Article published online: 2022-09-23

Malignant Ocular Melanoma with Intradural Cervical Metastasis: Case Report and Literature Review*

Melanoma ocular maligno com metástase cervical intradural: Relato de caso e revisão de literatura

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Arq Bras Neurocir 2022;41(3):e288–e292.

Abstract

Introduction The occurrence of malignant ocular melanomas is uncommon, and the association of these tumors with intradural extramedullary metastases in the cervical spine is exceptionally rare.

Case Report A 62-year-old woman undergoing adjuvant chemotherapy after surgical treatment for malignant ocular melanoma begins to experience vertigo and headache. The condition evolved with walking difficulty and neck pain that was exacerbated by swallowing and mobilizing the neck. During her ocular melanoma follow-up, lesions suggestive of metastasis in the central nervous system were not evidenced until this moment. The physical examination did not show significant findings, and a cranial computed tomography scan was performed. The image showed a hyperdense lesion with postcontrast enhancement inside the vertebral canal, at the level of C1-C2. Spinal decompression and subtotal resection were performed. The anatomopathological report revealed intradural metastasis of a malignant ocular melanoma. The postoperative period was uneventful, with significant pain improvement and no recurrences.

Keywords
- intradural extramedullary metastasis
- malignant ocular melanoma
- surgery

* *Study conducted at Hospital Erasto Gaertner, Curitiba - PR, Brazil.*

received
August 14, 2021
accepted
December 20, 2021

DOI https://doi.org/10.1055/s-0042-1743105.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Conclusion Intradural extramedullary metastases are rare presentations of malignant ocular melanoma. In addition, less than ten similar cases have been reported in the literature. When caring for a patient with melanoma and neurological deficits, always consider evaluating central nervous system metastases. To evaluate this patient, a sensible and detailed neurological exam is extremely important to recognize the location of the deficits and guide the best approach, such as an indication for surgery.

Resumo

Introdução É infrequente a ocorrência dos melanomas oculares malignos, e menos frequente ainda é a sua associação às metástases intradurais extramedulares na região cervical.
Relato de Caso Uma mulher de 62 anos, submetida a quimioterapia adjuvante após tratamento cirúrgico para melanoma ocular maligno, abre um quadro de vertigem e cefaleia. O quadro evoluiu com dificuldade para deambular e dor cervical que se exacerbava ao se alimentar e mobilizar o pescoço. Durante o seguimento do melanoma ocular, não foram evidenciadas lesões sugestivas de metástase no sistema nervoso central até este momento. O exame físico não denotou alterações significativas, sendo então realizada tomografia computadorizada de crânio, cuja imagem evidenciou lesão hiperdensa com realce após contraste no interior do canal vertebral, no nível de C1-C2. Foram realizadas descompressão medular e ressecção subtotal, cujo laudo anatomopatológico revelou metástase intradural do melanoma ocular maligno. O pós-operatório seguiu sem intercorrências, com melhora significativa da dor e ausência de recidivas.
Conclusão As metástases intradurais extramedulares são apresentações raras de melanoma ocular maligno. Além disso, há menos de dez casos similares relatados na literatura mundial. Ao tratar de um paciente com melanoma e déficits neurológicos, sempre considere avaliar metástases no sistema nervoso central. Para avaliar este paciente, um exame neurológico criterioso e detalhado é essencial para reconhecer a localização dos déficits e guiar o manejo adequado, como a indicação cirúrgica.

Palavras-chave
- metástase intradural extramedular
- melanoma ocular maligno
- cirurgia

Introduction

Melanoma is a potentially-fatal malignant disease, and its frequency is higher in fair-skinned individuals.[1] Epidemiological studies[1,2] indicate melanoma as the fifth and sixth most common cancer among men and women in the United States respectively. In addition, an increase in the incidence of cases is observed between 25 and 50 years of age, with 57 years as the median age at diagnosis.[1] Ocular malignant melanoma occurs in less than 5% of all melanomas, and the liver is the most frequent metastatic site.[2]

Studies indicate that early identification of these lesions is the most important factor in terms of prognosis.[1] Such lesions can cause distant metastases, mainly in the lungs, brain, liver, bones, and intestines, most of them with low rates of success regarding treatment.[3] However, intradural extramedullary (IDEM) metastases are exceptionally rare, especially when there is no other metastasis in the central nervous system (CNS).[1–3]

We herein describe a rare presentation of IDEM metastasis, with an ocular malignant melanoma as the primary site of the lesion. So far, less than ten similar cases have been reported in the literature, and the present report aims to contribute to this context.

Case Report

A 62-year-old female patient was referred to the oncology surgery service due to a diagnosis of ocular malignant melanoma, initially investigated due to progressive decrease in left visual acuity and local pain. There was a history of prolonged exposure to sunlight since the age of 10 years. She denied smoking and drinking, and reported a family history of leukemia. A cranial computed tomography (CT) scan (►**Fig. 1**) identified intraocular hyperdense heterogeneous material. The patient initially refused to get surgical treatment, and sought the service three years later, due to a progressive increase in the lesion over the past six months. At the time, surgical treatment was suggested for the purpose of providing her comfort. A brain magnetic resonance imaging (MRI) scan (►**Fig. 2**) revealed an expansive ocular and extraocular lesion in the left eye, with a large mass extending to the preseptal region and retrobulbar fat, measuring ~ 46 mm in the anteroposterior direction, compatible with primary neoplasia (melanoma), and the presence of left optic nerve atrophy, without unequivocal evidence of intracranial extension. The procedure performed included orbital exenteration and maxillectomy of the orbital floor. There was an absence of lymph node metastases at the time of the

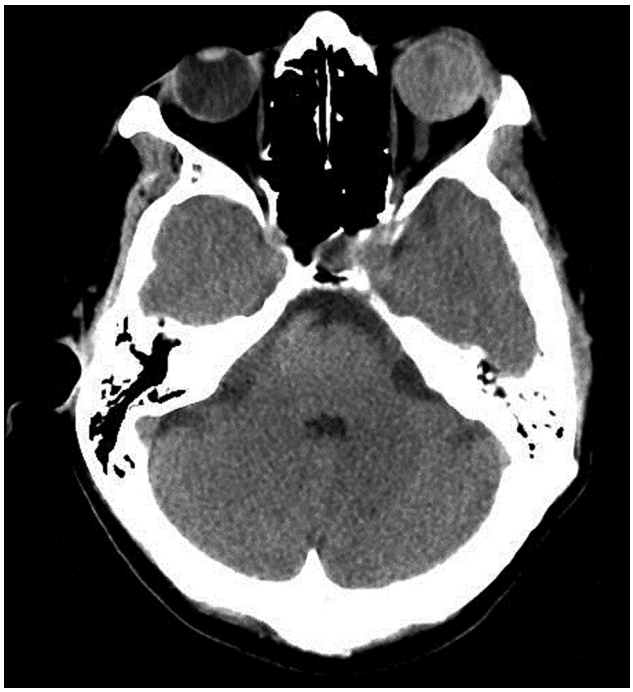

Fig. 1 Brain computed tomography scan showing heterogeneous material inside the left eyeball.

surgery. The histopathological analysis of the specimen revealed mixed-cell melanoma (spindle cell and epithelioid – grade II). The immunohistochemical analysis showed a type III receptor tyrosine kinase, which is localized in various neoplasms, CD117 (cKIT), with diffuse weak positivity.

The postoperative control brain CT revealed no expansive lesions. After the procedure, the patient was referred to start

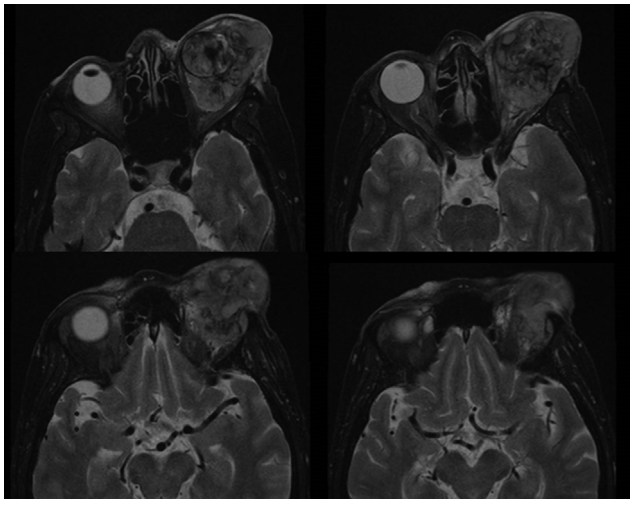

Fig. 2 Brain magnetic resonance imaging scan showing an expansive lesion in the left eye, measuring $\sim$ 46 mm in length in the antero-posterior direction, presenting heterogeneous signs with hypo- and hyperintense foci on T1- and T2-weighted images and postgadolinium heterogeneous enhancement. Impression of discrete postgadolinium enhancement in the canalicular portion of the left optic nerve, with atrophy of its prechiasmatic segment, is also observed.

adjuvant therapy. Chemotherapy with interferon-α 2A and radiotherapy (34 Gy) were indicated for locoregional control of the orbit. She remained in bimonthly outpatient follow-up but did not complete the recommended time for adjuvant therapy, having undergone 1 year and 8 months of chemotherapy. She was lost to follow-up for 8 months due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, reporting isolation. Upon return, in agreement with the patient and family, we identified that there was no benefit from the continuation of the treatment with interferon, but the bimonthly follow-up was maintained. Despite this, she did not perform the imaging exams requested. Three months after resuming follow-up, the patient started to present vertigo and headache. A CT scan of the brain revealed a spontaneously hyperdense, contrast-enhanced nodule within the vertebral canal, at the level of C1-C2. The nodule had approximate dimensions of 14×10 mm in the axial plane and 19 mm in the sagittal plane. The lesion was not present in previous exams. In addition, a hypoattenuating area was identified in the left frontal lobe, adjacent to the anterior horn of the lateral ventricle, mainly affecting the white matter, and not promoting effacement or retraction of the cerebral sulci. We identified the presence of a tenuous nodular enhancement focus measuring 2 mm in the cortical-subcortical transition. We recommended that the investigation should proceed with a cervical spine MRI.

One month after identifying the changes in imaging exams, the patient sought the emergency room of the service due to difficulty in walking, dizziness, and neck pain, which had evolved for weeks, in addition to an episode of emesis the day before. The pain was exacerbated with neck mobilization and swallowing, leading to reduced food intake. Upon physical examination, muscle strength was normal in all four limbs, and sensitivity was preserved. She was admitted for a specialized evaluation, which determined the need for surgical management for spinal-cord decompression. Dexamethasone 4 mg was started every 6 hours until the procedure, which was performed two days later. The cervical spine MRI (►**Fig. 3**) showed a solid intradural extramedullary nodule located posteriorly to the vertebral canal at the level of C1 and C2, measuring $28 \times 17 \times 15$ mm.

Intraoperatively, after laminectomy of C1 and opening of the dura mater, a black lesion measuring $\sim$2.5 cm in the longitudinal direction (►**Fig. 4**) was observed, which partially infiltrated nerve roots and vascular structures and compressed the left lateral region of the spinal cord. Most of the tumor was resected, except for the infiltrated regions, considering the risks to mobility and sensitivity. The patient had no neurological deficits on the first postoperative day, reporting only pain in the left ear canal.

Discussion

Intradural extramedullary metastases (IDEM) from malignant melanomas are exceptionally rare. Also, IDEM metastases correspond to approximately 5% of spinal metastases.[4]

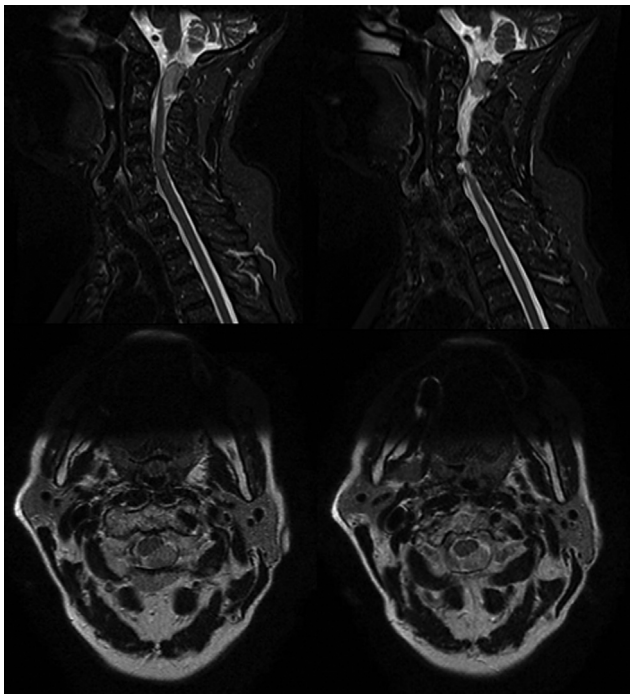

Fig. 3 Magnetic resonance imaging scan of the cervical spine showing a solid intradural extramedullary nodule located posteriorly to the vertebral canal at the level of C1 and C2 measuring 28 × 17 × 15 mm, compressing the posterior surface of the medullary cord. It presents isosignal on T1 and hypersignal on T2 with the musculature and moderate/slightly heterogeneous post-gadolinium uptake.

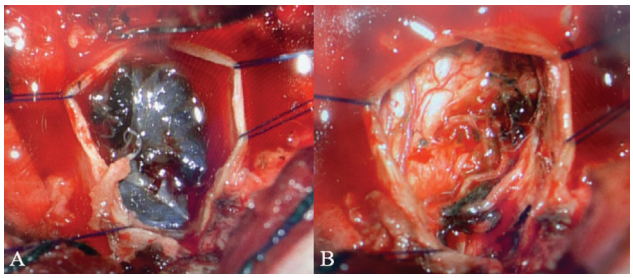

Fig. 4 (A) Intraoperative appearance of the lesion. (B) Intraoperative appearance after subtotal resection.

The overall prevalence of spinal melanoma metastases estimated by clinical studies[5] is only 2.4%, and the ocular site corresponds to 10% of the primary melanoma sites. Metastases to the brain are more prevalent than those to the spinal, and CNS metastases occurs in 10% to 40% of melanoma patients, and in up to 90% of the cases in autopsy studies.[6]

The first report of IEMs occurred in 1982, when Perrin et al.[7] analyzed 200 patients with non-neurogenic spinal metastases, and found that 10 cases occurred in the intradural space. By 2020, 14 cases of IEM metastasis of malignant melanoma had been published,[2] and only 3 were located between cervical vertebrae. The comparison of those 3 studies[3,5,8] and the present case are shown in ►**Table 1**.

Multiple theories have been proposed to explain the spread to the intradural space. Among them, the most accepted and which corroborates the fact that most IEMs are associated with other metastases in the CNS is the theory of dissemination through the cerebrospinal fluid (CSF), also called "drop metastases."[2,4] In a review,[8] a rate of positivity of 50% for malignant cells was observed in the CSF analysis. Even though a CSF examination was not performed in the present study during the reported period, the authors agree with its importance, notably when leptomeningeal commitment is a plausible differential diagnosis.

In those patients without coexisting CNS metastasis, other theories of hematogenous spread seem more plausible. When analyzing tributary veins of the vertebral venous plexus, it is possible to establish drainage routes communicating the eyes and the maxilla (primary surgical sites) to the craniovertebral junction. A possible drainage route is after the ophthalmic veins reach the cavernous sinus, the hematogenous metastasis would be drained to the basilar venous plexus, and via the marginal sinus disseminate to vertebral venous plexus. However, due to the drainage anatomy, the most plausible route is the hematogenous metastasis draining to the inferior petrosal sinus and reaching the superior bulb of the internal jugular vein, which does not corroborate to explain the dissemination of the present case.

Among the 14 similar cases reported in the literature,[2] the thoracic and lumbar regions were the most affected, and the predominant symptoms in these cases were weakness in the lower limbs and paresthesia. Lumbar, radicular or cervical pain, urinary dysfunction or incontinence, and loss of thermal sensitivity were other symptoms reported according to the location of the metastasis.[2] The time from the diagnosis of malignant melanoma to the diagnosis of cervical IDEM metastasis was also variable, as reported by Knafo et al.,[8]

Table 1 Literature review of intradural extramedullary metastasis of malignant melanoma in the cervical region

Reference	Age and gender	Vertebrae	Symptoms
Shakur et al.,[5] 2012	66, female	C1–2	Weakness and sensory loss
Knafo et al.,[8] 2013	74, male	Cervical (not specified)	Cervical pain
Stein et al.,[3] 2018	63, male	C1–2, C7-T1, conus medullaris, L4-S1	Cervical pain, weakness, and sensory loss
Present case, 2021	62, female	C1–2	Cervical pain, headache, dizziness, walking difficulty, and emesis

occurring in less than 1 year, and by Shakur et al., after 14 years.[5] In the present case, the time from the diagnosis of melanoma until the patient manifested symptoms of IDEM metastasis was of 6 years.

Regarding treatment, the information available in the literature is scarce. Only a few authors[2,4,9] report good recovery after surgery with or without adjuvant radiotherapy, yet resection is still indicated with a strictly palliative purpose to try to preserve neurological function.[5,9] Among patients with spinal metastasis deficits from malignant melanoma, Donaldson et al.[10] reported a median survival of 5.3 months with surgery, and of 1.2 months without surgery. However, although the prognosis remains unfavorable, there has been a trend toward better results since 2012 compared with the results observed between 1982 and 1999, which may be related to advances in imaging diagnosis, chemotherapy, and early diagnosis.[2]

Conclusion

In the present article, we report a rare form of intradural extramedullary metastatic tumor in an elderly patient. In our review, only a few studies have reported such a presentation. When caring for a patient with melanoma and neurological deficits, always consider evaluating CNS metastases. Brain metastases are more probable, and can spread as "drop metastases" through the CSF, predisposing spinal metastases. To evaluate this patient, a sensible and detailed neurological exam is extremely important to recognize the location of the deficits and guide the best approach, such as an indication for surgery.

Ethics Statement

The present study was approved by the Ethics in Research Committee of Centro de Projetos de Ensino e Pesquisa (CEPEP) from Hospital Erasto Gaertner, in the city of Curitiba, Southern Brazil, and approved under CAAE number 87548518.2.0000.0098. Written consent was obtained from the patient.

Funding Statement

The authors declare that no funding has been received pertaining to the present article.

Conflict of Interests

The authors have no conflict of interests to declare.

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