

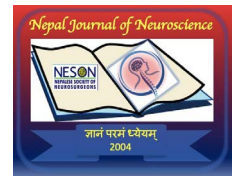
Central Nervous System Melanoma: Report of two cases

Prasanna Karki¹, Rupesh Shakya¹, Shoshan Raj Acharya², Apurva Sharma³,
Sumit Joshi¹, Prakash Paudel¹, Damber Bikram Shah¹, Gopal Raman Sharma¹

¹Department of Neurosciences, Nepal Medici Hospital, Bhaisepati, Lalitpur, Nepal

²Department of Pathology, Medici Hospital, Bhaisepati, Lalitpur, Nepal

³ St. John's College, Annapolis, Maryland, USA



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Abstract

Primary brain melanomas are exceedingly rare, and metastasis outside of the central nervous system is an uncommon occurrence. The patients initially presented with an intraparenchymal hematoma with associated symptoms. Extensive diagnostic tests did not reveal any tumor-related or vascular patterns contributing to these bleedings. A comprehensive surgical resection was conducted, and the diagnosis of Central Nervous System (CNS) melanoma was confirmed through histological examination. Despite the generally poor prognosis associated with malignant melanomas, the combination of complete surgical resection and emerging therapies is extending overall survival and enhancing the quality of life. In cases where primary brain melanoma is suspected, even in the presence of extracerebral metastasis, aggressive treatment may be a viable consideration.

Keywords: Primary Melanoma, Metastatic Melanoma, Neurosurgery.

Introduction

Melanoma is a tumor that develops when melanocytes undergo malignant transformation. Despite the fact that they typically occur on the skin as melanocytes are produced from the neural crest, melanomas can develop in any other organs where neural crest cells migrate, including brain.¹ Malignant melanomas could originate from melanocytes, most of which are of cutaneous origins. Primary cerebral melanomas, derived from the melanocytic element normally present in the leptomeninges, are rare and occur in around 1% of all melanoma cases.² Approximately 1% of all melanoma cases and 0.07% of all brain tumors are primary intracranial melanomas, which are rare. These initial melanomas are highly aggressive in nature and have the potential to spread to other organs.³ Primary

cutaneous head and neck melanomas (HNM) are reported to be associated with a higher incidence of brain metastasis than trunk and limb melanomas (TLM).⁴ We herein report two cases of Melanoma, first case being primary melanoma of right temporal lobe and a second case of the secondary cerebral melanoma in the left frontal lobe, which was confirmed by histopathological examination of the excised mass. Also, related literatures were reviewed.

Case 1

A 43 year old man presented with the complaint of occipital headache, vomiting for 8 days and blurring of vision for 4 days with weakness of left upper and lower limbs. His neurological examination was normal. His previous medical history and family history were insignificant. The CT scan of head showed non-enhancing well-defined lobulated heterogeneous density mass with large calcified and cystic component encasing the branches of right middle cerebral artery with mild surrounding edema in right temporal lobe (Figure 1A). The contrast CT head showed well enhancing lesion on right temporal lobe encasing right MCA and its branches along with cystic component (Figure 1B). Pre-operative MRI brain images. (Figure 1C) T1 pre-contrast shows a large lobular tumour with intrinsic high T1 signal and internal heterogeneity. (Figure 1D) Approximately 5.5 x 3.9 x 3.8 cm size lobulated outline heterogeneous T2 mass is noted in right frontal lobe anterior inferior aspect extending to right Temporal lobe and right basal ganglia. (Figure 1E) T1 post-contrast highlights an enhancing dural-based, extra-axial lesion against the greater wing of sphenoid bone. The lesion compresses the prechiasmatic right intracranial optic nerve,

basi-frontal and temporal pole and was suspected to be a sphenoid wing meningioma. MRI, magnetic resonance imaging.

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Address for correspondence:

Dr. Prasanna Karki
Department of Neurosciences, Neurosurgery Division,
Nepal Medici, Sainbu, Bhaisepathi, Lalitpur, Nepal
E-mail: prasannakarki7@gmail.com

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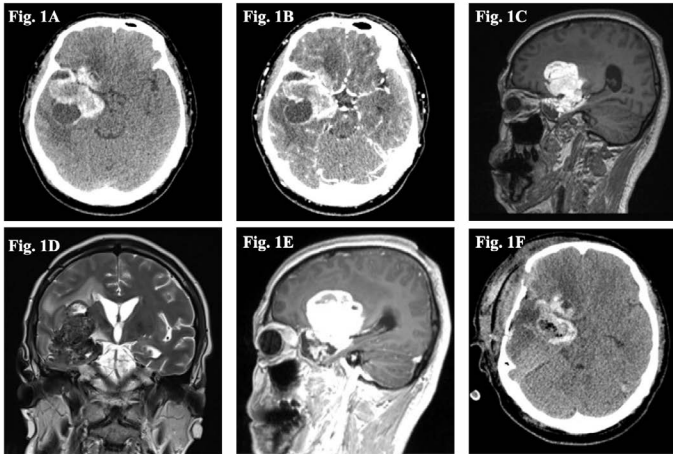


Figure 1: A: CT head plain showing right temporal lobe heterogeneous mass encasing right middle cerebral artery and its branches. B: CT head post contrast showing enhancing right temporal mass with cystic hypodense area. C: MRI T1 weighted sagittal images showing hyperintense right temporal mass. D: MRI T2 weighted coronal image showing hypointense right temporal mass. E: MRI post Gadolinium sagittal view showing heterogeneous enhancing right temporal mass. F: Post operative CT head plain showing small residual tumor on right temporal region with perilesional edema.

The differential diagnosis made after the analyzing MRI images were: DNET, Diffuse glioneuronal tumor with oligodendroglial features and nuclear clusters, Oligodendroglioma.

A craniotomy and excision of mass (near total) was performed and around 4x5cm intra-axial greenish black in color, soft to firm in consistency arising from right temporal lobe compressing right lateral ventricle suggestive of melanoma was observed. The patient underwent the right pterional approach and partial excision of the lesion was achieved as it was highly vascular. A biopsy specimen was sent to the laboratory. Post operative CT head showed subtotal removal of the lesion (Figure 1F).

Histopathological examination showed hypercellular sheets (Figure 2) and nest of pleomorphic round to epithelioid cells exhibiting indistinct cell membrane, vesicular to coarse chromatin with prominent nucleoli and abundant intracytoplasmic melanin pigment noted infiltrating into the glial tissue with areas of necrosis (Figure 2B). The cytology of smear showed abundant extracellular melanin pigment deposits and sheets of pleomorphic round to epithelioid cells with abundant intracytoplasmic melanin pigment (Figure 2C-D). These findings were suggestive of Primary cerebral melanoma. The patient was discharged 13 days postoperatively without any

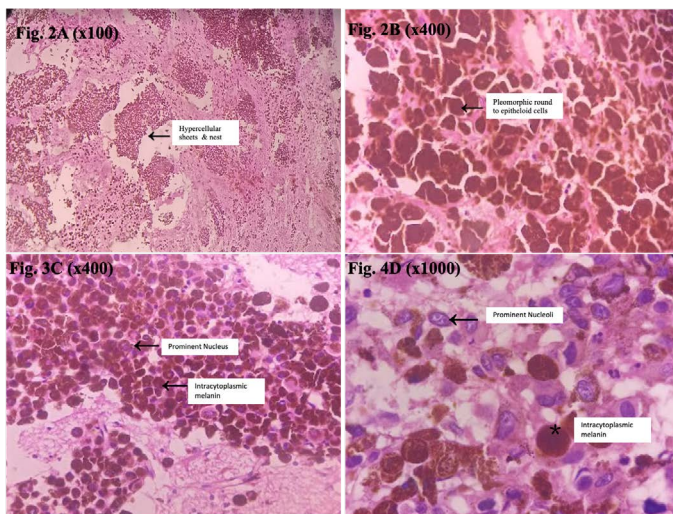


Figure 2: A: Hematoxylin and eosin (H&E) stain showing Hypercellular sheets and nest X100. B: Pleomorphic round to epithelioid cells X400. C: Prominent nucleus and abundant intracytoplasmic melanin x 400 and D: Prominent nucleoli and abundant intracytoplasmic melanin x 1000

Case 2

A 74-year-old woman presented with the complaint of headache after waking up from sleep at night. In the morning she developed facial drooping along with slurring of speech. She is a known case of Hypertension under medication and osteoporosis. She underwent surgery in 2016 for a scalp melanoma. CT scan of head showed heterogeneously enhancing lesion in left frontal lobe with areas of necrosis and hemorrhage with adjacent vasogenic edema (Figure 3A). T1 weighted MRI showed heterogeneous mass with hematoma in left frontal lobe (Figure 3B). T2 MRI showed white matter hyperintensity around the lesion suggestive of perilesional edema (Figure 3C). Variable thickness and irregular mild to moderate rim enhancement is noted in post contrast T1 MRI (Figure 3 D-E).

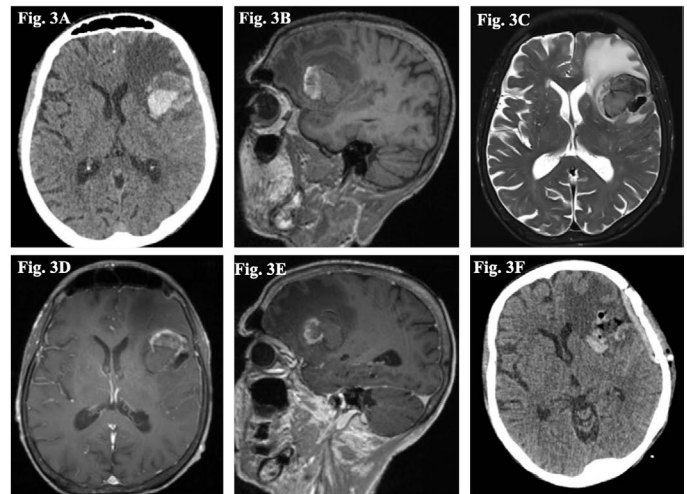


Figure 3: A: CT head plain showing left frontal lobe heterogeneous mass with necrosis and hemorrhage and adjacent edema. B: MRI T1 weighted sagittal images showing iso to hyperintense left frontal mass with hematoma. C: MRI T2 weighted axial image showing hypo to isointense left frontal mass. D: MRI post gadolinium axial image showing heterogeneous cystic mass. E: MRI post Gadolinium sagittal view showing heterogeneous enhancing left frontal mass with vasogenic edema. F: Post operative CT head plain showing complete excision of mass in left frontal region with perilesional edema.

The differential diagnosis made after the analyzing MRI images were: metastasis or tumor bleed. The patient underwent the right pterional approach and complete excision of the lesion was achieved as it was highly vascular. A biopsy specimen was sent to the laboratory. Post operative CT head showed complete removal of the lesion (Figure 3F).

Histopathological examination showed Hypercellular sheets (Figure 4A-B) and nest of pleomorphic round to epithelioid cells exhibit indistinct cell membrane (Figure 4C) with areas of necrosis, hemorrhages and mitosis at places, vesicular to coarse chromatin with intracytoplasmic melanin pigment (Figure 4C) and prominent nucleoli (Figure 4D) noted. These findings were suggestive of melanoma.

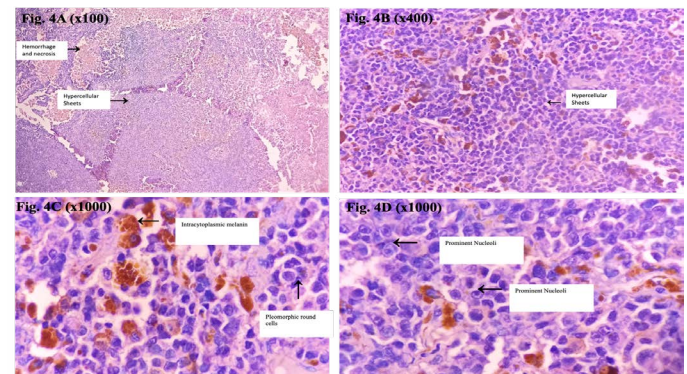


Figure 4: A: Hematoxylin and eosin (H&E) stain showing Hypercellular sheets and nest X100. B: Hypercellular sheets and nest X400. C: pleomorphic round to epithelioid cells X1000. D: prominent nucleoli X1000.

Discussion

The condition known as primary cerebral melanoma is rare. Intracranial melanomas can be divided into metastatic type or primary type, and primary cerebral melanoma accounts for 1% of all melanomas and 0.07% of all brain tumors are CNS melanoma.⁵ Leptomeningeal cells, glial cells, adrenal medulla cells, and melanocytes are all derived from the neural crest, a collection of multipotent cells, on day 22 of development. The pia matter surrounding the inferior surface of the cerebellum, the spinal medulla, and the upper cervical medulla are where melanocytes are primarily found.⁶ The predominant sites for primary brain melanoma typically include the cerebral lobe (accounting for 53.1%), the posterior fossa (constituting 17.3%), and the pineal region (making up 13.6%).⁶ In our patient (Case-1), clinical examinations did not reveal any systemic melanomas; instead, a single isolated mass was identified with histological confirmations of melanoma. Concerning primary cerebral melanomas, the origins of melanin cells remain incompletely understood.

In CT scans, primary solitary cerebral melanomas often present as a hyperdense mass situated close to the brain's surface, and this hyperdensity significantly intensifies following the administration of contrast material. This heightened attenuation is thought to be a result of intratumoral bleeding and/or the presence of melanin before the contrast CT image. These features commonly resemble those of meningiomas, though they can also suggest a diagnosis of melanoma rather than glioma.⁷ Our patient's condition appeared on CT as a predominantly hyperdense region along with iso to hypodense areas, indicative of older, partially clotted blood.

Typical radiological features of cerebral melanomas, whether primary or metastatic, observed in MRI scans, include a hyperintense signal in T1 and a hypointense signal in T2, mainly due to the paramagnetic properties of melanin. Additionally, they tend to display uniform enhancement in post-contrast images. The MRI appearance can vary significantly, contingent upon the melanoma subtype and whether intratumoral hemorrhages are present or not.⁸ Both of our cases had intertumoral hemorrhage evident in imaging. Shinomiya et al. explained the reason for these hemorrhages: intracranial melanomas have fenestrated endothelial cells promoting intralesional bleedings.⁹ There are no globally recognized treatment guidelines tailored specifically for Primary cranial melanoma, and its infrequency makes it challenging to study distinct treatment approaches in a prospective manner. Given melanomas typical resistance to treatment, surgical intervention should be the primary approach. Subsequently, adjuvant radiotherapy although these tumors are considered radio-resistant and/or chemotherapy may be considered. While the prognosis is generally grim, it tends to be more favorable than that of patients with metastatic melanoma. Median survival reports fall within the range of 11 to 31 months.¹⁰

Melanoma is one of the primary causes of malignant metastases to the central nervous system (CNS), accounting for 6–12% of all metastatic brain tumors.¹¹ The incidence of brain metastasis is highest in the subset of patient with scalp melanomas i.e.: 12.7% after 5 years.¹² As the metastatic CNS melanoma has median survival of 8.9 months, it is considered to have worse prognosis than primary CNS melanoma.

Standard treatments for melanoma with CNS metastasis include whole-brain radiation therapy (WBRT) and stereotactic radiosurgery (SRS), alone or in combination, and cytotoxic chemotherapy.¹³ With the use of targeted immunotherapy, surgery and stereotactic Radiosurgery, the prognosis has slightly improved when compared to historical cohorts.¹¹ New treatments approved from 2011 to 2015, including BRAF inhibitors (BRAFi)¹⁴ and MEK inhibitors (MEKi)¹⁵ as Approximately 45 % of melanomas have BRAF mutation.

Distinguishing between primary melanoma and melanoma brain metastasis remains a contentious issue, primarily due to the overlap in radiological and histological characteristics, making an accurate diagnosis particularly challenging.¹⁶ Clinically, they often exhibit similar presentations. One differentiating factor, as highlighted by Terao and colleagues, is the age of onset. Primary CNS melanoma tends to manifest in relatively younger patients, typically under the age of 50¹⁷, as was the case with our patient.

Conclusion

Despite the generally grim outlook associated with malignant melanomas, the combination of complete surgical resection and novel therapeutic approaches is enhancing both overall survival and the quality of life. Our case study and the review of existing literature suggest that for a patient with suspected primary brain melanoma, even in the presence of extracerebral metastases, aggressive treatment should be contemplated.

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