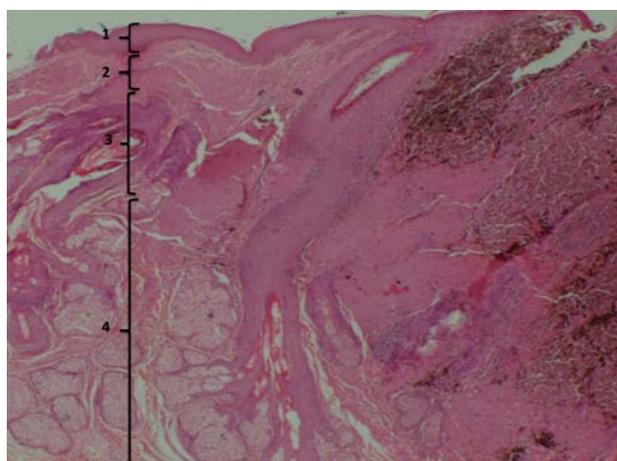


Figure 1: Clark's levels in nodular melanoma case (X10, H&E)

Permission for the study was obtained from the Eskişehir Osmangazi University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee, and IBM SPSS Statistics (Version 25.0. Armonk, NY: IBM Corp.) was used for the statistical analysis of the data. Descriptive statistics for continuous variables were presented as Mean±Standard Deviation, while count and percent (%) for categorical variable. Spearman's

Rho correlation coefficient was computed to determine the relationships between continuous variables and life expectancy. Statistical significance level was considered as 5% for all statistical computations.

Results

Among the 57 cases included in the study, the youngest patient was 26 years old and our oldest was 88 years old, and the mean age was 63.18±16.54 years; 26 (45.6%) were female and five (3 female, 2 male) (8.78%) were 40 years of age or younger and 52 (23 female, 29 male) (91.22%) were over 40 years of age. The lesions were located in the head and neck in 21 patients (36.8%), in the lower extremities in 16 patients (28.1%), in the upper extremities in 11 patients (19.3%) and on the trunk in nine patients (15.8%) (Table 2). In the male cases, the most common localization was the head-neck (15 cases), while the lower extremities (12 cases) were the most common location in females. No statistically significant relationship was observed between gender and localization (p:0.125). During the minimum 1- and maximum 10-year follow-up of the cases, nine (15.8%) patients experienced

Table 2: General Characteristics of the Cases

Cutaneous Malignant Melanoma	Parameter	Number (n)	Percentage (%)
General Characteristics	Number of Patients	57	100
Age	≤40	5	8.78
	>40	52	91.22
Gender	Male	31	54.40
	Female	26	45.60
Localization	Head&Neck	21	36.80
	Upper Extremity	11	19.30
	Lower Extremity	16	28.10
Histological Type	Trunk	9	15.80
	Nodular	40	70.20
	Superficial Spreading	8	14.00
	Acral lentiginous	7	12.30
Breslow Thickness (mm)	Lentigo maligna	2	3.50
	<0.75mm	5	8.80
	0.76-1.5mm	16	28.10
	1.51-4mm	16	28.10
Clark's level of invasion	>4mm	20	35.10
	Level 1	5	8.80
	Level 2	6	10.50
	Level 3	9	15.80
Ulceration	Level 4	31	54.40
	Level 5	6	10.50
	Present	30	52.60
Inflammatory Response	None	27	47.40
	None	5	8.80
	Mild	27	47.40
	Moderate	22	38.60
	High	3	5.30

Table 3: Relationships between life expectancy Lifespan

	Lifespanlife expectancy	
	Correlation	p
Histopathological Type	0.256	0.055
Tumor localization	0.006	0.963
Ulceration	-0.313	0.018
Inflammatory Response	-0.063	0.641
Metastasis	-0.126	0.351
Clark's level of	-0.346	0.008
Breslow Thickness	-0.504	0.001

metastasis and 48 (84.2%) did not during the follow-up period. The metastases were to the regional lymph nodes in six patients (10.5%), to the brain in one patient (1.8%) and to different regional soft tissues in two patients (3.5%). Tumors on the lower extremities were more

frequently observed in the metastatic lesions, and no statistically significant relationship was observed between localization and metastasis (p:0.365). Of the patients enrolled in the study, 24 (42.1%) died during the follow-up period among which the lesions were located in the lower

extremities in five patients, in the upper extremities in five patients, on the trunk in four patients and on the head-neck in 10 patients. No statistically significant relationship was observed between tumor localization and survival ($p:0.963$). In the study, 40 patients (70.2%) were diagnosed with nodular melanoma, eight (14%) with superficial melanoma, two (3.5%) with lentigo and seven (12.3%) with acral melanoma. No statistically significant correlation was observed between tumor localization and histopathological tumor type ($p:0.042$). While ulceration was present in 30 cases (52.6%), no ulceration was observed in 27 cases (47.4%); and while no inflammatory response was observed in five cases (8.8%), mild inflammatory response was observed in 27 cases (47.4%), moderate in 22 cases (38.6%) and intense in three cases (5.3%). The Breslow thicknesses of the cases were <0.8 mm in five cases (8.8%), 1–2 mm in 16 cases (28.1%), 2–4 mm in 16 cases (28.1%), and >4 mm in 20 cases (35.1%). No statistically significant correlation was observed between Breslow thickness and tumor localization ($p:0.985$). The Clark's level were Level 1 in five cases (8.8%), Level 2 in six cases (10.5%), Level 3 in nine cases (15.8%), Level 4 in 31 cases (54.4%) and Level 5 in six cases (10.5%). Among the cases, the lesions located in the lower extremities in 11 cases were of Clark Level IV, which was the most common in all localizations. Localization and Clark's level were not statistically significant ($p:0.143$). The shortest life expectancy was 3 months and the longest was 131 months, and the mean life expectancy was found to be 56.60 ± 41.04 years in our cases. A statistically significant relationship was observed between Breslow thickness ($p:0.001$) and Clark's level of invasion ($p:0.008$) and life expectancy, and it was observed that tumor ulceration also affected survival ($p:0.018$). No statistically significant correlation was identified between gender, age, tumor localization, metastasis, localization of metastatic foci, tumor type and tumor periphery, inflammatory response and survival (Table 3). In the present study, a statistically significant relationship was identified between ulceration and tumor localization ($p:0.046$), tumor type ($p:0.002$), Clark's invasion ($p:0.001$), Breslow thickness ($p:0.008$) and metastasis ($p:0.017$). In addition, a significant correlation was observed between metastasis with Clark's invasion ($p:0.015$) and Breslow thickness ($p:0.001$).

Discussion

Primary cutaneous melanomas originating from the melanocytic system and localized on the skin

account for 1–2% of all cancer deaths in humans worldwide. Although cutaneous melanoma accounts for only 4% of all skin cancers, it is the main cause of death associated with skin cancers (8). In our country, Eser et al. (9) published a study in 2006 in which they analyzed data garnered from eight geographical locations (İzmir, Eskişehir, Bursa, Edirne, Antalya, Trabzon and Samsun) and reported an incidence of melanoma in men of 1.4 per 100,000 in Turkey. In the present study, 0.29% of all patients with skin cancer who presented to our pathology clinic were diagnosed with melanoma. An analysis of data on the incidence of melanoma in literature reveals, that although the prevalence among men and women is similar, it is more common in women aged <40 years and men aged $40 >$ years (10). Although the number of patients aged 40 and under were very small in the present study, the findings concurred with literature. In a study by Zhang et al. (11) involving 98 patients in China, the age range of the patients was 36–96, and the male/female ratio was 1.88/1. Taş et al. (12) found the mean age of cases to be 50 in their study, while in the study by Şimşek et al. (13), the mean age was reported as 59.5, and 63 in the study conducted by Şahin et al. (14). In the present study, the youngest patient was 26 years old, the oldest was 88 years old and the mean age was 63.18 years. Şimşek et al. (13) reported a male/female ratio of 0.83/1 in their study, while Şahin et al. (14) found the male/female ratio to be 1.32/1. In the present study, the male/female ratio was found to be 1.19/1. An analysis of the studies conducted in Turkey to date reveals an average age of between 50 and 63 years and a male/female ratio of 0.83-1.2. The results of the present study also fall within these ranges. Melanomas can develop on the skin, in the mucosa and on other parts of the body (15). While Zhang et al. (11) and Taş et al. (12) reported lesions to be most common on the extremities, Şimşek et al. (13) found the most common localization to be the head and neck, concurring with the findings of the present study. An analysis of the studies conducted in Turkey to date reveals the most common locations to be the head, neck and extremities, with localization differences observable between genders. This difference in tumor localization is usually attributed to the socio-cultural differences between the East and West, geographical features and economic causes. Although superficial spreading melanoma is the most common histopathological type in literature, superficial spreading and nodular melanomas are most frequently reported in our country.

Lentiginous acral melanomas were reported to be the most common in the study by Zhang et al. (11). In a study conducted by Taş et al. (12) based on data collected from the Istanbul region, the most common type was superficial spreading melanoma. In contrast, in the study conducted by Şimşek et al. (13) based on data collected from the Samsun region, and in the study conducted by İbiliğlü et al. (16) based on data collected from the Diyarbakır region, the most common melanoma type was nodular melanoma, as was the case also in our study. This supports the suggestion made at the beginning of the study that patients in Turkey are unable to detect melanoma and other cutaneous malignancies over the changes in the skin with age and benign lesions, and so tend to present to hospitals only when lesions reach an advanced stage. Clark's Level and Breslow thickness are now accepted worldwide as the most common indicators of life expectancy, and it is generally Clark's Level IV reported in studies in Turkey. In the study by Taş et al. (12), the most common Breslow thickness was 2–4 mm and showed an equal distribution. In the studies by Şahin et al. (14), Şimşek et al. (13) and İbiliğlü et al. (16), Breslow thicknesses of 4 mm and above were reported. In the present study, the results comply with the general findings, with 4 mm and above being the most commonly seen Breslow thickness. Therefore, Clark's Level was also observed as stage 4 in our study. While ulceration is reported to be rare in Western literature, it was reported to be common in the study by Zhang et al. (11). Balch et al. (7), on the other hand, suggested that ulceration increases in direct proportion to tumor thickness. Ulceration was seen in more than half of the cases in the present study (52.6%) (6), while Taş et al. (12) observed ulceration in 47.6% of cases, and Büyükpınarbaşı et al. (17) in 53.8% of the cases. Furthermore, Taş et al. (12) reported no significant relationship between ulceration and survival, while Büyükpınarbaşı et al. (17) reported a significant relationship between ulceration and survival, and a similar result was found also in the present study. This is consistent with the assumption of Balch et al. (7) that ulceration is the second most accurate prognostic indicator. The American Joint Committee on Cancer (AJCC) staging system (8th edition) identify Breslow thickness and ulceration as important predictive factors for survival for patients with melanoma (18). In our study, a significant relationship was identified between Clark's Level ($p:0.000$) and Breslow thickness ($p:0.008$) and ulceration. The most effective and reliable approaches to the treatment of melanoma

involve wide surgical excision, and regional lymph node curettage where necessary. It is possible to achieve 95% regression in early stage lesions (19), but as seen in the present study, cases in our country usually present to hospital only after reaching an advanced stage.

Conclusion

In our study, the majority of our patients were over 40 years old and male patients, and melanoma was most commonly located in the head and neck region. Histopathologically, the tumor is the most common nodular and ulcerous type. Most of our patients have advanced Breslow thickness and Clark's stages. There is a statistically significant relationship between Breslow thickness, Clark's stage, ulceration and survival in our study. This shows us that most of our cases applied to health institutions late and therefore they were diagnosed late. The most important known risk factor in the etiology of melanoma is exposure to the sun. Therefore, preventive methods gain importance.

Ethical Consent: This study was approved by the Osmangazi University Faculty of Medicine Ethics Committee and it was done according to the declaration of Helsinki.

Conflict of Interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Financial Support: No financial support has been received for this study from any institution and/or fund.

Author Contributions: BPC: conceived and designed the study; FT, BPC: collected the data; BPC, FT: analyzed and interpreted the data; BPC: supervised the study.

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