Early diagnosis of cutaneous melanoma: an observation in southern Brazil *

A precocidade diagnóstica do melanoma cutâneo: uma observação no sul do Brasil

Raquel Bonfá [1]
Rafael Bonfá [3]
Roque Domingos Furian [4]
Renan Rangel Bonamigo [2]
Kauê Marcolin Duro [3]
Alice de Medeiros Zelmanowicz [5]

Abstract: BACKGROUND: The incidence of melanoma cutaneous and the mortalities rates are rising in most countries worldwide.
Objective: to describe the histopathological characteristics of cutaneous melanoma, according to the criteria established by the Brazilian Group of Melanoma, and to evaluate early diagnosis in a cancer treatment referral center.
Methods: we performed a cross-sectional descriptive study of cases of primary cutaneous melanoma identified after excisional biopsy and processed at the pathology laboratory of Complexo Hospitalar Santa Casa between Jan 1st 2000 and Jan 15th 2005. The following variables were analyzed: age, gender, topography, histopathologic subtype, Breslow thickness, growth phase, Clark level, mitotic index, peritumoral and intratumoral lymphocytic inflammatory infiltrate, angiolymphatic invasion, ulceration, regression, type of regression, microscopic satellitosis, and surgical margins.
Results: 328 cases, 57% female and 43% male, were analyzed. Mean age was 55.6 years. For women, the most common tumor location was in inferior(29.26%) and superior limbs(23.94%), while for men melanoma was mainly found in the back(35%), followed by anterior chest/abdomen(14.29%) ($p<0.05$). Prevalence of histologic subtypes was the following: superficial spreading melanoma(62.8%), lentigo maligna(14.9%), nodular(14.6%), acral(7.3%), and desmoplastic(0.3%) types. Regarding Breslow, 26.2% were in situ, 36.9% had ≤1 mm, and only 15.9% were ? 4mm in depth.
Conclusion: the distribution of histopathologic subtypes, as well as Breslow thickness, was in accordance with previous studies in outpatient populations. The profile of cases of cutaneous melanoma diagnosed in a tertiary hospital seems to be experiencing some changes over the last two decades, with a current trend for earlier diagnosis.
Keywords: Early diagnosis; Epidemiology; Melanoma; Risk factors; Skin neoplasms

Resumo: FUNDAMENTOS: A incidência do melanoma cutâneo e as taxas de mortalidade a ele associadas estão crescendo na maioria dos países do mundo.
OBJETIVO: Descrever as características histopatológicas do melanoma cutâneo, segundo critérios do Grupo Brasileiro de Melanoma, e avaliar a precocidade diagnóstica em hospital de referência do sul do Brasil para o atendimento de melanoma.
MÉTODOS: Estudo transversal com casos de melanoma cutâneo primário reconhecidos após biópsia excisional, processados no laboratório de Patologia do Complexo Hospitalar Santa Casa de Porto Alegre entre 1º/1/2000 e 15/1/2005. Outras variáveis analisadas: idade, sexo, topografia da lesão, subtipos histopatológicos, índice Breslow, fase de crescimento, índice de Clark, índice mitótico, infiltrado inflamatório linfocitário peritumoral e intratumoral, invasão angiolinfática e perineural, presença de úlcera e regressão, tipo de regressão, satelitose microscópica e margens cirúrgicas.
RESULTADOS: Incluídos 328 casos, sendo 57% mulheres e 43% homens, com média de idade de 55,63 anos. A localização foi preferencialmente nos membros inferiores (29,26%) e superiores (23,94%) nas mulheres. Nos homens, predominou no dorso (35%) e no tórax anterior/abdome (14,29%) ($p<0,05$). Os subtipos histológicos se apresentaram com as seguintes frequências: espalhamento superficial (62,8%), lentigo maligno (14,9%), nodular (14,6%), acral (7,3%) e desmoplásico (0,3%). Quanto ao Breslow: 26,2% dos casos eram in situ, 36,9% eram ≤1mm, enquanto apenas 15,9% apresentavam mais de 4mm de profundidade.
CONCLUSÃO: A distribuição dos subtipos histológicos e o nível de profundidade (Breslow) foram semelhantes aos encontrados em estudos anteriores em população de base não hospitalar. O perfil dos casos de melanoma cutâneo avaliados em hospital terciário parece estar se modificando nas últimas duas décadas, com tendência a diagnósticos mais precoces, atualmente.
Palavras-chave: Diagnóstico precoce, Epidemiologia, Fatores de risco, Melanoma,Neoplasias cutâneas

Received on 14.06.2009.
Approved by the Advisory Board and accepted for publication on 04.07.10.
* Work conducted at the Health Sciences Federal University of Porto Alegre (UFCSPA) - Faculty of Medicine - Department of Internal Medicine/Dermatology, Santa Casa Hospital Complex - Santa Rita Hospital - Pathology Laboratory - Porto Alegre (RS), Brazil.
Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding / *Suporte financeiro:* Financial aid granted through a scientific initiation scholarship offered by the Rio Grande do Sul Research Foundation (FAPERGS) for 12 months

[1] MD - Resident in Dermatology, Health Sciences Federal University of Porto Alegre (UFCSPA) - Porto Alegre (RS), Brazil.
[2] Ph.D - Professor, Department of Internal Medicine - Division of Dermatology, Health Sciences Federal University of Porto Alegre (UFCSPA). Head of the Dermatology Service. Residency Supervisor for Dermatology Residents and Professor of the Postgraduate Course of Pathology, Health Sciences Federal University of Porto Alegre (UFCSPA) - Porto Alegre (RS), Brazil.
[3] Dermatologist - Assistant at the Service of Dermatology, Health Sciences Federal University of Porto Alegre (UFCSPA) - Porto Alegre (RS), Brazil.
[4] Pathologist - Professor of Pathology, Health Sciences Federal University of Porto Alegre (UFCSPA). Responsible for the Residency Program in Pathology, Health Sciences Federal University of Porto Alegre (UFCSPA). Pathologist at the Santa Casa de Misericordia Hospital Complex - Porto Alegre (RS), Brazil.
[5] PhD – Oncologist, Santa Casa de Misericordia Hospital Complex - Porto Alegre (RS). Coordinator of the Center for Cancer Prevention and Hospital-based Cancer Registry, Santa Rita Hospital - Santa Casa de Misericordia Hosital Complex - Porto Alegre (RS), Brazil.

INTRODUCTION

The incidence of melanoma and its mortality rates are increasing in most countries worldwide where data about the disease are recorded. Brazil appears to follow this trend, despite the lack of information. [1]

Even though incidence of the disease has increased, a great improvement in the survival of patients with this type of cancer has been observed, primarily due to early detection. Educational programs designed to improve the early diagnosis of melanoma are probably responsible for this phenomenon, since treatment of the disease has not changed significantly. [2]

For 2008, the National Cancer Institute (INCA) estimates that 140 new cases of melanoma will be diagnosed in Porto Alegre. Rio Grande do Sul had the second largest gross rate of incidence among the Brazilian states during that year, an estimated 8.2 new cases per 100,000 inhabitants for men and 7.29 new cases per 100,000 inhabitants for women. Rio Grande do Sul was second to Santa Catarina, the Brazilian state with the highest annual rates. [3]

In Brazil, the population of Rio Grande do Sul is more prone to developing melanoma due to the higher proportion of fair-skinned individuals in relation to other states, as well as the high environmental concentration of UVA due to geographic location and cultural habits such as sun exposure on the beaches during the summer. [4]

There are four main types of primary cutaneous melanoma: lentigo maligna melanoma, superficial spreading, nodular and acral lentiginous-. [5] In a study conducted in a hospital in Porto Alegre in 1992, the most common histological type of primary cutaneous melanoma was nodular (36.6%). [6] However, these data refer to a tertiary care hospital, where cases are likely to have been diagnosed later, so lesions would already be growing vertically, masking eventual histopathological findings of other types of melanoma.

Another study conducted in 1997 in laboratories of Pathology of Porto Alegre-RS showed that superficial spreading melanoma accounted for 80.6% of cases. [7] This finding is similar to those of world literature, probably for not presenting the selection pattern mentioned, which suggests rates close to 70% for cases of superficial spreading melanoma, and only 15% for cases of nodular melanoma. [5]

The thickness of the tumor on histopathologic examination is the main prognostic factor studied. [8] Increases in the maximum thickness of the tumor and the presence of microscopic ulceration are inversely correlated with survival. [9] In Porto Alegre, the diagnosis of melanoma generally appears to be late. Only 2.15% are diagnosed at the *in situ* stage, and only 52% of cases present with tumor thickness of up to 1.5 mm (mean survival of 93% in 5 years) [7].

Given the increasing number of melanoma cases and the combination of risk factors for the population of southern Brazil, the expansion of epidemiological data on melanoma in Rio Grande do Sul is necessary.

The objectives of this work are to assess the main clinical and histopathological features of melanomas treated in a referral hospital in Porto Alegre (Santa Casa Hospital Complex - CHSC), identify age and sex of the patient with primary cutaneous melanoma, as well as the topography of the lesion, check early diagnosis in a tertiary level health care facility and analyze the association between these characteristics and the depth of the tumor using prognostic criteria in accordance with the guidelines established in 2003 by the Multicentric and Multidisciplinary Brazilian Group for the Study of Melanoma (GBM). [10] Very few papers have been published since the publication of these guidelines; therefore, studies of these variables are scant in the national literature.

MATERIALS AND METHODS

This was a descriptive, cross-sectional observational study of primary cutaneous melanoma cases diagnosed after excisional biopsy and processed in the laboratory of Pathology of CHSC between January 1, 2000 and January 15, 2005. We also evaluated variables such as age, sex, topography of the lesion, histopathological subtypes, in situ lesions, association of nevi and the histopathological criteria established by GBM - growth stage, Clark level, Breslow depth, mitotic index, peritumoral and intratumoral lymphocytic inflammatory infiltrate, perineural and angiolymphatic invasion, presence of ulcer, presence of regression, regression type, microscopic satellitosis and surgical margins. Clinical variables were obtained from the patients' medical records, whereas anatomopathological reports provided the histological variables. Cases with incomplete medical reports were reviewed by a CHSC pathologist and classified according to GBM's guidelines.

Data obtained from incisional biopsies and cases with incomplete information regarding the variables under study, even after histological analysis and review of the patient's chart, were excluded.

The statistical analysis was conducted based on an electronic database (Excel for Windows ®).

SPSS ® version 13.0 was used in the analysis of

the data and the Chi-square and Fisher's exact tests were performed with Monte Carlo methods. A level of significance of 0.05 was considered significant for association of the variables. A subsequent residual analysis was conducted.

The study was approved by the Ethics Research Committee of CHSC.

RESULTS

The study sample included 328 cases; 57% were women and 43%, men. The mean age was 55.63 years. The mean age of women was lower than that of men - 54.87 and 56.64 years, respectively. The age ranged from 13 to 93 years. There was a peak of incidence of 46.95% for those aged between 50 and 69 years (Graph 1).

With regard to the topography of lesions, the most common site was the back (27.74%) followed by lower limbs (24.09%), head and neck (19.51%), upper limbs (18.29 %) and thorax and abdomen (10.37%). Melanomas mainly affected the lower (29.26%) and upper (23.94%) limbs in women. In men, they were predominant in the back (35%), chest and abdomen (14.29%). These differences were statistically significant ($p < 0.05$) (Table 1).

The histological subtypes of melanoma showed the following frequencies: superficial spreading melanoma (SSM) (62.8%), lentigo maligna (LM) (14.9%), nodular (14.6%), acral (7.3 %) and desmoplastic (0.3%) (Table 2).

As to Breslow depth, the lesions were *in situ* in 26.2% of the cases; 36.9% were ≤ 1 mm, 10.3% were between 1.01 and 2mm, 10.7% between 2.01 and 4mm and 15.9% were more than 4 mm thick (Graph 2).

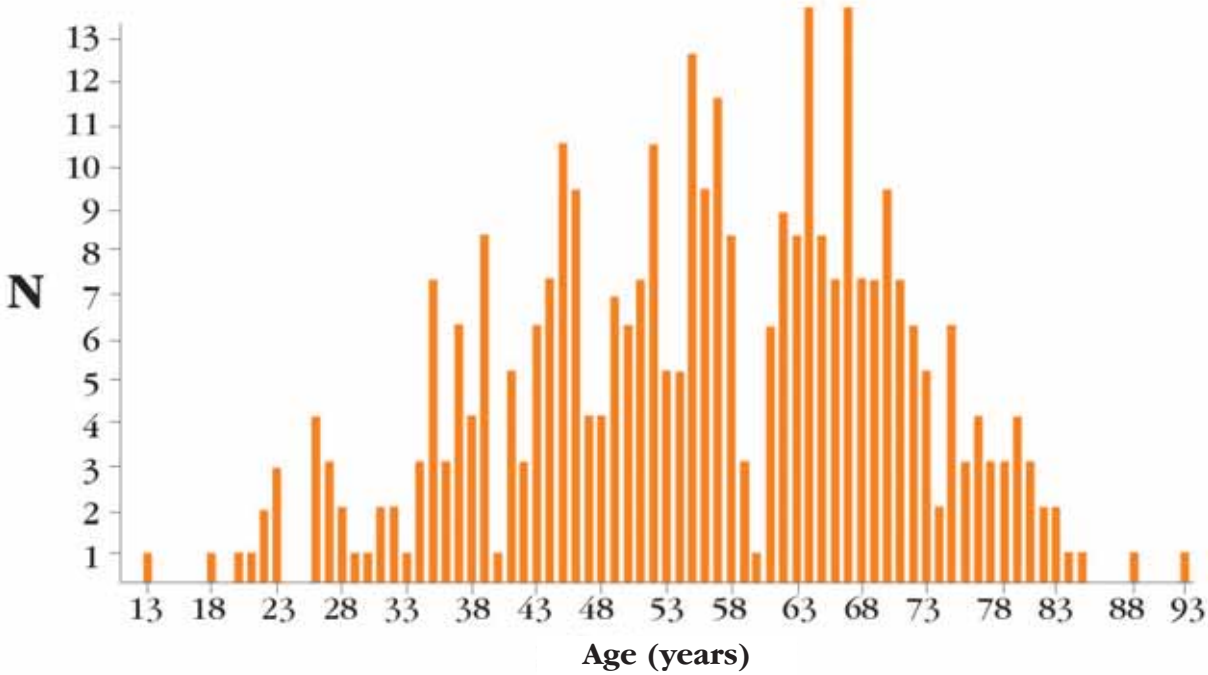
There was no significant association between sex and Breslow depth ($p = 0.275$).

The comparison between age and Breslow depth resulted in a significant association between the age range of 30 to 39 years and Breslow depth of £1mm and between the age of 80 years or more and Breslow depth ranging from 2.01 to 4 ($p < 0.05$).

There was also a significant association between Breslow depth and topography ($p < 0.05$); head and neck melanomas were associated with Breslow depth of £ 1 mm. Location in the lower limbs was associated with Breslow depth between 1.01 and 2mm and ? 4mm.

Results concerning the frequencies of other histopathological variables in the study sample (Clark level, mitotic index, growth stage, ulceration, regression, regression type, surgical margins, associated nevus, angiolymphatic invasion, perineural Invasion, Intratumoral lymphocytic inflammatory infiltrate, peritumoral lymphocytic inflammatory infiltrate and microscopic satellitosis) are presented in Table 3 .

Cases of *in situ* melanoma were only analyzed for Clark level, growth stage, surgical margins and associated nevus.



Graph 1: Age distribution of patients

Table 1: Distribution of topography in relation to gender

	Topography					
	Head/neck n (%)	**back n (%)**	**LL n (%)**	**Antherior thorax / abdomen n (%)**	**UL n (%)**	**Total n (%)**
Men	32 (22.86)	49 (35)*	24 (17.14)	20 (14.29)*	15 (10.71)	140 (100)
Women	32 (17.02)	42 (22.34)	55 (29.26)*	14 (7.45)	45 (23.94)*	188 (100.0)
Total	64 (19.5)	91 (27.7)	79 (24.1)	34 (10.4)	60 (18.3)	328 (100,0)

*p<0,05

Table 2: Distribution of subtypes of primary cutaneous melanoma

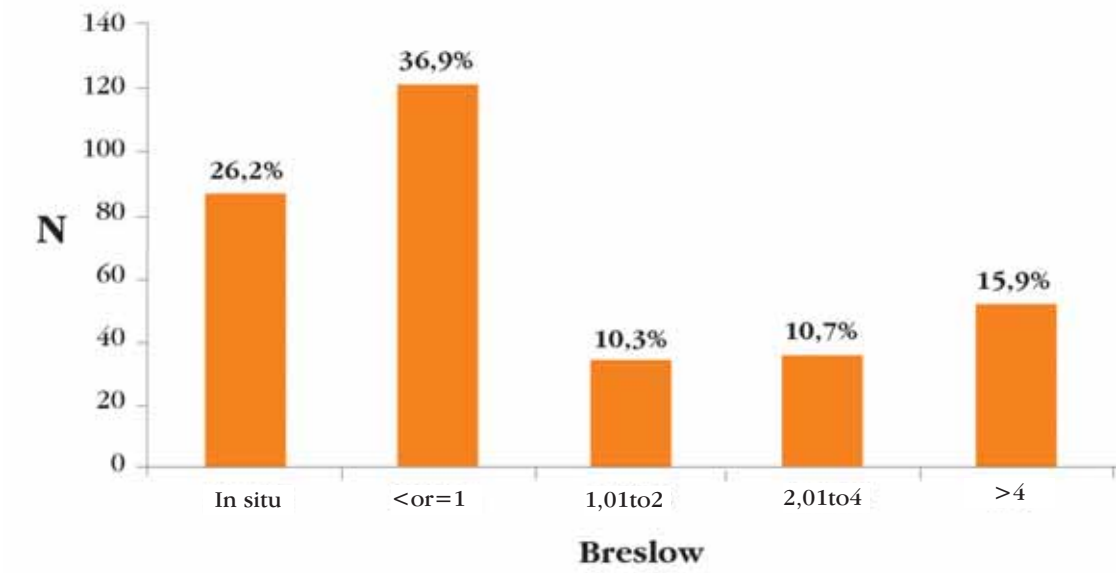
Histological subtype	Frequency	%
Acral	24	7,3
LM	49	14,9
SSM	206	62,8
Nodular	48	14,6
Desmoplastic	1	0,3
Total	328	100,0

DISCUSSION

As this is a hospital based study, screening of malignancies with a worse prognosis is expected due to a possible later diagnosis. However, even though this is a tertiary care hospital study, there is a predominance (63.1%) of melanomas considered thin (Breslow thickness ≤ 1 mm), with 26.2% of all cases being *in situ,* indicating a relatively early diagnosis. It is interesting to compare these data with previous studies conducted in the 90's in Porto Alegre-RS, because there are important differences regarding the early diagnosis of melanoma. For example, Venegas *et alin situ.* [6] In 1997, a study in laboratories of pathology in Porto Alegre-RS presented 2.15% of melanomas *in situ* and 31.5% with Breslow thickness ≤ 1.5 mm. [7] (1992), in hospital-based study, showed only 15.8% of melanoma with Breslow thickness ≤ 1.5 mm and only 1% of injuries

The distribution of histological subtypes of melanoma in this study was similar to that of non-hospital based studies, unlike expected, since at the tertiary care for a relative increase in the number of nodular melanomas and reduction of SSM. So [6.11] as the frequency of melanomas considered thin, the predominance of superficial spreading melanoma (62.8%) also draws attention.Benvegnú *et al in* a study conducted in the central region of Rio Grande do Sul between 1986 and 1995, found that 49% of the cases were nodular melanoma. [12] Hospital-based studies with data from the 80's and 90's in other Brazilian cities also follow this distribution with a predominance of the nodular subtype. [13.14]

A more recent study, using data collected



Graph 2: Breslow depth in the sample studied (n= skin melanoma cases)

Tabela 3: Distribuição dos subtipos de melanoma cutâneo primário

Clark Level	**Frequency**	**%**
I	86	26.2
II	49	23.8
III	51	15.5
IV	90	27.4
V	23	7.0
Total	328	100.0
Mitotic Index (number of mitoses in 10 fields)	**Frequency**	**%**
Less than 2	93	38.4
2	53	21.9
4	21	8.7
6	20	8.3
8	10	4.1
10	20	8.3
More than 10	25	10.3
Total	242*	100.0
Microscopic Ulcer	**Frequency**	**%**
Absent	183	75.6
Present	59	24.4
Total	242*	100.0
Growth Stage	**Frequency**	**%**
Radial	174	53.0
Vertical	154	47.0
Total	328	100.0
Intratumoral Lymphocytic Inflammatory Infiltrate	**Frequency**	**%**
Absent	207	85.5
Mild	10	4.1
Moderate	17	7.0
Marked	8	3.3
Total	242*	100.0
Peritumoral Lymphocytic Inflammatory Infiltrate	**Frequency**	**%**
Absent	23	9.5
Mild	132	54.5
Moderate	68	28.1
Marked	19	7.9
Total	242*	100.0
Perineural Invasion	**Frequency**	**%**
Absent	238	98.3
Present	4	1.7
Total	242*	100.0
Angiolymphatic Invasion	**Frequency**	**%**
Absent	230	95.0
Present	12	5.0
Total	242*	100.0
Microscopic Satellitosis	**Frequency**	**%**
Absent	239	98.8
Present	3	1.2
Total	242*	100.0
Regression	**Frequency**	**%**
Absent	193	79.8
Present	49	20.2
Total	242*	100.0
Regression	**Frequency**	**%**
Parcial	34	69.4
Total	15	30.6
Total	49	100.0
Surgical Margins	**Frequency**	**%**
Livres	309	94.2
Comprometidas	19	5.8
Total	328	100.0
Associated Nevus	**Frequency**	**%**
Sim	35	10.7
Não	293	89.3
Total	328	100.0

* Evaluation for in situ cases is not applicable. Frequencies of other GBM variables

between 1999 and 2004 in two hospitals in Florianópolis, SC, showed more positive results and a better outcome, similarly to the present work. *Weber et al* showed that 71.94% of anatomopathological reports, excluding metastases, were considered thin melanomas (Breslow thickness ≤ 1 mm), 60% were superficial spreading melanoma and 30% were nodular.[15]

Improvement of prognostic factors for melanoma is possibly the result of institutional prevention campaigns and media disclosures, as well as better access to public health care.In Brazil, the Brazilian Society of Dermatology has been holding an annual National Campaign Against Skin Cancer since 1998. It targets secondary prevention, offering treatment guidance to the population, as well as educating the public to recognize suspicious lesions and seek early treatment. The GBM also has educational campaigns such as the Summer Action, which informs the public about photoprotection and photoprevention. [16].

The peak of incidence occurs around the 7th decade of life and is in agreement with the literature. [17.18]

The predilection of the disease for the dorsum in men and extremities in women appears to show a significant contribution of behavior in cancer. Inappropriate habits of sun exposure, whether for leisure or work, can cause sunburns, an important risk factor of melanoma. [4] The number of sunburns throughout life, not only during childhood, increases the risk for the development of melanoma. [19]

The association between Breslow thickness and topography is possibly due to the distribution of the different histological types of melanoma. Thinner tumors such as LM and SSM occur more frequently in the head, neck and back, probably caused by chronic sun exposure. In turn, more aggressive histological subtypes such as nodular and acral have a predilection for the limbs.

The main histopathological variables found in Table 3 show that most skin melanomas diagnosed at this hospital are minimally invasive.

CONCLUSION

The profile of melanoma cases evaluated in a tertiary referral hospital appears to be changing with a tendency to early diagnosis in Southern Brazil.

Recognition of the presence of histopathologic prognostic factors and clinical characteristics of patients with cutaneous melanoma allows us to understand the real magnitude of the problem in our country, contributing to the development of new scientific studies and institutional interventions. ❑

REFERENCES

1. Azevedo G, Mendonça S. Risco crescente de melanoma de pele no Brasil. Rev Saude Publica. 1992;26:290-4.
2. Marks R. Epidemiology of melanoma. Clin Exp Dermatol. 2000;25:459-63.
3. Inca.gov.br [Internet]. Estimativa 2008: Incidência de Câncer no Brasil. Rio de Janeiro: INCA; 2007. [acesso 16 Fev. 2009] Disponível em: http://www.inca.gov.br/estimativa/2008/versaofinal.pdf
4. Bakos L, Wagner M, Bakos RM, Leite CS, Sperhacke CL, Dzekaniak KS, et al. Sunburn, sunscreens, and phenotypes: some risk factors for cutaneous melanoma in southern Brazil. Int J Dermatol. 2002;41:557-62.
5. Domonkos AN, Arnold HL, Odom RB. Andrew's diseases of the skin. 8th ed. Philadelphia: W.B. Saunders;1990. p. 808-30.
6. Venegas LFP, Flores C, Blacher GG, Daudt AW, Cerski CTS. Melanoma maligno cutâneo no Rio Grande do Sul: estudo de 101 casos. Rev Ass Med Brasil. 1992;38:122-6.
7. Hampe SV. Estudo da precocidade diagnóstica dos melanomas cutâneos primários em Porto Alegre, por análise de imagem computadorizada [Tese]. Porto Alegre (RS): Universidade Federal do Rio Grande do Sul; 1997. 132 p.
8. Barnhill RL, Fine JA, Roush GC, Berwick M. Predicting five-year outcome for patients with cutaneous melanoma in a population-based study. Cancer. 1996;7:427-32.
9. Tsao H, Atkins MB, Sober AJ. Management of Cutaneous Melanoma. N Eng J Med. 2004;351:998-1012.
10. Landman G, Muller H, Fillus Neto J, Maceira JMP, Marques M, Costa MB, et al. Consenso para o laudo anatomopatológico do melanoma cutâneo: Grupo Multicêntrico e Multidisciplinar Brasileiro para Estudo do Melanoma (GBM). Acta Oncol Bras. 2003;23:504-10.
11. Avilés JA, Lázaro P, Lecona M. Epidemiology and survival of cutaneous melanoma in Spain: a report of 552 cases (1994-2003). Rev Clin Esp. 2006;206:319-25.
12. Benvegnú LA, Pasqualotto AC, Santos RP, Copette FR. Melanoma cutâneo na região central do Rio Grande do Sul: análise de 79 casos. Rev AMRIGS. 1997;41:208-12.
13. Pinheiro AMC, Friedman H, Cabral ALSV, Rodrigues HB. Melanoma cutâneo: características clínicas, epidemiológicas e histopatológicas no Hospital Universitário de Brasília entre janeiro de 1994 e abril de 1999. An Bras Dermatol. 2003;78:179-86.
14. Lapa MS, Guedes KF, Schslch FO, Landman G. Melanomas malignos cutâneos tratados no Hospital do Câncer de São Paulo. Estudo retrospectivo para avaliação de distribuição, fatores prognósticos e sobrevida. An Bras Dermatol. 2002;77:313-20.
15. Lebsa-Weber A, Nunes DH, Souza Filho JJ, Carvalho-Pinto CJ. Avaliação de 496 laudos anatomopatológicos de melanoma diagnosticados no município de Florianópolis, Santa Catarina, Brasil. An Bras Dermatol. 2007;82:227-32.
16. Gbm.org [Internet]. Grupo Brasileiro de Melanoma. [Acesso 16 Fev. 2009] Disponível em: http://www.gbm.org.br/gbm/campanhas.aspx
17. Katalinic A, Kunze U, Schäfer T. Epidemiology of cutaneous melanoma and non-melanoma skin cancer in Schleswig-Holstein, Germany: incidence, clinical subtypes, tumour stages and localization (epidemiology of skin cancer). Br J Dermatol. 2003;149:1200-6.
18. Thörn M, Pontén F, Bergström R, Sparén P, Adami HO. Trends in tumour characteristics and survival of malignant melanoma 1960-84: a population-based study in Sweden. Br J Cancer. 1994;70:743-8.
19. Dennis LK, Vanbeek MJ, Beane Freeman LE, Smith BJ, Dawson DV, Coughlin JA. Sunburns and risk of cutaneous melanoma: does age matter? A comprehensive meta-analysis. Ann Epidemiol. 2008;18:614-27.

Mailing address / Endereço para correspondência:
Raquel Bonfá
Dr. Timóteo, 450/601 – Floresta
90570-040 Porto Alegre - RS, Brazil
E-mail: raqbonfa@gmail.com

How to cite this article/*Como citar este artigo*: Bonfá R, Bonamigo RR, Bonfá R, Duro KM, Furian RD, Zelmanowicz AM. Early diagnosis of cutaneous melanoma: an observation in southern Brazil. An Bras Dermatol. 2011;86(2):215-21.