

## Pseudomelanomas at a referral ocular oncology center in Brazil

## Pseudomelanomas em um centro de referência em oncologia ocular no Brasil

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**ABSTRACT****Objective:** To evaluate the epidemiological, clinical, and imaging profile of lesions that mimic choroidal melanoma.**Methods:** Retrospective study of medical records of suspected choroidal melanoma lesions referred to the Ocular Oncology Service from the Universidade Federal de São Paulo, from 2014 to 2020. Demographic data, clinical history, and exams were evaluated.**Results:** A total of 104 patients (mean age: 65.57 ± 13.18; 49.04% female) were referred to our service with suspected choroidal melanoma. Of these, 32 (30.77%) were classified as pseudomelanoma, while 72 (69.23%) had a confirmed diagnosis of choroidal melanoma. Pseudomelanoma cases manifested in older individuals ( $p < 0.001$ ), with smaller lesions in height ( $p < 0.001$ ), anteroposterior diameter ( $p = 0.008$ ), and lateral diameter ( $p = 0.003$ ) on ultrasound. Pseudomelanoma cases were associated with higher frequencies of vitreous hemorrhage ( $p = 0.014$ ) and lower rates of the presence of a mass ( $p = 0.001$ ) and retinal detachment ( $p < 0.001$ ). The main diagnoses of pseudomelanoma cases were choroidal nevus (40.63%), subretinal hemorrhage (18.75%) and choroidal neovascular membrane (18.75%).**Conclusion:** Almost one third of the cases referred with suspected choroidal melanoma were pseudomelanomas, which demonstrates that there is still a considerable path to improve the ability of general ophthalmologists to clinically discriminate melanoma from other conditions that can mimic it.**RESUMO****Objetivo:** Avaliar a frequência e o perfil epidemiológico, clínico e de imagem das lesões que simulam o melanoma de coroide.**Métodos:** Trata-se de estudo de revisão retrospectiva de prontuários de suspeita de lesões de melanoma de coroide de 2014 a 2020 no Setor de Oncologia Ocular da Universidade Federal de São Paulo. Foram avaliados dados demográficos, dados clínicos e exames complementares.**Resultados:** Um total de 104 pacientes (média de idade: 65,57 ± 13,18; 49,04% do sexo feminino) foram encaminhados ao nosso serviço com suspeita de melanoma de coroide. Destes, 32 (30,77%) foram classificados como pseudomelanoma, enquanto 72 (69,23%) tiveram diagnóstico confirmado de melanoma de coroide. Os casos de pseudomelanoma manifestaram-se em indivíduos mais velhos ( $p < 0,001$ ) e apresentaram lesões menores em altura ( $p < 0,001$ ), diâmetro anteroposterior ( $p = 0,008$ ) e diâmetro lateral ( $p = 0,003$ ) na ultrassonografia. Os casos de pseudomelanoma estão associados a maiores frequências de hemorragia vítrea ( $p = 0,014$ ) e menores taxas de presença de massa ( $p = 0,001$ ) e descolamento de retina ( $p < 0,001$ ). Os principais diagnósticos dos casos de pseudomelanoma foram nevo (40,63%), hemorragia sub-retiniana (18,75%) e membrana neovascular coroidal (18,75%).**Conclusão:** Quase um terço dos casos encaminhados com suspeita de melanoma de coroide foram pseudomelanomas, o que demonstra que ainda há um caminho considerável para melhorar a habilidade do oftalmologista geral em discriminar clinicamente o melanoma de outras condições que o simulam.

## INTRODUCTION

The intraocular tumors comprise an extensive cast of benign and malignant lesions that may not only cause vision loss but can lead to one's death if not detected and treated on a proper timeline. Early detection and accurate diagnosis are fundamental for a good prognosis. The definitive diagnosis of intraocular tumors requires histopathological confirmation, but the biopsy techniques for this confirmation are invasive and still not completely safe; therefore, diagnostic biopsy procedures are indicated only in a few selected cases.<sup>(1,2)</sup> On the other hand, the improvement of propaedeutic imaging methods increased the intraocular tumor diagnosis precision so that nowadays the diagnostic and therapeutic decision has often relied on information provided by these imaging methods.<sup>(3-5)</sup>

Choroidal melanoma is the most common primary intraocular tumor in adults, with an annual incidence of about 5.2 cases per million people, but many suspicious clinical findings of choroidal lesions can mimic it, as observed in pseudomelanoma.<sup>(6,7)</sup> The intraocular tumors originate predominantly from the uvea (iris, ciliary body and choroid), retina, optic disc and, more rarely, from the pigment epithelium. The choroid is the main site of intraocular tumors, including melanoma, metastatic tumors, and hemangioma. In addition to the tumors themselves, lesions of inflammatory nature, such as granulomas or cystic lesions, and hemorrhages can simulate a tumor and therefore must be considered in the differential diagnosis.<sup>(8)</sup>

When the direct view of the tumor by ophthalmoscopy and biomicroscopy is hampered by changes in the transparency of the optical media, such as in corneal opacities, cataracts, or vitreous clouding, the imaging exams have their importance not only by measuring tumor dimensions but also by evaluating the suspected lesion characteristics.<sup>(8)</sup> The ocular ultrasound (US) is particularly useful in this case of detecting intraocular tumors when the optics are not clear.<sup>(9)</sup> The ocular US associated with eye fundus examination is essential for the diagnosis of choroidal melanoma. These two exams allow the correct diagnosis in more than 90% of the cases. During the ocular US exam, it is important to evaluate the presence of a solid lesion, its shape, its measurements, and reflectivity.<sup>(10)</sup>

The purpose of the current study is to evaluate the epidemiological, clinical, and imaging profile of lesions that mimic choroidal melanoma.

## METHODS

Retrospective study with data collected from the medical records from patients referred to the Ocular Oncology Service of the Universidade Federal de São Paulo (Unifesp) with an initial diagnostic hypothesis of choroidal melanoma from 2014 to 2020. The study had approval from the Unifesp Ethics Committee and was carried out in accordance with the tenets of the Declaration of Helsinki.

The following information was collected: age, sex, laterality, clinical, and imaging findings. Patients with incomplete data whose diagnosis could not be confirmed were excluded.

Statistical analyses were performed using Stata/SE statistical software, release 14.0, 2015 (Stata Corp, College Station, Texas, USA). Frequency tables were used for descriptive analysis.

## RESULTS

A total of 104 patients with suspected choroidal melanoma referred to our service from 2014 to 2020 were included in the present study. Out of those, 32 (30.77%) were classified as pseudomelanoma, while 72 (69.23%) had a confirmed diagnosis of choroidal melanoma based on the pathology results. Table 1 shows the characteristics of melanoma and pseudomelanoma cases.

**Table 1.** Clinical and demographic comparison between groups

	Pseudomelanoma	Melanoma	p-value
Sex			0.160
Male	13 (40.63)	40 (55.56)	
Female	19 (59.38)	32 (44.44)	
Age	73.7 ± 9.68	62.25 ± 13.01	<0.001
Laterality			0.051
Right	15 (46.88)	37 (51.39)	
Left	14 (43.75)	35 (48.61)	
Both	3 (9.38)	0	
Lesion height (US)	4.18 ± 2.33	9.66 ± 3.71	<0.001
Lesion anteroposterior diameter (US)	9.72 ± 4.11	13.11 ± 3.40	0.008
Lesion Lateral diameter (US)	9.33 ± 3.40	13.31 ± 3.57	0.003
Hyperemia	3 (9.38)	10 (13.89)	0.386
Corneal abnormalities	1 (3.13)	4 (5.56)	0.510
Anterior chamber reaction/ flare	0	2 (2.78)	0.477
Vitreous hemorrhage	11 (34.38)	9 (12.50)	0.014
Posterior segment mass	2 (6.25)	46 (100.00)	<0.001
Retinal detachment	7 (21.88)	46 (63.89)	<0.001

Results expressed as n (%) or mean ± standard deviation.

There was no statistically significant difference in sex, laterality or anterior segment changes between the melanoma and pseudomelanoma cases ( $p > 0.05$ ). Pseudomelanomas, however, were associated with older age ( $p < 0.001$ ) and smaller lesions in height ( $p < 0.001$ ), anteroposterior diameter ( $p = 0.008$ ) and lateral diameter

( $p = 0.003$ ) in the ocular US. Moreover, pseudomelanomas showed a higher frequency of vitreous hemorrhage ( $p = 0.014$ ) and a lower rate of posterior mass ( $p = 0.001$ ) and retinal detachment ( $p < 0.001$ ).

Table 2 indicates the true diagnosis of cases classified as pseudomelanomas.

**Table 2.** Frequency of confirmed diagnosis of pseudomelanoma cases.

Diagnosis	n(%)
Nevus	13 (40.63)
Subretinal hemorrhage	6 (18.75)
Neovascular membrane	6 (18.75)
Hemangioma	2 (6.25)
High myopia	1 (3.13)
Macroaneurysm	1 (3.13)
Melanocytoma	1 (3.13)
Ocular metastasis	1 (3.13)
Osteoma	1 (3.13)
Total	32 (100.00)

The main correct diagnoses of pseudomelanoma cases were nevus (40.63%), subretinal hemorrhage (18.75%) and neovascular membrane (18.75%). Other diagnoses included hemangioma (6.25%), high myopia (3.13%), macroaneurysm (3.13%), melanocytoma (3.13%), ocular metastasis (3.13%) and osteoma (3.13%).

## DISCUSSION

The assertive diagnosis of choroidal melanoma implies better therapeutic planning for the patient, rationalization in the request for complementary exams and allows for improving the screening of clinical cases referred to the ocular oncology service.

Our data showed no significant difference in sex between choroidal melanoma and pseudomelanoma cases, which is in accordance with the literature that states the disease has no differential occurrence according to sex, nor a predominance in laterality or anterior segment abnormalities.<sup>(11)</sup>

Choroidal melanoma diagnosis is based on clinical and imaging findings. Those, however, can be quite variable, so the disease can be associated with different visual conditions as ectropion uveal, corectopia, and eye pain, or even asymptomatic cases, diagnosed during a routine ophthalmological examination.<sup>(8,12)</sup> In addition, different benign lesions can mimic choroidal melanoma at ophthalmoscopy, such as choroidal nevus, the most prevalent differential diagnosis in our study.

Choroidal nevus (40.63% of all pseudomelanoma in the study) may look remarkably similar to small choroidal melanoma; however, melanoma usually grow over time,

whereas the nevus is usually stable. Choroidal nevus appears generally as a flat lesion, with variable pigmentation, with a diameter between 1.5 and 5 mm. Most choroidal nevus do not require treatment, but follow-up is important, as there is a possibility of the nevus turning into choroidal melanoma, despite being a quite rare event. Suspicious lesions should be followed up carefully, with photographic documentation.<sup>(6)</sup> The larger the size of the observed lesion, the more challenging is the diagnostic differentiation.

It is important to remember retinal hemorrhages as differential diagnoses such as those seen in peripheral exudative hemorrhagic chorioretinopathy (PEHCR), hemorrhagic complications of age-related macular degeneration, or the idiopathic hemorrhagic retinal detachment itself that can mimic hemorrhagic complications of choroidal melanoma. In cases of amelanotic melanomas, the main differential diagnosis is hemangioma and ocular metastases. The sonographic appearance of hemangioma and ocular metastases are different from that seen in choroidal melanoma, making ocular US an important diagnostic tool.<sup>(6)</sup>

Our findings indicated that 30.77% of lesions suspected of choroidal melanoma were classified as pseudomelanoma, highlighting the need of improvement on the ability of general ophthalmologists to clinically discriminate melanoma and conditions that mimic it.

## CONCLUSION

Almost one third of the cases referred to the Ocular Oncology Service of the Universidade Federal de São Paulo from 2014 to 2020 with suspected choroidal melanoma were actually pseudomelanomas, which demonstrates that there is still a considerable path to improve the diagnosis of the general ophthalmologist, improving the ability to clinically discriminate melanoma from other conditions that may mimic it. The use of diagnostic tools such as ultrasound can help in this differential diagnosis. The present study retrospectively evaluated the cases of pseudomelanoma, but future studies with a larger group of cases are needed to better consolidate the evaluated data.

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