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Primary CNS Melanoma of Meckel's Cave: A Rare Case with Literature Review

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Abstract

Meckel's cave is a dural recess in the posteromedial portion of the middle cranial fossa, serving as a conduit for the trigeminal nerve and hosting various pathologies. The radiological diagnosis of Meckel's cave pathologies is often challenging, especially when they are atypical and rarely encountered. Here, we discuss the case of a 41-year-old woman who presented with right hemifacial pain, numbness, and binocular diplopia. Imaging features suggested a T2 hypointense, T1 hyperintense, and nonenhancing mass in the right Meckel's cave. Intraoperatively, an extra-axial black mass was observed, suggestive of melanoma, which was radically excised. Further postoperative workup and biopsy revealed it was a primary central nervous system (CNS) malignant melanoma, an exceedingly rare condition. Due to the rarity of the disease, a consensus regarding treatment regimens is lacking. This case report underscores the significance of considering uncommon diagnoses when faced with unusual radiological findings and emphasizes the importance of aggressive surgical resection and the evolving landscape of adjuvant treatments for primary CNS melanomas.

Keywords
- cavernous sinus
- Meckel's cave
- primary
- CNS
- malignant
- melanoma

Introduction

Meckel's cave, a natural aperture resembling a mouth in the medial part of the middle cranial fossa, serves as a crucial pathway for the trigeminal nerve (CN V), the largest cranial nerve. It links the cavernous sinus to the prepontine cistern in the posterior fossa. Meningiomas and schwannomas are frequently encountered lesions in Meckel's cave. Here, we present the rare case of a 41-year-old female who was diagnosed with a nonenhancing right Meckel's cave mass which turned out to be a melanoma.

Case Summary

A 41-year-old female patient presented with a 2-year history of decreased sensation on the right side of her face, binocular diplopia that had persisted for 6 months, and worsening right hemifacial pain over the past 2 months. Clinical findings included right lateral rectus paresis, atrophy of the right temporalis and masseter muscles, and decreased sensation in the V1, V2, and V3 dermatomes by 50%. Magnetic resonance imaging (MRI) brain revealed a $3 \times 2.6 \times 1.7$ cm extra-axial mass in the right Meckel's cave. The mass was T1 hyperintense and T2 hypo-isointense, and caused mass effect on the mesial temporal lobe structures. No enhancement was observed with gadolinium contrast. Compared with an MRI done 8 months earlier, the mass had doubled in size. Computed tomography (CT) brain imaging revealed hyperdensity within the mass (►**Fig. 1**). The petrous and cavernous portions of the internal carotid artery were medial to the mass.

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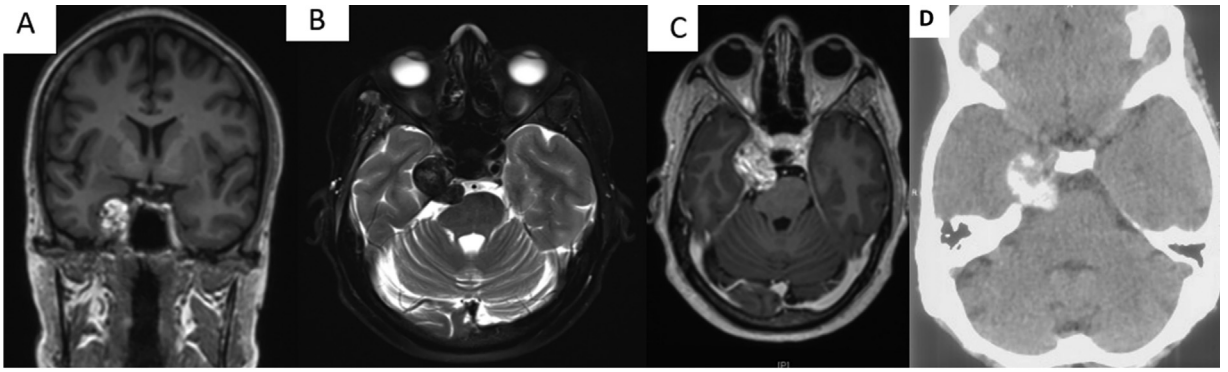

Fig. 1 Magnetic resonance (MR) imaging showing T1 hyperintense mass in posterior cavernous sinus in coronal section (**A**). The mass was T2 hypointense and extended from the right Meckel's cave to the posterior cavernous sinus (**B**). The mass was nonenhancing (**C**) and had areas of hyperdensity on plain computed tomography (CT) imaging (**D**).

We performed right temporal craniotomy with zygomatic osteotomy. The middle cranial fossa base was drilled. The superior orbital fissure, foramen rotundum and foramen ovale, and foramen spinosum were exposed. The foramen rotundum and foramen ovale were unroofed. The dural layer over the maxillary and mandibular divisions was sharply cut. The middle meningeal artery was coagulated and cut at the foramen spinosum. The temporal dura was peeled off from the cavernous dura. A blackish mass was seen in the anterolateral triangle suggestive of melanoma (►**Fig. 2A, B**). The grayish capsule was then opened, the soft black contents were debulked with gentle suctioning, and the capsule was peeled off the cavernous dura. At the end, a gush of cerebrospinal fluid was observed after removing the capsule. The dural rent was packed with fat, covered with temporalis fascia, and reinforced with fibrin glue.

Histopathological examination revealed abundant intracytoplasmic brown and black pigments, obscuring cell morphology (►**Fig. 3A**). Mitotic activity was observed in 2/10 high-power fields with evidence of necrosis. Immunohistochemistry revealed diffuse positivity for HMB-45 and Melan A (►**Fig. 3B–D**). BRAF mutation was negative. The biopsy was reported as malignant melanoma. Positron emission tomography-CT ruled out extracranial disease. There were no skin or eye lesions. Based on these findings, the patient was diagnosed with primary central nervous system (CNS) melanoma. There was no residual tumor in the postoperative brain MRI, suggestive of radical excision (►**Fig. 2C**). The patient underwent three-dimensional conformal radiotherapy to the tumor bed, as recommended by our multidisciplinary tumor board. She had resolution of facial pain and diplopia in the immediate postoperative period. At 1-year follow-up, there was no recurrence on imaging.

Discussion

Meningiomas and schwannomas are the most common lesions found in Meckel's cave and both demonstrate enhancement on gadolinium contrast imaging. However, the mass, in this case, was T1 hyperintense, T2 hypointense, and nonenhancing with hyperdensity on the CT. A black extra-axial lesion was identified intraoperatively, which was surprising given the rarity of primary CNS melanomas, accounting for approximately 1% of all melanoma cases and 0.07% of all brain tumors.[1] According to the 2021 World Health Organization classification, primary CNS melanocytic neoplasms are classified as diffuse meningeal melanocytic neoplasms and circumscribed meningeal melanocytic neoplasms.[2] Circumscribed meningeal melanocytic neoplasms are further classified as meningeal melanocytosis and meningeal melanomatosis.[2] These tumors arise from pigmented cells called melanocytes or their precursor cells, melanoblasts, which are most numerous in the meninges

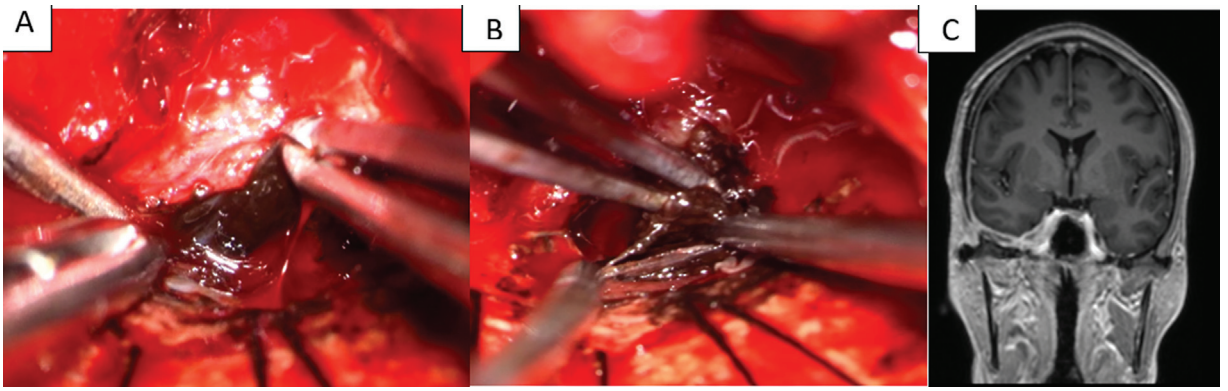

Fig. 2 Intraoperative picture showing the interdural mass with black capsule (**A**). The mass was debulked and the capsule peeled off from the surrounding dura (**B**). Postoperative T1 contrast showed no residual lesion (**C**).

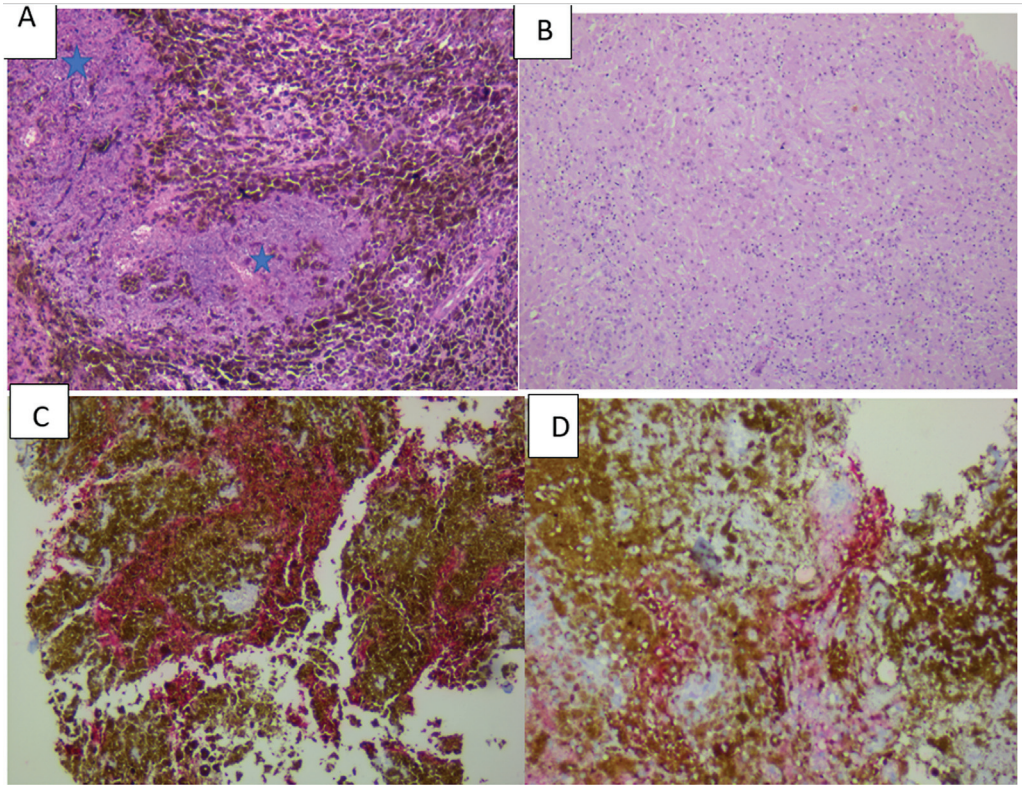

Fig. 3 (**A**) Histopathology showing sheets of tumor cells with intracytoplasmic brown-black pigment with areas of necrosis (hematoxylin and eosin [H&E] ×100). (**B**) Melanin bleach staining displaying epithelioid morphology of tumor cells after complete bleaching of melanin (magnification ×100). (**C**) HMB-45 immunostaining using red chromogen showing patchy positivity. (**D**) Melan A immunostaining using red chromogen showing patchy positivity.

investing the ventrolateral surfaces of the brain and spinal cord.[3,4] Leptomeningeal melanosis is a normal variant found in 85% of the population, but heterotrophic melanin in the dura is rare.[5] As a result, dural melanomas are rare, and melanomas of the fifth nerve are even rarer. Only two cases of primary malignant melanoma in the Meckel's cave have been reported in the literature so far.[5,6] Falavigna et al reported the case of a 55-year-old male who presented with worsening right-sided facial pain. The melanoma was radically excised and there was no recurrence at 9-month follow-up. Facial pain resolved postoperatively and no adjuvant therapy was given.[5] Haddad et al reported a neurofibromatosis type 1-associated melanoma in a 38-year-old female which was subtotally excised. The tumor recurred after 6 months and the patient succumbed to it.[6] Primary dural melanomas tend to have a less aggressive course compared with the leptomeningeal variant which has a median survival of around 1 month and an overall 2-year survival of 15%.[5] For dural melanomas, the progression-free survival ranges from 9 to 18 months.[5]

Microscopic examination of primary CNS melanomas reveals highly cellular tumors with an eosinophilic cytoplasm containing areas of necrosis, invasion, and hemorrhage. Pleomorphic cells with intracytoplasmic brown granular pigment, similar to cutaneous melanomas, are observed.[7] These tumors typically have a vasocentric arrangement of melanocytes throughout the neuroglial tissue.[8] Diffuse positivity for HMB-45, MART-1 (Melan A), S-100, and tyrosinase is typical, and melanomas do not stain for epithelial membrane antigen, which aids in differentiating them from meningiomas.[9] It is important to rule out melanin-containing primary CNS tumors such as medulloblastomas or meningiomas before labeling them as primary CNS melanomas.[9] There have been case reports of melanocytic schwannomas arising in Meckel's cave.[10] Cytogenetic abnormalities seen in cutaneous melanoma, including mutations in the BRAF, NRAS, and CDKN2A genes and abnormalities in the short arm of chromosomes 13 and 14, have also been found in primary CNS melanomas.[11]

There is little consensus on the treatment of primary CNS malignant melanoma in both adult and pediatric literature. It has been observed that patients who undergo gross total resection have better long-term survival compared with those who undergo subtotal or partial resection.[12] Furthermore, malignant melanomas are generally considered radioresistant.[12] It has been noted that a recent study indicates that the administration of adjuvant radiotherapy following tumor resection decreases the likelihood of local recurrence in comparison to surgery alone.[12]

Currently, there is no standard chemotherapy regimen advocated owing to the rarity of primary CNS melanomas. Although temozolomide has shown promise, no improvement in overall survival has been observed to date.[13] Recently, targeted therapies have gained popularity. For BRAF-mutated tumors, BRAF inhibitors such as vemurafenib and dabrafenib are recommended, while anti-PD-1-based therapy should be administered for BRAF wild tumors.[12]

Conclusion

In the case of primary malignant melanoma, it is crucial to aim for gross total resection when possible, as gross total resection has been established as the most reliable predictor of long-term survival. There is currently no widely agreed upon approach to adjuvant treatment, and new research is always emerging.

Authors' Contributions

K.R. was responsible for the conception or design of the work. C.M. and J.J. collected the data, while K.R. and G.C. performed the data analysis and interpretation. The article was drafted by C.M., J.J., and R.J., and K.R. conducted the critical revision of the article.

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Conflict of Interest

None declared.

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