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Case Report

A rare case of brain metastatic malignant melanoma coexisting with black colored dura mater: Management in low-resource setting

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ABSTRACT

Background: Brain metastases significantly contribute to morbidity and mortality in individuals with cancer, with melanoma exhibiting a high propensity for central nervous system dissemination. Early recognition and diagnosis are crucial, especially in low-resource settings where access to advanced diagnostics and treatment may be limited.

Case Description: We present the case of a 63-year-old male with a history of metastatic melanoma who presented with progressive neurological deficits. Imaging revealed a solitary brain metastasis in the cerebellopontine angle, further complicated by diffuse melanotic infiltration of the dura mater. The patient underwent surgical resection of the cerebellopontine angle mass, and histopathological examination confirmed metastatic melanoma.

Conclusion: This case highlights the importance of considering metastatic disease in the differential diagnosis of cancer patients presenting with neurological symptoms, even in atypical locations. The presence of dural melanosis underscores the aggressive nature of melanoma and the need for comprehensive evaluation. This case emphasizes the need for prompt diagnosis and management to optimize patient outcomes, particularly in resource-constrained environments.

Keywords: Black dura mater, Brain, Case report, Malignant melanoma, Rare case

INTRODUCTION

Brain metastases represent a devastating complication of malignant melanoma, often signifying advanced disease and a poor prognosis.[7] The incidence of brain metastases in melanoma patients is significant, with estimates suggesting up to 75% of patients develop brain metastases in their disease course.[6,7] While any area of the brain can be affected, melanoma demonstrates a predilection for certain sites, including the cerebellopontine angle, as highlighted in this case.[3,6,7]

The previous case report by Tang *et al.*, in 2017 [16] detailed the challenges in accurately diagnosing primary cerebral melanomas due to their varied radiologic appearance, often mimicking other intracranial lesions. The clinical presentation of brain metastases is often insidious and nonspecific, mimicking more common neurological conditions and posing a significant diagnostic challenge, particularly in resource-limited settings.[11,17] Facial pain, while a common

presenting symptom in various neurological disorders, can be misleading, as illustrated in this case where it masked a more sinister underlying pathology of the lesion in the left hemifacial. This diagnostic ambiguity underscores the importance of a comprehensive neurological evaluation and a high index of suspicion for metastatic disease in patients with a history of melanoma presenting with neurological symptoms.

This report describes a rare case of brain metastatic malignant melanoma presenting with left-sided facial pain and cranial nerve deficits, ultimately revealing a unique finding of diffuse melanotic infiltration of the black-colored dura mater, a rare occurrence even in the context of metastatic melanoma.

CASE DESCRIPTION

A 63-year-old male presented with a 7-month history of intermittent, left-sided facial pain. The pain, described as stabbing, was exacerbated by swelling around the left eye and was not relieved by over-the-counter analgesics. He reported a 2-year history of progressive swelling around the left eye, accompanied by 1 year of left-sided vision loss. In addition, he experienced 6 months of generalized weakness, 2 years of dizziness, and 3 years of left-sided hearing loss. His medical history is significant for hypertension, managed with Amlodipine 10 mg once daily. There is no family history of malignancy. The patient had previously undergone a skin biopsy at another institution, with a reported diagnosis of malignant melanoma. Unfortunately, we were unable to obtain the original pathology report.

On physical examination, the patient's vital signs were as follows: blood pressure 130/80 mmHg, heart rate 80 beats/minute, respiratory rate 20 breaths/minute, temperature 36.4°C, and oxygen saturation 99% of room air. A dermatological examination revealed a hemifacial nodule with well-defined borders, variegated black-to-greenish pigmentation, and proptosis of the left eye [Figure 1]. Neurological examination revealed a Glasgow Coma Scale score of E4M6V5. The patient was alert and oriented to person, place, and time. Cranial nerve examination showed no light perception in the left eye, with pupils measuring 3 mm on the right and 6 mm on the left, round, and anisocoric. Facial sensation was diminished in all three divisions (V1, V2, and V3) of the left trigeminal nerve. Left-sided lower facial weakness was evident by the asymmetry in smiling and grimacing. Motor examination revealed 5/5 strength in all extremities, normal tone throughout, and a normal gait.

A computed tomography scan of the head [Figure 2] revealed two distinct areas of concern. In the left cerebellopontine angle, a well-defined, dense mass measuring 1.7 cm across was found, showing signs of calcification. A larger, dense mass (3.8 × 4.3 cm) was identified in the area behind the left eye, pushing the eyeball forward. This mass also showed calcification and measured about 70 Hounsfield units, indicating its density.

The scan also revealed prominent grooves and folds in the frontal lobes of the brain, suggesting a degree of brain atrophy. The brain's fluid-filled spaces appeared normal, with no signs of pressure or displacement. Calcification of the choroid plexus, a structure within the brain's ventricles, was also noted. All other visible structures, including sinuses, air cells, and bones, appeared normal.

These findings point toward tumors in both the left cerebellopontine angle and the area behind the left eye. The characteristics of these tumors, particularly their density and calcification, align with the features of meningiomas. The prominent grooves and folds in the brain suggest the presence of cerebral atrophy.

The initial conclusion of brain magnetic resonance imaging (MRI) with the contrast of this patient [Figure 3] was a suspected left optic nerve sheath meningioma with the presence of multiple similar lesions raises concern for meningiomatosis in the brain, particularly in the left cerebellopontine angle. A brain MRI with contrast revealed a complex mass enveloping the left optic nerve. This mass, measuring about 3.8 cm across, appeared bright on the T1-weighted image and dark on the T2-weighted image, with unrestricted diffusion. Its appearance, including a characteristic "tram-track sign" and strong contrast enhancement, pointed toward a nerve sheath origin. This primary tumor extended beyond the optic nerve, reaching into the left cavernous sinus and pushing against the left side of the skull, causing a noticeable outward bulge of the eye (2.1 cm).

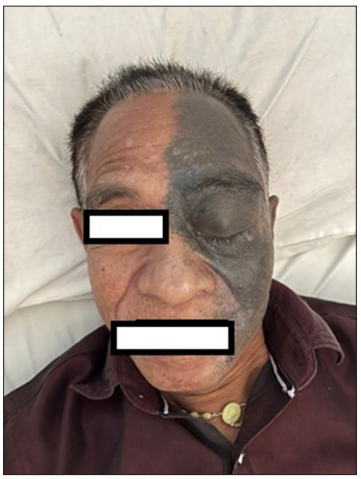

Figure 1: Left hemifacial hyperpigmentation of the patient with ptosis and proptosis of the left eye, with peripheral type paresis of cranial nerve (CN) VII.

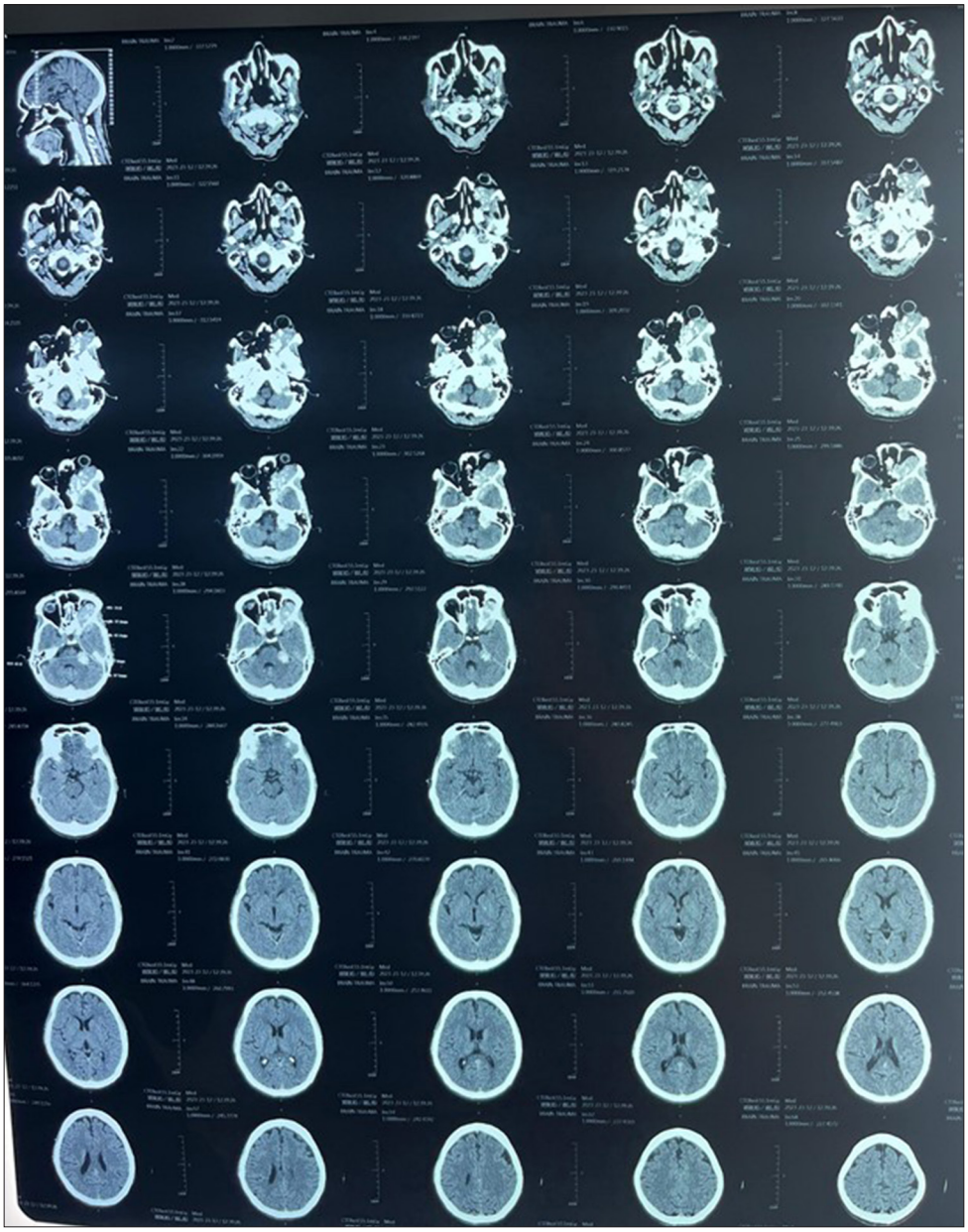

Figure 2: Head computed tomography scan: well-defined, hyperdense lesion with calcification, measuring approximately 1.7 × 1.7 cm, located in the left cerebellopontine angle. An additional larger lesion, measuring 3.8 × 4.3 cm, was observed in the left retrobulbar and temporal region, displacing the left eye globe anteriorly. This lesion also exhibited hyperdensity, measuring approximately 70 Hounsfield units, and contained calcifications.

Adding to the complexity, several similar lesions were scattered throughout the brain, suggesting a diagnosis of meningiomatosis. These additional masses were found in the left frontal lobe (0.5 cm), near the base of the skull (0.9 cm), and in the area where the cerebellum and brainstem connect (2 cm).

Apart from these masses, the rest of the brain appeared normal. The brain's structure, fluid-filled spaces, and other key areas, including the orbits and sinuses, were all unremarkable.

These findings strongly suggest a diagnosis of the left optic nerve sheath meningioma that has spread to the surrounding bone and sinus. The presence of multiple similar lesions raises concern for meningiomatosis, affecting various areas within the brain.

Based on the clinical presentation and preliminary imaging findings, the presumptive diagnosis is multiple intracranial lesions: left cerebellopontine angle tumor with possible

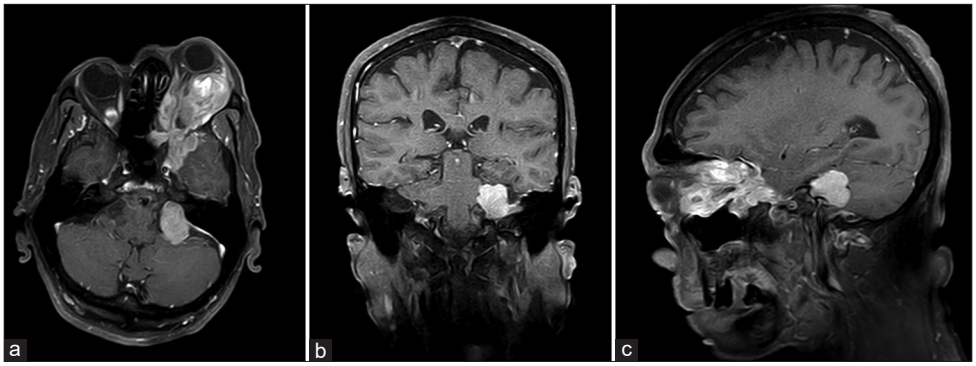

Figure 3: (a-c) Axial, coronal, and sagittal section of brain magnetic resonance imaging with contrast: A heterogeneously enhancing mass surrounding the left optic nerve. The lesion, measuring approximately 3.8 × 3.9 × 3.5 cm, exhibited hyperintensity on T1-weighted images and hypointensity on T2-weighted images. Diffusion-weighted imaging demonstrated unrestricted diffusion within the lesion. Notably, the mass displayed a "tram-track sign" and exhibited strong contrast enhancement, suggestive of a nerve sheath origin. This primary lesion extended through the left optic canal into the left cavernous sinus and abutted the left sphenoid convexity, resulting in a proptosis of approximately 2.1 cm. Furthermore, multiple similar lesions were identified, suggestive of meningiomatosis. These included a 0.5 cm lesion in the left frontal convexity, a 0.9 cm lesion in the left lesser sphenoid wing, and a 2 cm lesion in the left cerebellopontine angle.

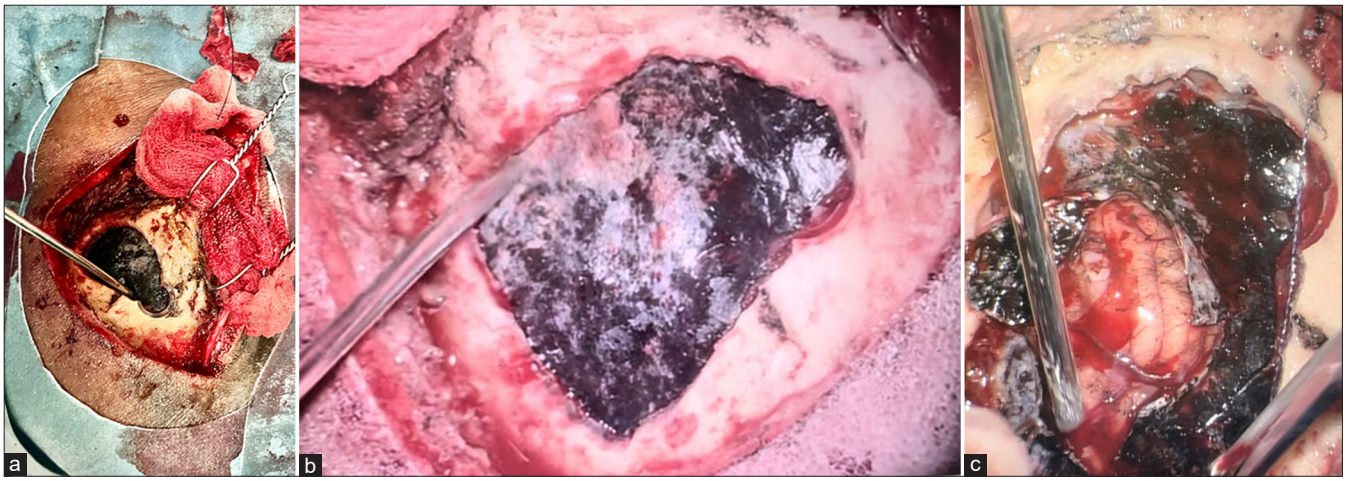

Figure 4: (a and b) The black-colored dura mater was strikingly found after the removal of the scalp and cranium during the retrosigmoid craniotomy. (c) After the incision of the dura mater, the cerebellum color appears normal.

extension and left retro-orbital tumor suspect brain metastases with differential diagnoses of meningioma.

The patient underwent a left retrosigmoid craniotomy for resection of the cerebellopontine angle mass. A curvilinear incision is made behind the ear, extending from the mastoid tip to a point superior and posterior to the pinna. The scalp and muscles are reflected to expose the skull. After the removal of the cranium, a striking black discoloration of the dura mater was observed, corroborating the suspected melanotic infiltration [Figure 4].

A retrosigmoid craniotomy is performed, exposing the transverse and sigmoid sinuses, as well as the posterior fossa dura. The dura mater is opened in a curvilinear fashion, exposing the cerebellum and the cerebellopontine angle (CPA). Cerebrospinal fluid (CSF) is drained from the cisterna magna to relax the brain and improve visualization. The tumor is carefully identified within the left CPA [Figure 5]. Microsurgical techniques are employed to dissect the tumor from surrounding structures, including cranial nerves V, VII, and VIII, the brainstem, and the cerebellum. The tumor is internally debulked using ultrasonic aspiration. Once debulked, the tumor capsule is carefully dissected from the surrounding structures and removed *en bloc*. After meticulous hemostasis, the dura is closed in a watertight fashion. The bone flap is replaced and

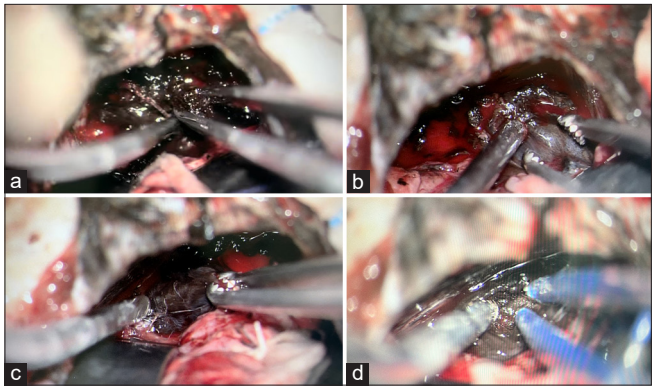

Figure 5: (a-d) Intraoperative view of black-colored mass in the left cerebellopontine angle compressing the nearby structures, including cranial nerve (CN) V, VII, and VIII.

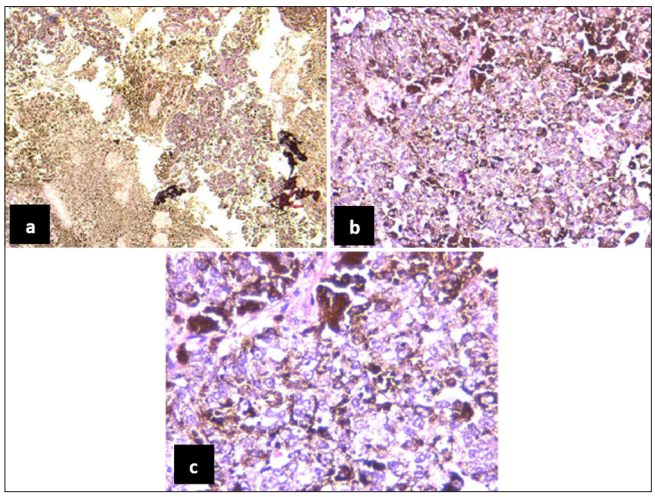

Figure 6: (a-c) Microscopic view of the tumor in ×4, ×20, and ×40 magnification**.** The stain used is hematoxylin and eosin.

secured with titanium plates and screws. The muscle and scalp layers are closed in layers.

This case presents a unique constellation of multiple left-sided abnormalities, including left hemifacial skin efflorescence, a black-pigmented mass in the left cerebellopontine angle, and abnormal pigmentation of the dura mater observed in the left retrosigmoid region [Figures 1, 4 and 5].

Histopathological analysis [Figure 6] demonstrated a dense cellular proliferation of malignant tumor cells arranged in nests and sheets. The tumor cells exhibited significant pleomorphism, appearing predominantly round to oval in shape, with irregular nuclear contours and abundant coarsely granular chromatin. Mitoses were readily identifiable. The ample cytoplasm of these cells frequently contained brown pigment granules, consistent with melanin. Areas of necrosis were interspersed throughout the tumor, along with a reactive stroma composed of connective tissue, lymphocytes, neutrophils, and extravasated red blood cells. In conclusion, the microscopic features of the tumor are definitively characteristic of metastatic malignant melanoma.

Due to the specimen processing occurring at an external referral institution, we were unable to obtain photographic documentation or a separate pathology report for the dura mater. While acknowledging this limitation, the histopathological diagnosis of metastatic malignant melanoma from the intracranial lesion, combined with the clinical presentation and imaging findings, strongly supports the diagnosis of dural metastasis.

Following surgical intervention, the patient was managed in the intensive care unit for a period of 48 h, subsequently transferred to a general ward for an additional 48 h, and transitioned to outpatient care on the 5th postoperative day. While the complete resolution of hemifacial pain was observed by the 2nd postoperative day, peripheral cranial nerve VII paresis and left-sided hearing loss persisted without noticeable improvement.

During a follow-up appointment at the neurosurgery outpatient clinic in the 2nd postoperative week, the patient presented with signs of CSF leak. A second craniotomy was performed for debridement and exploration, successfully sealing the leak. No further signs of CSF leakage were observed.

The patient was consulted by the oncology department and was treated with dacarbazine 350 mg per oral single dose within 5 days and given premedication with dexamethasone 5 mg intraveonus (IV), diphenhydramine 10 mg iv, and omeprazole 40 mg iv.

Surgical resection of the retrobulbar mass, in conjunction with ophthalmology, is planned following the stabilization of the patient's condition.

DISCUSSION

This case report unveils the complexities of managing a rare presentation of metastatic malignant melanoma, characterized by a cerebellopontine angle tumor and striking black-colored dura mater, all within the constraints of a low-resource setting. Several critical aspects warrant in-depth discussion.

The initial presentation with facial pain, while common, belied the sinister underlying pathology. This case underscores the challenges of diagnosing brain metastases, particularly in resource-limited settings where access to advanced imaging modalities such as MRI might be delayed or unavailable. A high index of suspicion is paramount in patients with a history of melanoma presenting with neurological symptoms, even if seemingly unrelated to the original malignancy.

The intraoperative finding of black-colored dura mater [Figure 4], a visual testament to diffuse melanotic infiltration,

is a rare occurrence.[1] While melanoma is known for its propensity for hematogenous spread, dural metastases often present with nonspecific symptoms, making early diagnosis difficult.[3] This case highlights the importance of considering dural involvement in melanoma patients with neurological symptoms, even in the absence of classic radiological signs.

Managing complex neurosurgical cases such as this in resource-constrained settings presents unique ethical and logistical dilemmas. Surgical resection, while offering the best chance for local control, might be limited by tumor extent and available expertise.[4] Adjuvant therapies such as stereotactic radiosurgery and immunotherapy, proven to improve survival in melanoma brain metastases, are inaccessible due to cost or infrastructure limitations.

In such scenarios, where curative intent might be limited by disease stage and resource availability, the focus shifts to optimizing quality of life. Palliative care, encompassing pain management, symptom control, and psychosocial support, becomes paramount. This case emphasizes the need for a holistic approach, addressing not just the physical but also the emotional and spiritual needs of the patient and their families.

By presenting this unusual case, we aim to raise awareness among clinicians about the atypical presentations of metastatic melanoma, emphasize the importance of early diagnosis and prompt intervention, and advocate for equitable access to quality healthcare for all. The presence of dural metastases suggests a higher likelihood of leptomeningeal spread, a devastating complication characterized by the dissemination of tumor cells throughout the CSF, which is notoriously difficult to treat.[8]

Here's how dural involvement influences treatment decisions, particularly in low-resource settings: Surgical Resection: while surgery might be considered for localized brain metastases, extensive dural involvement can make complete resection challenging or impossible.[5,8] In low-resource settings, where surgical expertise and technology might be limited, the risks and benefits of surgery need to be carefully weighed against the potential for complications and the likelihood of achieving meaningful tumor control.

Adjuvant Therapies: dural involvement often necessitates more aggressive adjuvant therapies, such as whole-brain radiotherapy, to target both the primary brain metastasis and potential microscopic spread within the meninges.[7] However, access to advanced radiotherapy techniques, such as stereotactic radiosurgery, which offers more targeted treatment with fewer side effects, might be limited in low-resource settings. Palliative Care: given the aggressive nature of dural involvement and the potential limitations in treatment options, early integration of palliative care is crucial. This approach focuses on symptom management, pain control, and psychosocial support to optimize the patient's quality of life.

Treatment decisions require a multidisciplinary approach, considering the patient's overall health, disease stage, available resources, and individual goals of care.

Dural involvement in melanoma brain metastases is a significant negative prognostic factor. It indicates a more aggressive disease phenotype and is associated with an increased risk of leptomeningeal spread: the dura mater is in close proximity to the CSF. Dural involvement increases the likelihood of tumor cells infiltrating the CSF, leading to leptomeningeal disease, a highly challenging condition to treat.[7,8] Higher tumor burden and microscopic spread: dural involvement often suggests a higher overall tumor burden and a greater likelihood of microscopic disease spread beyond the primary brain metastasis. This makes complete surgical resection difficult and increases the risk of recurrence.[12] Poorer response to treatment: patients with dural involvement tend to respond less favorably to standard treatments such as surgery, radiotherapy, and even systemic therapies. The presence of dural disease might necessitate more aggressive treatment approaches, which may not be feasible or accessible in all settings.[7,12] Decreased overall survival: studies have shown that patients with dural involvement in melanoma brain metastases generally have shorter overall survival compared to those without dural involvement.[12]

It is important to note that while dural involvement is a negative prognostic factor, it is not an absolute determinant of outcome. Individual patient factors, such as overall health, functional status, and the presence of other metastases, also play a significant role in determining prognosis. Therefore, a comprehensive assessment considering all these factors is crucial for appropriate treatment planning and prognostication.[12,13]

Personalized treatment planning: tailoring treatment plans based on individual patient factors, disease stage, available resources, and overall goals of care. Early integration of palliative care: providing symptom management, pain control, and psychosocial support to optimize quality of life, especially in cases where curative intent is limited.[13]

As mentioned above in the case presentation, the patient is treated with dacarbazine as a monochemotherapy. The mechanism of action of dacarbazine is an alkylating agent that disrupts Deoxyribonucleic acid (DNA) replication and ultimately leads to cancer cell death. Dacarbazine's role in melanoma: historically, dacarbazine was considered a standard chemotherapy option for metastatic melanoma, including brain metastases. Dacarbazine monotherapy generally demonstrates modest response rates in patients with melanoma brain metastases, and its impact on overall survival is limited. Dacarbazine can cause significant side effects, including nausea, vomiting, bone marrow suppression, and liver toxicity.[2]

With the advent of targeted therapies and immunotherapies, which have shown improved efficacy and tolerability, the use of dacarbazine as a first-line treatment for melanoma brain metastases has significantly decreased.[9]

The treatment of melanoma brain metastases has evolved rapidly in recent years. While chemotherapy, including dacarbazine, was once a mainstay of treatment, its role has been significantly impacted by the emergence of more effective and targeted therapies. Targeted therapies (e.g., B-Raf proto-oncogene, serine/threonine kinase. [BRAF] and mitogen-activated protein kinase kinase [MEK] inhibitors) and immunotherapies (e.g., immune checkpoint inhibitors) have demonstrated superior efficacy compared to chemotherapy in many cases of melanoma brain metastases. These therapies can cross the blood-brain barrier and target tumor cells more specifically, leading to improved outcomes. While side effects can occur, targeted therapies and immunotherapies often have more favorable toxicity profiles compared to dacarbazine, which can cause significant nausea, vomiting, and bone marrow suppression.[2,9]

Combination therapies, such as combining targeted therapies with immunotherapy or radiotherapy, are also being explored to enhance treatment response further and potentially improve survival.

While dacarbazine was previously used to treat brain metastases from malignant melanoma, its impact on overall survival was limited. The advent of more effective targeted therapies and immunotherapies has led to a shift in the treatment paradigm, and dacarbazine is now less.

Managing this patient in the resource-constrained setting of East Nusa Tenggara presented significant challenges. Our facility lacks access to several key treatment modalities currently considered standard of care for melanoma brain metastases in more developed settings. Specifically, we cannot administer combination therapies, such as targeted therapies combined with immunotherapy or radiotherapy. Advanced radiotherapy techniques, including stereotactic radiosurgery, are also unavailable. The absence of these treatment options limited our ability to offer the patient the most effective and potentially life-extending therapies.

Had these resources been available, the patient's management would have likely included BRAF/MEK inhibitors combined with immunotherapy, stereotactic radiosurgery, or whole-brain radiotherapy. These therapies have demonstrated improved outcomes in patients with melanoma brain metastases.[10,14,15]

CONCLUSION

This case underscores the critical need to include metastatic disease as a potential diagnosis in cancer patients experiencing neurological symptoms, even when presenting in uncommon locations. The observed dural melanosis emphasizes the aggressive behavior of melanoma and the importance of a thorough diagnostic approach. Furthermore, this case highlights the necessity of timely diagnosis and intervention to improve patient outcomes, particularly within environments where resources are limited.

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