

Brain Metastasis as Initial Manifestation of Melanoma (A Case Report)

Vitorino M. Santos^{1,2*}, Renata F. Silva¹, Viviane V. Passini¹, Mayza L. Duarte¹, Leandro P. Flores³

¹*Catholic University of Brasilia, Brasilia-DF, Brazil*

²*Internal Medicine Department from Armed Forces Hospital, Brasilia-DF, Brazil*

³*Neurosurgery Division from Armed Forces Hospital, Brasilia-DF, Brazil*

*Corresponding: Email: vitorinomodesto@gmail.com

Background: Melanoma is a malignancy derived from the neural crest, constituted of melanocytes found in the basal layer of epidermis, with the main function of melanin production. **Case:** A 64-year-old woman was admitted with headache and dyslalia and reported some episodes of vertigo and falls in the last six months. A superficial red and dark skin discoloration in the scalp and a node in the right parotid gland were observed. Computed tomography of the brain showed nodular lesions in the left parietal and right temporal and occipital lobes with hemorrhagic features, in addition to mass effect. Furthermore, PET-CT images were suggestive of brain, lung, and adrenal metastasis. The patient evolved with intracranial hypertension and a neurosurgery was performed. Histopathological and immunohistochemistry studies revealed metastatic melanoma. **Conclusions:** She underwent schedules of radiation therapy and chemotherapy, but developed uncontrolled sepsis and died in spite of clinical management and intensive care support. Cutaneous primary site of this malignancy in the scalp was previously neglected; therefore, neurological disturbances were the initial manifestations of melanoma. Immunohistochemistry findings allowed ruling out the main differential hypotheses.

Key words: Brain metastasis, immunohistochemistry diagnosis, melanoma.

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INTRODUCTION

Melanoma is a malignancy derived from the neural crest, constituted of melanocytes found in the basal layer of epidermis, with the main function of melanin production. During embryogenesis, melanocyte precursors migrate from the neural crest to the skin, uveal tract, leptomeninges, and mucous membranes. In general, they remain in undifferentiated status till some stimulus will induce them to transform in melanocytes. Therefore, these sites are more prone for the development of malignant melanoma. The main primary sites are skin, mucous membranes, eyes, urinary bladder, peripheral nerves, leptomeninges, and lungs, but the diagnosis depends on immunohistochemistry.¹⁻⁴

Corresponding author:

Prof. Dr. Vitorino Modesto dos Santos
Armed Forces Hospital. Estrada do Contorno
do Bosque s/n, Cruzeiro Novo, 70630-900,
Brasilia-DF, Brazil. Tel#55-61 32330812.
Fax#55-61 32331599.
Email: vitorinomodesto@gmail.com

Metastases to the central nervous system (CNS) represent the most common intracranial tumors in adults, usually occurring in advanced stages of malignancy. The incidence of CNS metastasis is 100,000 to 300,000 patients per year with Malignant melanoma as the third most common etiology.¹⁻³ CNS metastasis generally presenting very poor prognosis with mean survival time is approximately six months after diagnosis.³

The prognosis of melanoma usually determined by a Karnofsky performance score and the number of brain metastases. Interestingly, age and extra cranial metastases usually not significant prognostic factors.² In melanoma, up to 60% cases will develop CNS metastasis with manifestations that depends on the respective localizations and often pose challenges in diagnosis establishment.^{1,3} Accurate evaluations include immunohistochemistry are mandatory to confirm the diagnosis.^{1,2}

CASE REPORT

A 64-year-old woman was admitted because of vertigo and falls during the last six months. Four days before admission, she started with dyslalia and

bilateral parietal headache. There was no fever, mental confusion, weight loss, or other remarkable symptoms. Physical examination revealed dyslalia, diplopia with absence of motor focal changes.

Patient also had red dark-colored skin changes in the right parietal area of the scalp and enlarged lymph node over the right parotid area. Furthermore, she also claimed of intense headache, loss of visual acuity and vomiting. CNS imaging studies showed mass effect and intraventricular brain hemorrhage (**Figure 1. A to C**). In addition, there also expansive lesions involving the left parietal and the right temporal and occipital lobes associated with hemorrhagic phenomenon and mass effect (**Figure 1. D**) which lead to CNS metastases as possible diagnosis.

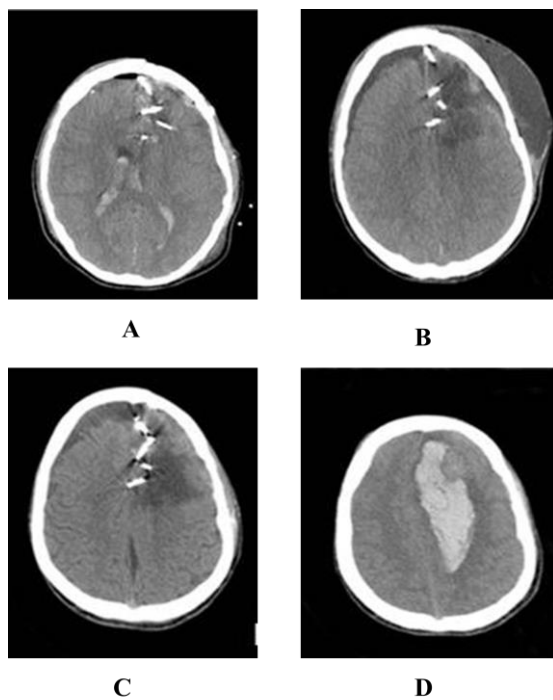


Figure 1. (CT images of the brain). **A to C.** Multiple large heterogeneous implants of malignant melanoma, hyperdense to brain and with cortical or subcortical localization. **D.** Indicative images of the hemorrhagic phenomena, which were associated with the CNS metastatic melanoma, including the evidence of intraventricular bleeding

Several implants were also detected by Computed tomography (CT) in lung and kidney which then confirmed by PET-CT. Blood clots were drained and a ventricle-peritoneal device was inserted by neurosurgical procedure in which patient clinically improved. Histopathology study of samples from implants showed a pleomorphic malignant tumor with areas of rhabdoid aspect which was suggestive of metastatic melanoma⁵. High expression of gp100 (HMB45) and S-100 protein were detected in immunohistochemistry procedure which consistent with melanocytic

histogenesis of tumor cells. **Table 1** summarize the result of hematological and blood chemistry analysis on day 1 and during patient control and treatment. The patient underwent ten sessions of radiation therapy followed by chemotherapy but patient condition finally worsens because of uncontrolled sepsis spite of management in the Intensive Care Unit.

DISCUSSION

The primary site of her cutaneous malignant melanoma was longstanding neglected and severe neurological disturbances constituted initial manifestations of this malignancy. Moreover, the parotid lymph nodes have been considered a frequent site of metastasis from melanoma with origin on the ipsilateral side of the scalp, like herein described^{6,7}. On admission, our major concern was about the routine differential diagnosis of stroke and several condition which includes diverse primary or secondary conditions of benign or malignant origin. CT and PET-CT studies revealed suggestive images of brain metastases.

Table 1. Laboratory controls of a 64-year-old woman with CNS metastatic melanoma

Parameters (normal ranges)	D1	D20	D61	D75	D87	D98	D108
Hemoglobin (13.5-18.0 g/dL)	13.5	14.8	11.3	10.9	10.8	9.4	10.6
Hematocrit (42-52%)	40.0	43.1	32.2	31.9	30.9	28.4	32.4
Leukocytes (4-11 x 10 ⁹ /L)	13.4	3.99	13.8	4.6	15.3	10.1	7.3
Neutrophils (40-70%)	88	86	79	62	78	87	79
Platelets (140-450 x 10 ⁹ /L)	264	279	196	344	657	225	250
ESR (< 15 mm/h)	31	20	-	-	39	95	-
C-RP (0.5-0.9 mg/dL)	0.7	-	1.6	1.6	0.9	0.3	0.3
Sodium (135-145 mmol/L)	138	128	151	138	138	134	133
Potassium (3.5-5.2 mmol/L)	4.6	4.2	2.6	3.8	5.0	4.4	4.1
Urea (10-50 mg/dL)	43.3	58.6	12.3	47.8	122	54	61.7
Creatinine (0.7-1.3 mg/dL)	0.7	0.6	0.3	0.2	0.7	0.2	0.2

D1: May 17th 2015; Patient's death was on D126; ESR: Erythrocyte sedimentation rate; C-RP:C-reactive protein. Abnormal data are in bold.

The hypothesis then confirmed by consistent histopathological and immunohistochemistry findings. Initial concern would be about the mimicked rhabdoid aspect in the surgical samples. However, this variant of melanoma is rare and should be characterized by polygonal cells with abundant cytoplasm, eosinophilic inclusions, and

peripherally-sited nuclei.⁵ Additionally, S-100 protein and HMB-45 can be negative in 16% and 19% of the cases while vimentin is 100% positive which is related to the distribution of eosinophilic inclusions.⁵ In this case, the immunohistochemistry analysis revealed that the brain metastatic cells significantly expressed both gp100 (HMB45) and S-100 protein, consistent with malignant melanoma. The specimens were also tested for cytokeratin's (40, 48, 50, and 50.8 kDa) and Melan A/ MART-1 clone A103 which yielded negative results.

CNS metastases are the most common intracranial tumors in adults with nonspecific manifestations depending on their specific localization.^{1,2} Imaging studies can be useful to differentiate between this condition and other lesions. Some points of consideration in imaging studies include the presence of multiple lesions, localization at the limit between the gray and white substances, circumscribed margins, and accentuated vasogenic edema out of proportion with the diameter of the lesion.^{3,4,6}

CNS metastases usually present with clinical features mimicking primary brain tumors but the evolution of symptoms is faster, often sub-acute, and with duration of few days or few weeks. At least in part, this rapid evolution is associated with accentuated perilesional edema.⁶ Progressive symptoms of behavioral disturbances, focal neurologic signs, seizures, and headache are usual manifestations of CNS metastases and intracranial hypertension.^{1,3,6}

Contrasted CT and magnetic resonance are the main neuro imaging tools for diagnosis. Nevertheless, in some cases the sole imaging characteristic did not allow to distinguish CNS metastases from primary malignant tumors and biopsy should be then performed. CT of the brain should be the first imaging exam to be done and have good sensibility in cases of lesions presenting hemorrhagic phenomenon even without contrast medium. Hemorrhages secondary to intracranial neoplasia are uncommon, in special when the diagnosis is metastasis; primary tumors more frequently associated with hemorrhage manifestations are renal and thyroid cancers, as well as melanoma and coriocarcinoma.³ CT shows single (54.2%) or multiple (45.8%) lesions in patients with brain metastases of melanoma and 84% of solitary lesions appear in hemispheres which 62.5% located in frontal area.³ Non-contrast CT detects 75% of the lesions as hyperdense, 22% hypodense and 3% isodense. The main distinguishing characteristic is they have contrast enhancement with homogeneous nodular or ring pattern. Magnetic resonance shows hyperintense lesions on T1 and hypointense on T-2 images.³ Despite of the recognized value of imaging studies, histopathological evaluation of tissue specimens

with immunohistochemistry is essential to clarify these CNS lesions.

Melanoma of the scalp tend to spread to the cervical and the parotid lymph nodes.^{6,7} In this case, the patient had more than three CNS metastases with hemorrhage and mass effect, and implants in lungs, right adrenal gland, and parotid gland lymph node.^{6,7} She underwent neurosurgical resection plus whole brain irradiation as well as chemotherapy.³ Despite rigorous treatment, the patient developed uncontrollable sepsis. Patient died after 108 days after first admission. Patient's short life expectancy is consistent with prognostic characteristic of melanoma arising in head and neck.^{6,7}

CONCLUSION

Malignant melanoma is one of serious dermatologic malignancy because of its elusiveness, invasiveness and has a great tendency to metastasize early during the course of the disease development. Primary lesion of malignant melanoma usually shows no symptoms other than change in skin colouration. The first initial symptom almost always arises due to distant metastases which often unrelated with primary lesion. In this case, patient was admitted because of CNS related symptoms. Following assessment by CNS imaging, immunohistochemistry analysis finally reveals the true nature of the disease. Examination of the scalp lead to discovery of primary lesion which had neglected for long time. This case suggests that through physical examination was needed in order to rule this common malignancy in CNS lesion suspected due to malignancy.

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