International Journal of Medical Science and Clinical Invention 5(08): 3970-3973, 2018
DOI:10.18535/ijmsci/v5i8.01 **ICV 2016: 77.2**
e-ISSN:2348-991X, p-ISSN: 2454-9576

Research Article

Clınıcopathologıcal Features of Melanoma In Muğla

Özgür İLHAN ÇELİK

Muğla Sıtkı Koçman University Faculty of Medicine Department of Pathology, Kötekli, Muğla, Turkey.

Abstract:

Introduction: Melanoma, a neoplasm of melanocytes is the most aggressive and life-threatening skin cancer. The incidence of it is higher in fair skinned people as the Ultraviolet-light exposure is the most important risk factor with the malignant transformation of the nevi. So here we aimed to determine the clinical and histopathological findings of our Melanoma cases.

Method: We reviewed the tumors of the patients who received the diagnosis of Melanoma at our Pathology Laboratory, between 2011 and 2018 retrospectively.

Results and Discussion: There were 43 skin Melanoma cases. 21(48.8%) of the patients were female, 22(51.2%) were male. The median-age in females was 68, while 64 in males. 35(81.4%) of the 43 cases were Nodular Melanoma(NM), 3(7%) were Superficial-spreading melanoma(SSM) and 5(11.6%) were Melanoma-in-situ(MIS). None of the SSMs and MISs had metastasis to anywhere.

7(20%) of the NMs had lymph-node and 3(8.6%) had soft tissue metastasis at the time of diagnosis. 4 developed lung, brain, stomach and nasopharinx metastases in the following 2 years. The ratio of the Clark Level 2,3,4,5 of NMs were 11.4%, 28.6%, 45.7% and 14.3% respectively. Most of the metastatic cases were Clark Level 3 or 4. This study showed that Melanoma is generally diagnosed at WHO-Stage 2 or 3 and this cause worse prognosis as the cure rates depend greatly on the stage.

Conclusion: As a result it's very important to self-examine the existing nevi on our skin in order to detect the early malignant transformation to Melanoma and protect our skin from Ultraviolet-light.

Keywords: Melanoma, Skin tumor, histopathology.

Introduction:

Melanoma is a malignant neoplasm of melanocytes. It accounts for 4% and 5% of all new diagnosed malignancies in females and males respectively(1). It predominantly affects older people; however it can present occasionally in younger adults and also in children. The incidence of it is higher in fair people as the exposure to Ultraviolet-light is the most important risk factor(1-3). With the increase in exposure to Ultraviolet-light because of the defect of Ozon layer and global warming, the incidence of Melanoma has been increasing. Etiological factors other than Ultraviolet-light and fair skin are family story (Familial melanoma), Xeroderma Pigmentosum, Familial dysplastic nevus syndrome, congenital bathing-trunk nevus and immunosuppression. It can also arise denovo(1,4). It is the most aggressive and life-threatening skin tumor as it has a very high tendency to spread to other parts of the body and has a high mortality(5). As Melanoma is such an important disease especially in more sunny countries like ours, we here aimed to determine the clinical and histopathological findings of Melanoma cases diagnosed in our Pathology Laboratory.

Method:

We reviewed the slides and the clinical data of the patients Who received the diagnosis of Melanoma at Pathology Laboratory of Muğla Sıtkı Koçman University Education and Research Hospital, between 2011 and 2018 retrospectively. Clinical parameters of the patients were obtained from the hospital automation system. The parameters evaluated were age, gender, histological type of the tumors, Breslow tumor thickness, Clark Level, mitosis, lymphovascular invasion, perineural and intraneural invasion, regression and tumor infiltrating lymphocytes. Breslow tumor thickness was calculated according to AJCC (The American Joint Committee on Cancer) guidelines (6). The level of tumor invasion was classified according to Clark levels. (Level 1: in situ melanoma, Level 2: invasion of the papillary dermis by single cells or small nests, Level 3: invasive tumor usually as an expansile nodule abutting on the reticular dermal interface, Level 4: invasion of the reticular dermis, Level 5: invasion of the subcutaneous fat)(1). Mitotic rate was counted in $1mm^2$ area. >1 mitosis was accepted as present, ≤ 1 mitosis was accepted as absent(1). Lymphovascular invasion, perineural and intraneural infiltration and regression were evaluated as absent or present. Tumor infiltrating lymphocytes were evaluated as; Brisk (lymphocytes present throughout the whole vertical growth phase or extending across its entire base), Nonbrisk(tumor infiltrating lymphocytes implies focal

infiltration only) and absent (no lymphocytes at all or lymphocytes are present but do not infiltrate the tumor) (7,8).
This Project was evaluated by Muğla Sıtkı Koçman University Research and Publication Ethics Committee with 180150/18 registration number and it was approved in terms of scientific researches and patient ethics.
In statistical analysis of data, mean and standard deviation for continuous variables and percentages for categorical variables were used. Descriptive statistics and categorical variables were given as frequencies (percentages).

Results and Discussion:

There were 43 cutaneous Melanoma cases. 21(48.8%) of the patients were female, 22(51.2%) of them were male. The median age at the time of diagnosis in females was 68, while 64 in males. Other detailed results of the parameters evaluated are listed in the Table 1.

Table 1: Parameters evaluated in patients with Cutaneous Melanoma

Parameter		**Number**	**Ratio (%)**
Histological tumor type	Nodular Melanoma	35	81.4
	Superficial-spreading melanoma	3	7
	Melanoma-in-situ	5	11.6
Total		**43**	**100**
Breslow Thickness of Melanomas (mm)	-	5	11.63
	<1	2	4.65
	1-2	9	20.93
	>2-≤4	13	30.23
	>4	14	32.56
Total		**43**	**100**
Clark level	-	5	11.63
	1	1	2.33
	2	5	11.63
	3	12	20.90
	4	16	37.21
	5	4	9.30
Total		**43**	**100**
Mitosis	Absent (≤1/1mm^2)	6	13.95
	Present (>1/1mm^2)	37	86.05
Total		**43**	**100**
Lymphovascular invasion	Absent	33	76.74
	Present	10	23.26
Total		**43**	**100**
Perineural/intraneural infiltration	Absent	34	79.07
	Present	9	20.93
Total		**43**	**100**
Tumor infiltrating lymphocytes	Absent	13	30.23
	Nonbrisk	11	25.58
	Brisk	19	44.19
Total		**43**	**100**
Regression	Absent	38	88.37
	Present	5	11.63
Total		43	100

Most of the cases were Nodular Melanoma(NM), 3 were Superficial-spreading melanoma(SSM) and 5 were Melanoma-in-situ(MIS). None of the SSMs and MISs had metastasis to anywhere.
7(20%) of the NMs had lymph-node metastasis (Table 2) and 3(8.6%) had soft tissue metastasis (without lymph-node metastasis) at the time of initial diagnosis.

Among these lymph-node metastatic patients, 1 patient had synchronous lung, soft tissue metastasis with Non-Hodgkin Lymphoma as an additional disease. He was the youngest patient (31 years old) and he was being treated for Lymphoma for 3 years at the time of melanoma diagnosis. Unfortunatelly he lost his life in 1 year. This poor disease course was linked to immunosuppression (1)(Table 2).

Table 2: The features of Nodular Melanoma cases with lymph-node metastasis at the time of diagnosis.

case	Age	Breslow thickness(mm)	Cark level	Lymphovascular invasion	Peri/intraneural invasion	Other synchronous metastasis	Metachronous metastasis	Additional disease
1	63	10	5	+	-			
2	73	9	5	+	-			

3	68	15	5	+	+		-Nasopharinx	
4	75	13	5	+	+		-Stomach	
5	72	14	5	+	+	-Brain		
6	60	8	4	+	_			
7	31	10	5	+	+	-Lung-Soft tissue		Non-Hodgkin Lymphoma

Also among these lymph-node metastatic patients, 1 patient had synchronous brain metastasis and 2 patients developed metachronous metastases to the stomach and nasopharinx in the following 2 years (Table 2). Metastatic patients had Clark level 4 or 5 and high Breslow thickness; however none of them had regression and tumor infiltrating lymphocytes. Also 1 of these 7 patients presented with a lymph-node metastasis at first and later the primary skin tumor was found on his scalp.

When all patients are considered; most of the tumors had higher Breslow thickness than 2mm (62.79%) and the average Breslow tumor thickness was 4.75mm in NMs. Also most of the tumors had 3 or higher Clark Level (67.41%) at the time of diagnosis.

In our study we presented that Cutaneous melanoma is predominantly a disease of older people and is seen more common in males especially in our geographical region in paralel to the study of Ozgen(9). It is a very interesting disease that makes frequent, early and unusual organ metastases (10). The worst prognostic histological type of melanoma was NM with the higher rates of metastasis, higher Breslow thickness, higher Clark Level, higher mitotic rates, with more lymphovascular-peri/intraneural infiltrations, with lesser tumor infiltrating lympocytes and with poorer course as seen in the literature (2,3,5,9,11). Most of the melanomas arise de novo. Only 2 of our patients mentioned previous presence of a blue and a melanositik nevus. So it is important to recognise the melanomas early with these signs: diameter larger than 6mm, irregular lesion borders, irregular and variable pigmentation, asymmetry, recent and rapid change in a pre-existing lesion. Older and male patients have worse course(12). The prognostic parameters have to be evaluated carefully in the surgical materials with the clinical parameters like age, gender and localization in order to determine the tumors which have the capacity for spread and shorten the life. The most important prognostic indicator is the Breslow tumor thickness measured from the superficial level of granular cell layer to the deepest point of invasion(13,14). Breslow tumor thickness, presence of mitosis, skin ulceration and satellit lesions with lymph node and distant metastasis are the features used in AJCC staging system in order to determine the need of adjuvant chemotherapy, immunotheraphy or other treatment regimens (15,16). The level of tumor invasion is evaluated according to the Clark level system. Clark level formerly was believed to provide independent prognostic information for thin tumors than 1mm (17,18); however recent studies present that mitotic rate assessment was enough in even thin tumors and so Clark level was not suggested anymore(19,20). Tumor infiltrating lymphocytes are also important independent prognostic parameter. Thin melanomas tend to have brisk response while thick tumors frequently have no lymphocytic response as we found in our study(7,8). They tend to make more metastasis to lymph nodes as Taylor et all presented in their study in paralel with our study (8). The importance of regression is still controversial. Some authors claim that it correlates with aworse prognosis in thin tumors(21). The precence of lymphovascular invasion facilitates metastasis as we saw in our study(22) and diminishes the survival as presented in many other studies (23-25). The presence of perineural and/or intraneural infiltration increases the risk of recurrence (1).

Conclusion:

This study showed that Melanoma is generally diagnosed at advanced stage and this cause worse prognosis as the cure rates depend greatly on the stage. So as a result it's very important to self-examine our skin, detect the newly emerging lesions and the existing nevi on our skin in order to diagnose the Melanomas earlier. Also another very important attitude is to protect our skin from Ultraviolet-light especially in the countries with excess sun exposure like our country; Turkey.

References

[1] Calonje E, Brenn T, Lazar A, McKee PH. Malignant Melanoma in McKee's Pathology of the skin. Elsevier Saunders, 4th ed. 2012, Philadelphia. P:1221-1267.

[2] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65(1):5-29.

[3] Chang C, Murzaku EC, Penn L, Abbasi NR, Davis PD, Berwick M, et al. More skin, more sun, more tan, more melanom. Am J Public Health. 2014;104(11):92-9.

[4] IARC Working group reports. Exposure to artificial UV radiation and skin cancer. Lyon, France. IARC Working group on risk of skin cancer and exposure to artificial ultraviolet light, International Agency for Research on cancer World Health Organization 2005;1:21-33.

[5] Sula B, Uçmak F, Kaplan MA, Urakçi Z, Arica M, IsikdoganA. Epidemiological and clinical characteristics of malignant melanoma in Southeast Anatolia in Turkey. Pan Afr Med J. 2016; 24: 22.

[6] Balch CM. Melanoma of the skin. In: Edge SB, Byrd DR, Compton CC, et al. AJCC Cancer Staging Manual. Ed 7thNew York: Springer Verlag, 2010, p:325-44.

[7] Clemente CG, Mihm MC Jr, Bufalino R, et al.: Prognostic value of tumor infiltrating lymphocytes in the vertical growth phase of primary cutaneous melanoma. Cancer. 1996;77:1303-10.

[8] Taylor RC, Patel A, Panageas KS, et al.: Tumor-infiltrating lymphocytes predict sentinel lymph node

positivity in patients with cutaneous melanoma. J Clin Oncol. 2007;25:869–75.
[9] Ozgen A. A single institution retrospective analysis of malignant melanoma. J Can Res Ther. 2014;10(1):38-42.
[10] Ljubacev A, Medved I. Multiple Melanomas of the Right Atrium as a First Sign of a Metastatic Disease. IJMSCI. 2017;4(7):3116-8.
[11] Rastrelli M, Tropea S, Rossi CR, Alaibac M. Melanoma: epidemiology, risk factors, pathogenesis, diagnosis and classification. In Vivo. 2014;28(6):1005-11.
[12] Weiss SA, Hanniford D, Hernando E, Osman I. Revisiting determinants of prognosis in cutaneous melanoma. Cancer. 2015;121(23):4108-23.
[13] McGovern VJ, Shaw HM, Milton GW. Prognostic significance of a polypoid configuration in malignant melanoma. Histopathology. 1983;7:663–72.
[14] Breslow A. Thickness, cross-sectioned areas and depth of invasion in the prognosis of cutaneous melanoma. Ann Surg. 1981;172:902–8.
[15] Dvir E, Gellei B, Hirshowitz B. Measurement of tumor thickness as a prognostic tool in primary melanoma of the skin. Ann Plast Surg. 1980; 5:216–21.
[16] NIH Consensus Development Panel on Early Melanoma: Diagnosis and treatment of early melanoma. J Am Med Assoc. 1992; 268:1314–19.
[17] Balch CM, Soong SJ, Gershenwald JE, et al. Prognostic factors analysis of 17,600 patients: validation of The American Joint Committee on Cancer melanoma staging system. J Clin Oncol. 2001;19:3622–34.
[18] Masback A, Olsson H, Westerdahl J, et al. Prognostic factors in invasive cutaneous melanoma: a population-based study and review. Melanoma Res. 2001;11:435-45.
[19] Balch CM, Buzaid AC, Soong SJ, et al. Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. J Clin Oncol. 2001;19:3635–48.
[20] Blessing K, McLaren KM.Histological regression in primary cutaneous melanoma: recognition, prevalence, and significance. Histopathology. 1992; 20:315–22.
[21] Cooper PH, Wanebo HJ, Hagar RW. Regression in thin melanoma; microscopic diagnosis and prognostic importance. Arch Dermatol. 1985;21:1127–31.
[22] Thorn M, Ponten F, Bergstrom R, et al. Clinical and histopathologic predictors of survival in patients with malignant melanoma: a population-based study in Sweden. J Natl Cancer Inst. 1994;86:761–69.
[23] Straume O, Akslen LA. Independent prognostic importance of vascular invasion in nodular melanomas. Cancer. 1996;78:1211–19.
[24] Kashani-Sabet M, Sagebiel RW, Ferreira CMM, et al. Vascular involvement in the prognosis of primary cutaneous melanoma. Arch Dermatol. 2001;137:1169–73.
[25] Nagore E, Oliver V, Botella-Estrada R, et al. Prognostic factors in localized invasive cutaneous melanoma: high value of mitotic rate, vascular invasion and microscopic satellitosis. Melanoma Res. 2005;15:169–77.