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Case Report

Ocular melanoma: Keep your eyes open for late brain metastases

Danilo O. de A. Silva[1,2], Georgios K. Matis[1], Leonardo F. Costa[2], Matheus A. P. Kitamura[2], Eduardo V. de C. Júnior[2], Breno J. A. P. Barbosa[2], Isaac B. Santiago[2], Tatiane I. Silva[2], Fabiana Q. de P. A. Silva[3], Carlos U. Pereira[4], Hildo R. C. Azevedo Filho[2]

[1]Department of Neurosurgery, Weill Cornell Medical College, New York, USA, [2]Department of Neurosurgery, Restauração Hospital, [3]Department of Ophthalmology, Hospital de Olhos Santa Luzia, Recife PE, Brazil, [4]Department of Neurosurgery, Universidade Federal de Sergipe, Aracaju SE, Brazil

E-mail: *Danilo O. de A. Silva - daniloncr@gmail.com; Georgios K. Matis - gkmatis@yahoo.gr; Leonardo F. Costa - leosport2000@yahoo.com.br; Matheus A. P. Kitamura - matheus_kitamura@yahoo.com.br; Eduardo V. de C. Júnior - eduardov@gmail.com; Breno J. A. P. Barbosa - brenojb@gmail.com; Isaac B. Santiago - Isaacb@gmail.com; Tatiane I. Silva - Tatianeindrusiak@gmail.com; Fabiana Q. de P. A. Silva - fabiqueiroga@gmail.com; Carlos U. Pereira - umberto@infonet.com.br; Hildo R. C. Azevedo Filho - azevedoh@uol.com.br

*Corresponding author

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Abstract

Background: The most frequent intraocular malignant tumor is choroidal melanoma (CM). Although brain metastasis is a common feature of other types of cancers, metastasis of CM to the brain is a rare entity.

Case Description: The authors report a case of a 28-year-old woman presenting with a single brain metastasis, 10 years after the treatment of a CM. She underwent a total en-bloc resection of the lesion, and the diagnosis was confirmed histopathologically. The patient concomitantly received whole-brain irradiation therapy combined with chemotherapy, with a survival period of 24 months.

Conclusion: The present case report draws attention to the necessity of a close and lifelong follow-up of patients treated for this malignancy. The international literature is also reviewed.

Key Words: Brain metastasis, choroidal melanoma, surgical treatment

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INTRODUCTION

Choroidal melanoma (CM) is the most frequent intraocular malignant tumor in adulthood.[11] Brain metastases are relatively rare, accounting for 2–5% of the overall incidence of metastases, and they are associated with a poor outcome, usually appearing concomitantly with liver metastases.[18] The authors describe a rare case of an isolated brain metastasis, appearing 10 years after treatment of the primary lesion that responded favorably to local resection combined with whole-brain irradiation therapy (WBRT) and chemotherapy. To the authors' knowledge, there are only two similar articles in the English literature.[1,16] Patient's family consent along with the institutional ethical committee's permission for publication was granted.

CASE REPORT

A 28-year-old female patient was admitted to the Neurosurgery Unit of the Hospital da Restauração (Recife, PE, Brazil) with a recent history of intense headache that was not responsive to any kind of medical therapy. She complained of continuous headache almost every morning for the last 2 months. At the time of presentation, despite the mentioned symptoms, she was

neurologically intact. She showed neither any evidence of peripheral lymphadenopathy nor any pigmented lesions at the physical examination. Of note, she had a prosthetic eye on the right side. The medical history revealed that she had been operated on for a CM 10 years ago. The surgical procedure involved enucleation of the right eye. The histopathologic study was consistent with a malignant CM. During the follow-up, no skeletal scintigraphy or magnetic resonance imaging (MRI) tests were performed.

All laboratory tests revealed nothing abnormal. Computed tomography (CT) and MRI scans were performed at day 2 and a left frontal lobe lesion was illustrated. This lesion appeared hyperdense on CT scan [Figure 1], a finding that drew the attention to a possible recent intratumoral bleeding. However, it did not behave as blood on MRI study. It was hyperintense on T1-weighted images [Figure 2] and isointense on T2-weighted images. But when analyzing the gradient echo sequence (GRE), the lesion was isointense to the brain [Figure 3]. Since blood usually appears hypointense on GRE, the possibility of a late single brain metastatic melanoma became the most prominent diagnosis.

On the fourth day of hospitalization, the patient experienced worsening of the headache and became drowsy. New emergency CT scan showed increase of the midline shift, subfalcine and uncus herniation. The patient was taken to the operating room for a total resection of the tumor. The surgical procedure consisted of a left frontotemporal craniotomy and standard microsurgical techniques were employed to achieve an "en bloc" resection of the tumor. The histology of the lesion confirmed a metastatic melanoma of the brain [Figure 4]. Typical hyperchromatic and pleomorphic cells were recognized and special melanin stains [S100, Melan-A, homatropine methylbromide (HMB) 45]

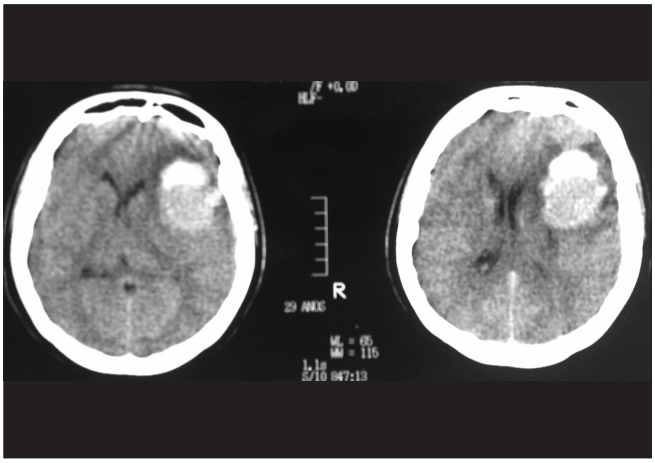

Figure 1: Hyperdense frontal lesion mimicking an intratumoral hemorrhage

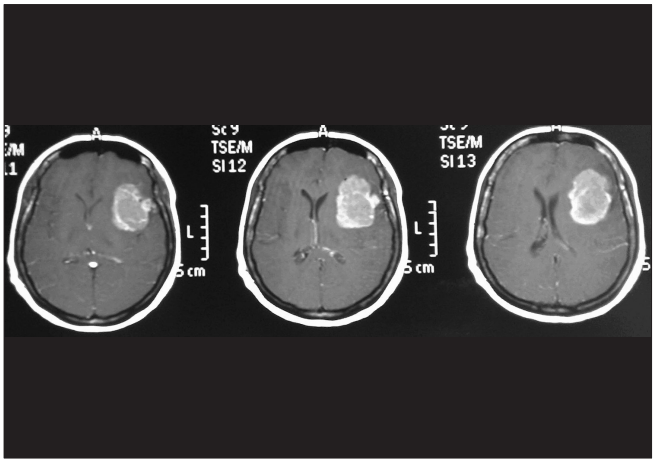

Figure 2: T1-weighted images (contrast-enhanced) demonstrating a hyperintense left frontal lobe lesion

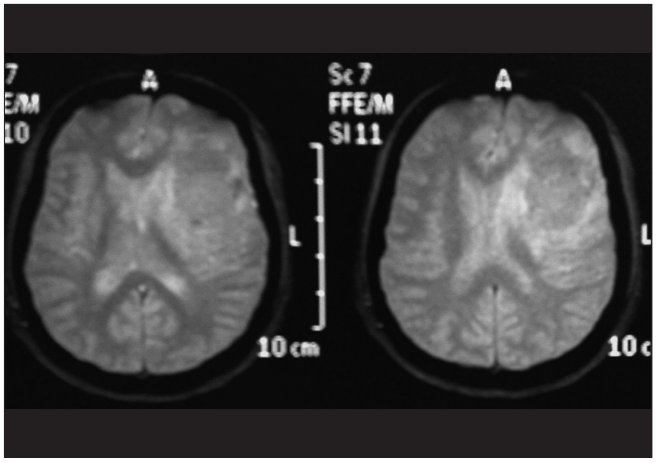

Figure 3: Gradient echo sequence: the lesion is isointense to the brain

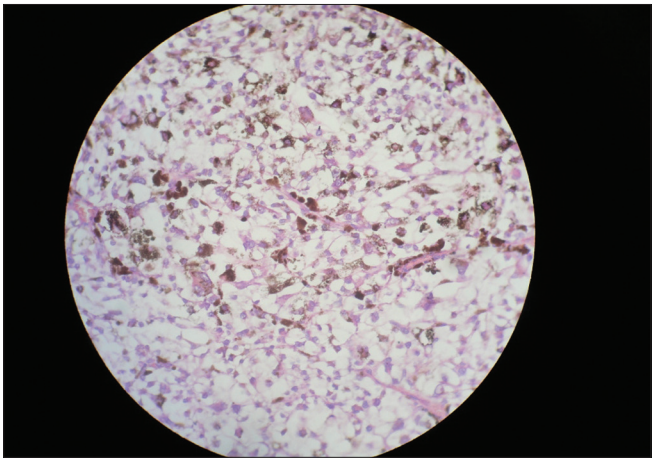

Figure 4: Histopathologic findings included dense deposit of melanin, intense tumoral necrosis and nuclear atypism with surrounding secondary lesions (H and E, ×300)

confirmed the diagnosis.

The patient received WBRT for 3 months with a total dose of 54 Gy combined with chemotherapy, consisting of increasing doses of temozolamide (Temodal®, Merck and Co., Inc., Whitehouse Station, NJ, USA) up to 150 mg/m^2/day. Thereafter, she had been closely followed up in the Ambulatory Department with no recurrence on serial MRI scans. She was asymptomatic for 24 months, when she was admitted to the hospital with shortness of breath and eventually died from pulmonary embolism. No autopsy was conducted due to her family's religious beliefs.

DISCUSSION

CM is the most frequent intraocular malignant tumor in adulthood.[11] It has been estimated that the incidence of CM in the United States is six to seven cases per million per year.[18] Several risk factors for malignant CM have been identified. Women are slightly more affected than men and Whites have an eightfold increased risk than more darkly pigmented persons.[9] People with lightly colored irises have also increased risk to develop CM.[9,17] Prevalence increases with age as follows: 1 in 1 million before 30 years of age, 7 in 1 million before the age of 70 years, and 50 in 1 million after 70 years of age.[6,9]

Multiple known and unknown factors may influence the prognosis of CM. Brain metastases from CM are relatively rare (2–5% of all brain metastases) and they are associated with poor prognosis, with life expectancy being less than 1 year. They are usually concomitant with liver metastases.[6,11,17] Liver metastases usually occur within the first 4 years after the treatment of the primary tumor. Other sites of disseminated disease are the lungs, bones, kidneys and brain.[1,3,11,16] Shields *et al*. reported on one case of a liver late metastasis from a CM, 42 years after the treatment of the primary tumor.[15]

In the early 90s, Lorigan *et al*. studied the clinical and radiological findings of 110 patients with metastatic CM, of which only 5 had brain metastases.[10] More recently, some studies have used positron emission tomography (PET) for staging the metastatic disease from CM. Using this method, Finger *et al*. evaluated a series of 52 patients where the liver (100%), bone (50%) and lymph nodes (50%) were the main sites of metastases from CM. In this case series, only one patient had an isolated metastatic brain tumor.[5]

Although CMs are clinically not as aggressive as skin melanomas, they present substantial risk of developing metastases.[3] The biological malignancy of CM depends on its morphological, clinical and histological type, mitotic activity, cytomorphometric parameters, tumor size, tumor location and patient age.[11] Among these factors, tumor size is the main indicator for the possibility of metastatic disease and, therefore, an indicator of survival, as suggested by the Collaborative Ocular Melanoma Study (COMS).[2]

In an elegant experimental study, Schackert *et al*. suggested that different human melanoma cells injected into the internal carotid artery of nude mice produced different patterns of brain metastases.[14] They appeared to depend on the source of the original patient's metastases from which the cell lines were derived. Thus, only cells originating from brain metastases produced parenchymal lesions, while non-brain cells (lymph nodes, subcutaneous tissue) produced changes preferentially in the meninges, choroid plexus and ventricles.[14]

From the standpoint of molecular biology, it is believed that the brain metastatic cells have properties that favor the passage through the blood brain barrier. There may be a specific interaction with the microenvironment of the brain, especially in terms of specific binding to endothelial cells and local growth factors receptors.[12] Recently, researchers have focused on the expression of p75 NGF receptor (NGF-R), which correlates with brain metastases and survival of brain-metastatic cell lines of epithelioid melanomas, such as CM.[19]

Diagnosing CM can be problematic because the symptoms vary greatly, and in some cases, it may be easily confused with other common ocular conditions.[4] The differential diagnosis includes meningiomas, schwannomas, epidermoid cysts, or metastases.[1] The treatments include chemotherapy, brachytherapy, thermotherapy, and transpupillary enucleation.[9] The latter is historically the mainstay of treatment for CM.[3] COMS data published in 1998 showed no benefit on survival of patients with tumors of large size treated with radiotherapy before enucleation.[2] This may be because melanoma is resistant to radiotherapy or chemotherapy.[16] Thus, some authors have reinforced the need for long follow-up of patients treated for CM in order to early detect possible late metastases.[1,11]

Metastatic melanoma to the brain is characteristically multi-focal and can be hemorrhagic.[7] The treatment for solitary lesions is the combination of surgical excision and radiotherapy.[8] Multiple lesions can be treated with radiation and chemotherapy only.[13] The patient had a good outcome (survival of 2 years) with resection, radiation therapy, and chemotherapy. This case report along with the only two other similar articles found in the literature[1,16] show the importance of close, lifelong follow-up for all patients treated for CM.

REFERENCES

1. Achtaropoulos AK, Mitsos AP, Detorakis ET, Georgakoulias NV, Drakonaki EE, Kozobolis VP. Late isolated brain metastasis following enucleation for choroidal melanoma. Ophthalmic Surg Lasers Imaging 2005;36:151-4.

2. Anonymous. The Collaborative Ocular Melanoma Study (COMS) randomized trial of pre-enucleation radiation of large choroidal melanoma II: Initial mortality findings. COMS report No. 10. Am J Ophthalmol 1998;125:779-96.
3. Bell DJ, Wilson MW. Choroidal melanoma: Natural history and management options. Cancer Control 2004;11:296-303.
4. Bloch-Marcotte C, Ambrosetti D, Novellas S, Caramella T, Dahman M, Thyss A, *et al*. Ovarian metastases from choroidal melanoma. Clin Imaging 2008;32:318-20.
5. Finger PT, Kurli M, Reddy S, Tena LB, Pavlick AC. Whole body PET/CT for initial staging of choroidal melanoma. Br J Ophthalmol 2005;89:1270-4.
6. Gragoudas ES, Egan KM, Seddon JM. Survival of patients with metastases from uveal melanoma. Ophthalmology 1991;98:383-90.
7. Guzel A, Maciaczyk J, Dohmen-Scheufler H, Senturk S, Volk B, Ostertag CB, *et al*. Multiple intracranial melanoma metastases: Case report and review of the literature. J Neurooncol 2009;93:413-20.
8. Hoffman M, Kiecker F, Wurm R, Schlenger L, Budach V, Sterry W, *et al*. Temozolamide with or without radiotherapy in melanoma with unresectable brain metastases. J Neurooncol 2006;76:59-64.
9. Kearns C, Boyer S, Gay D. Two differing presentations, treatments, and outcomes of malignant choroidal melanoma. Optometry 2008;79:365-70.
10. Lorigan JG, Wallace S, Mavligit GM. The prevalence and location of metastases from ocular melanoma: Imaging study in 110 patients. AJR Am J Roentgenol 1991;157:1279-81.
11. Midena E, de Belvis V, Dei Tos AP, Antonini C. Isolated brain metastasis of malignant choroidal melanoma 27 years after enucleation. Arch Ophthalmol 1999;117:1553-6.
12. Nicolson GL. Cancer metastasis: Tumor cell and host organ properties important in metastasis to specific secondary sites. Biochim Biophys Acta 1988;948:175-224.
13. Panagiotou IE, Brountzos EN, Kelekis DA, Papathanasiou MA, Bafaloukos DI. Cerebral metastases of malignant melanoma: Contemporary treatment modalities and survival outcome. Neoplasma 2005;52:150-8.
14. Schackert G, Price JE, Zhang RD, Bucana CD, Itoh K, Fidler IJ. Regional growth of different human melanomas as metastases in the brain of nude mice. Am J Pathol 1990;136:95-102.
15. Shields JA, Ausburger JJ, Donoso LA, Bernardino VB, Portenar M. Hepatic metastasis and orbital recurrence of uveal melanoma after 42 years. Am J Ophthalmol 1985;100:666-8.
16. Shields JA, Perez N, Shields CL, Singh AD, Eagle RC Jr. Orbital melanoma metastatic from contralateral choroid: Management by complete surgical Resection. Ophthalmic Surg Lasers 2002;33:416-20.
17. Van Wiltenburg R, Sevick RJ, Clark AW, Burger PC, LeBlanc FE. Choroidal melanoma metastasis as a rare cause of cerebellopontine angle lesion: Two case reports. Can Assoc Radiol J 1998;49:185-9.
18. Wilkes S, Kurland L, Campbell RJ, Robertson DM. Incidence of uveal malignant melanoma. Am J Ophthalmol 1979;88:629-30.
19. Zbytek B, Carlson JA, Granese J, Ross J, Mihm MC, Slominski A. Current concepts of metastases in melanoma. Expert Rev Dermatol 2008;3:569-85.