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ANALYSIS OF THE EPIDEMIOLOGICAL AND HISTOPATHOLOGICAL PROFILE OF CASES OF CUTANEOUS MELANOMA IN A REFERENCE HOSPITAL IN THE WEST OF PARANÁ

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ABSTRACT

Introduction: Cutaneous melanoma (CM) is considered the most aggressive malignant neoplasm of the skin due to its high metastatic power and has been showing an increasing incidence, becoming a public health problem. **Objective:** To analyze the epidemiological and histopathological profile of patients diagnosed with CM, taking into account the primary location, Breslow thickness, Clark Levels, as well as demographic variables such as sex, age, skin color and profession. **Methods:** A retrospective, descriptive and cross-sectional study with a quantitative approach was carried out on 124 medical records of patients diagnosed with CM through histopathology, treated at a reference hospital in the city of Cascavel-PR, Brazil, from 2012 to 2018. **Results:** The profile of the patients was: male (60.5%), caucasian (96%), 57.4 years old, farmer (35.4%), with lesions predominantly on the trunk (40.32%), lower limbs (16.93%) and face and/or or scalp (16.12%). The Breslow index ≥ 4.01mm was expressed with the highest frequency (33.75%). As for Clark's levels, the highest incidence was observed at level IV (44.87%). Conclusion: We can hypothesize that most of the diagnoses in this study were performed late, taking into account the histological variables analyzed. Therefore, primary and secondary prevention measures should be widely discussed in order to diagnose CM early and prevent its worsening.

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INTRODUCTION

Cutaneous melanoma (CM) is considered the most important skin cancer (SAMPAIO, 2001). It originates from melanocytes, melanin-producing cells and despite having a low incidence, 3% in the Brazilian population, it is considered the most aggressive of skin neoplasms, due to its high metastatic power (INCA, 2018). The incidence of CM has been increasing worldwide, mainly in white individuals (ALMEIDA et al., 2001). In Brazil, according to the National Cancer Institute (INCA), 8,450 new cases of CM are expected for 2020, with 4,200 new cases in men and 4,250 new cases in women, mainly in the southern region of the country, where concentrate the highest rates of CM in the country in recent decades (INCA, 2020). The risk factors for the development of such pathology have been discussed for years, and can be divided into constitutional and environmental: skin with lighter phototypes (types I and II of Fitzpatrick and Path), the quantitative presence (more than 50 acquired nevi) and qualitative (presence of atypical nevi) of nevi and the family history of melanoma are the main constitutional factors for its appearance (OSOBA, 1993; HARRIS, 1991). Regarding environmental factors, exposure to solar radiation becomes a potent risk factor, therefore, intermittent sun exposure, in the form of sunburn, as well as the modification of nevi due to radiation, are the

main etiologies of the disease. 1993; HARRIS, 1991). The diagnostic hypothesis of CM should be questioned in all skin lesions that present asymmetry, irregular borders, color variation, diameter greater than 6mm and very fast evolution (DIMATOS et al., 2009). One of the criteria used to assess the depth of the CM is the Breslow Index. This scale is closely linked to patient survival: the greater the thickness of the tumor, the shorter the survival. The Breslow Index is classified according to Table 1, where, according to Sampaio et al, (2008) the 10-year mortality is proportional to the deep involvement of the layers (TSAU et al., 2004; SAMPAIO et al., 2008) (Table 1). Clark's Levels describe anatomical invasion of the MC in the skin (PROENÇA et al., 2001). (Table 2) According to the Joint American Committee on Cancer Staging (AJCC) this classification is no longer recommended as a staging criterion (BALCH, 2009). However, the presence of the Clark level in the anatomopathological report for staging purposes is recommended by the Brazilian Society of Dermatology (TOVO, 2019).

Table 1. Breslow index related to 10-year survival

Survival	Depth
≤ 1mm	22.50%
1.1-2mm	21.25%
2.1-4mm	22.50%
≥ 4.01mm	33.75%

Source: Sampaio SA, Rivitti EA, 2001.

Table 2. Clark Level

Level	Anatomic Invasion
I	Confined to the epidermis (in situ)
II	Invasion of the papillary dermis
III	Invasion of the dermal papillary-reticular junction
IV	Invasion of the reticular dermis
V	Subcutaneous fat invasion

Source: Ministry of health of Brazil, 2013.

In this sense, the present study aims to analyze the epidemiological and histopathological profile of patients diagnosed with CM, in a reference hospital in western Paraná, taking into account the primary location, Breslow thickness, Clark levels, as well as demographic variables such as sex, age, skin color and profession performing correlation between variables.

METHODOLOGY

The present study was approved by the Ethics and Research Committee of the Centro Universitário Assis Gurgacz and data collection began after signing the Free and Informed Consent Form from the head of the hospital unit involved in the study. A retrospective, descriptive and cross-sectional study was carried out with a quantitative approach of 124 medical records of patients diagnosed with Cutaneous Melanoma through histopathology, treated at CEONC - Hospital do Câncer, in the city of Cascavel-PR, Brazil, from 2012 to 2018. All medical records of patients whose primary site of the tumor was cutaneous were included, regardless of sex, age, race, origin or profession with anatomopathological diagnosis. The dependent variable studied was primary cutaneous melanoma and the independent variables were: sex, age, skin color, occupation, lesion topography, Clark level and Breslow index. Data were entered into Excel and analyzed using EpiInfo software.

RESULTS

The total sample consisted of 124 patients with primary CM, including 75 males (60.5%) and 49 females (39.5%). The mean age of the study population at diagnosis was 57.4 years, ranging from 19 to 89 years of age. The average female age was lower than the male, 56.1 and 58.4 years, respectively. As for the distribution by age, 4 patients (3.22%) were aged below 30 years, 8 (6.45%) aged between 31 and 40 years, 26 (20.96%) were aged between 41 and 50 years old, 37 (29.83%) between 51 and 60 years old, 24 (19.35%) between 61 and 70 years old, 16 (12.90%) between 71 and 80 years old, and 9 (7.25%) above 80 years. Regarding skin color, the number of white patients totaled 119 (96%). Of the remaining patients, 4 (3.2%) were brown and 1 (0.8%) yellow. There is no incidence of CM in black patients. As for the patients' occupation, the profession that stood out was the farmer/farmer, 44 patients (35.4%). As for the topography of the lesions, 20 patients (16.12%) had lesions on the face, 9 patients (7.25%) had lesions in the cervical region, 50 (40.32%) had lesions on the trunk, 17 (13.70%) %) had injuries to the upper limbs, 21 (16.93%) had injuries to the lower limbs, 3 (2.41%) had injuries to the palm/plantar region, and 4 (3.22%) had injuries to the genitalia. (Table 3). With regard to the Breslow Index, there was no information in 44 medical records as well as in the histopathological reports.

Table 3. Distribution of CM according to topography

Breslow Index	N	% Total
Face/Scalp	20	16.12
Cervical	9	7.25
Stem	50	40.32
Upper limbs	17	13.70
Lower members	21	16.93
Span	3	2.41
Intimate Region	4	3.22

Table 4. Distribution of cases according to the Breslow index

Breslow Index	N	% Total
≤ 1mm	18	22.50%
1.1-2mm	17	21.25%
2.1-4mm	18	22.50%
≥ 4.01mm	27	33.75%

Among the remaining 80 (64.5%) records, the tumor thickness varied between 0 and 9.1 mm, with an average of 3.46 mm. 18 (22.5%) patients had Breslow in situ being ≤ 1mm, 17 (21.25%) had Breslow between 1.01 and 2mm, 18 (22.5%) had Breslow between 2.01 and 4mm and 27 (33.75%) had Breslow ≥ 4.01mm (Table 4). There was no significant association between gender and Breslow index ($p=0.255$). The comparison between age and Breslow, in turn, showed significant associations between the age group below 40 years and Breslow ≤1mm and the age group above 71 years with Breslow level ≥ 2.01mm ($p<0.05$). When associated with topography, there was significance, and trunk melanomas were associated with Breslow level ≥ 2.01mm ($p<0.05$). As for the Clark Level, there was no information in 46 medical records as well as in the histopathological reports. Among the 78 (62.9%) remaining records, 4 (5.12%) presented Clark II, 19 (24.35%) presented Clark III, 35 (44.87%) presented Clark IV and 20 (25.64%) presented %) featured Clark V. There was no description of Clark I.

Table 5. Distribution of cases according to Clark's levels

Clark Levels	N	% Total
I	0	0.00%
II	4	9.30%
III	19	44.19%
IV	20	46.51%

DISCUSSION

In the present study, there was a predominance of CM in males (60.5%), which contradicts those in the national literature where there is a greater predominance in females (BORGES et al., 2007; CARVALHO et al., 2017; BAKOS et al., 2007; CARVALHO et al., 2017; BAKOS et al. al., 2012). Some authors even consider the female gender as a risk factor for the occurrence of CM (MIRANDA, 2001; OUMEISH, 1997). However, there are studies in the national literature whose data coincide with those of this work, one of which was carried out in Goiânia, which reveals a ratio of 1.6 men for each woman. This fact was associated with more frequent and intense sun exposure by males (SORTINO-RACHOU et al, 2006). In the sample, the mean age was 57.4 years, confirming data from the literature that

consecrates middle-aged adults as the most susceptible to CM (BORGES et al., 2007; CARVALHO et al., 2017; BAKOS et al., 2012). This average age was above the national average, which is 52 years, reflecting a late diagnosis of CM. Although these results are known, it is still unclear why melanoma shows a tendency to increase diagnosis rates in middle age. In fact, one would expect a greater occurrence in more advanced age groups, due to the cumulative effect of solar radiation and deterioration of the immune system (DENNIS, 1997). The white color prevailed in the sample (96%), which coincides with the national literature and corroborates with data from the Brazilian Society of Dermatology (2019) on the incidence of cutaneous neoplasms - occurring more in individuals with Fitzpatrick and II phototypes Path (TOVO, 2019). The southern region of the country is responsible for presenting a population of Caucasians who are exposed to solar radiation during several months of the year, due to climatic conditions and leisure options in the region, contributing to the appearance of CM (INCA, 2010). In this context, the profession most affected in this study was farming (35.4%), which corroborates exposure to sunlight as an extrinsic risk factor of great relevance for the development of skin cancer (CARVALHO, 2004). According to the above, professional casuistry proved to be very relevant in our study. In our region, located in western Paraná, the economy is based on agriculture, more specifically on soybean and corn plantations, as well as in other states, such as Mato Grosso, Mato Grosso do Sul, Santa Catarina and Rio Grande do Sul, and that require, in the vast majority of farmers, sun exposure for a prolonged period to carry out their activities.

A study carried out in Santa Catarina in 2019 evaluated farmers' knowledge and care about sun exposure. The results revealed that 80% of farmers are aware of diseases caused by sun exposure and recognize the importance of prevention, however, 80% of them say they do not use any protection against sun exposure (COLOMBO, 2019). that the culture of using photoprotection measures, such as barrier methods or sunscreen, is not widespread and fully accepted in this professional environment. As for topography, the highest percentage of patients with melanoma presented the trunk (40.32%) as the primary lesion sites, followed by the lower limbs (16.93%) and face/hair (16.12%). These results coincide with current published studies.22,23 Differences in clothing and lifestyle are factors that determine differences in the topography of lesions according to gender. Statistically, women had more injuries (57%) on the limbs than men, and men had more injuries on the face and trunk (64%) (FERRARI, 2008). Regarding the Breslow level, in situ lesions only corresponded to 22.5% of the cases, indicating a low diagnostic precocity. On the other hand, 33.75% of the patients presented Breslow≥ 4.01mm, coinciding with a study by the Cancer Hospital of São Paulo.24 Some authors confirmed that the measurement of tumor thickness is the strongest predictor of the prognosis of patients with melanoma, for be associated with an increased risk of local recurrence and regional and distant metastases. The prognosis worsens with increasing thickness as a continuous logarithmic function (CARVALHO et al., 2004; BAKOS et al., 2002; MIRANDA, 2001; BALCH et al., 2001). As for the Clark classification, 44.87% of the patients had Clark IV, coinciding again with the study by the Cancer Hospital of São Paulo (PURIM et al., 2020) In Londrina-PR, there was a predominance of Clark II and III, (70.3%) (GON et al., 2001) In Blumenal-SC and HU/UFSC there was a higher prevalence of Clark I, 24.9% and 51.4% respectively (NASSER, 1993).

CONCLUSION

As for the histopathological profile of the cases of CM evaluated in our study, the majority showed a predominance of Breslow≥ 4.01mm and Clark Level IV and V, which is considered an unfavorable prognosis, since the large thickness of the tumor and the high level of invasion are strongly linked to local recurrence and regional and distant metastases, favoring the theory that the studied population received a late diagnosis. The early diagnosis of skin cancer should be widely associated with education and prevention campaigns, as already carried out by the Brazilian Society of Dermatology since 1998, on a national basis, which aims at secondary prevention, providing therapeutic guidance to the population, as well as education for the recognition suspicious lesions, leading to an early search by a dermatologist. As for the epidemiological aspects, the results of the studies showed some similarities with national and international studies, highlighting the prevalence of middle-aged, male individuals with white skin, mainly phototypes I and II of Fitzpatrick and Path. In our region, there are a large number of farmers, who tend to expose themselves daily and for a long time to ultraviolet radiation to perform their duties. Similar studies report that even knowing the damage that solar radiation causes to the skin, most farmers do not use photoprotective measures. In this context, it is concluded that studies like this one allow mapping the current context of the problem in our environment, contributing to the development of new scientific studies and institutional interventions. The objectives of this study were achieved and further research on the subject is suggested, bringing information to the population of this region that needs photoprotection and that they become aware of the need to use sunscreen in the prevention of diseases such as skin cancer, melasma and premature aging, which is caused by solar radiation.

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