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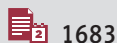
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Primary Brain Melanoma in a Pediatric Patient: A Case Report

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Puerto Rico**Corresponding Author:** Gretchen A. Otero-Soto, e-mail: gretchen.otero@upr.edu**Conflict of interest:** None declared**Patient:** Male, 17-year-old
Final Diagnosis: Primary malignant melanoma of brain
Symptoms: Tonic-clonic seizure
Medication: —
Clinical Procedure: Resection of brain tumor
Specialty: Neurosurgery • Pediatrics and Neonatology • Radiology**Objective:** Rare disease**Background:** Primary malignant melanoma of the brain is a challenging radiological diagnosis and a high index of suspicion is required about patients with the condition. In the pediatric population, only a few cases have been reported in the literature. The purpose of this report was to describe the expected imaging characteristics and the importance of a multidisciplinary approach in the diagnosis of this rare entity.**Case Report:** A 17-year-old Hispanic male who presented with new-onset tonic-clonic seizures had no focal neurologic deficits on physical examination. An initial computed tomography scan showed a hyperdense, right frontal, parafalcine mass. Brain magnetic resonance imaging was performed and revealed a T1 hyperintense and T2 hypointense, right-frontal-lobe, extra-axial mass with foci of susceptibility. Resection of the mass revealed a lesion that had a dark, pigmented macroscopic appearance. Histopathologic analysis confirmed that it was a primary intracranial malignant melanoma after no primary site was identified on dermatologic and ophthalmologic evaluations.**Conclusions:** Diagnosing a primary intracranial melanoma with imaging alone is virtually impossible if clinical data and findings from a thorough physical examination are unavailable. Intracranial primary malignant melanoma remains a complex radiological diagnosis that relies on the exclusion of other potentially more common entities and an optimal multidisciplinary approach.**Keywords:** Adolescent • Brain • Melanoma**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/926749>

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Background

The incidence of melanoma in the pediatric population has steadily decreased, although it remains the second most common cancer in adolescents. The majority of diagnoses are in non-Hispanic Whites [1] and the prevalence is higher in female patients than in male patients. Risk factors are similar to those in the adult population and include fair skin, family history of melanoma, and cumulative exposure to ultraviolet light [1]. Furthermore, primary brain melanoma in the pediatric population is uncommon and only a few cases have been reported in the literature.

Melanocytes are naturally found in the leptomeninges, and thus, melanoma would be expected to occur in any tissue within the central nervous system (CNS) where leptomeningeal tissue is present [2]. Nevertheless, this is not the case and primary melanomas continue to be rare. Although some imaging findings are suggestive of the diagnosis of malignant melanoma, their features tend to overlap with those of more commonly encountered diagnoses, specifically meningiomas (melanocytic or hemorrhagic) and hemorrhagic primary brain tumors, such as gliomas. Specific magnetic resonance imaging (MRI) characteristics found in these lesions may be due to the presence of melanin and blood products within the tumor related to their paramagnetic properties, making the distinction difficult. It is important to note that melanocytic tumors also have a propensity to bleed, and often, the features of melanin and hemosiderin can be found in the same tumor. Despite their peculiar imaging characteristics and specific immunological features, primary brain melanomas are indistinguishable from melanotic metastasis to the brain from an extra-CNS primary tumor; therefore, a thorough clinical analysis must be done [3]. Often, this is a diagnosis of exclusion and is made when skin or uveal melanocytic lesions are not found to account for a primary malignancy.

Radiologists have a critical role in diagnosing primary brain melanoma. Although the condition is rare, especially in pediatric patients, identifying it in timely fashion is critical to ensure appropriate management and proper selection of therapy, and to assess prognosis.

In this report, we present a rare case of primary intracranial brain melanoma in a young patient who presented with new-onset seizures.

Case Report

We report the case of a 17-year-old male with a medical history of hypotonia, unspecified metabolic disorder, and bronchial asthma who presented to our institution with tonic-clonic

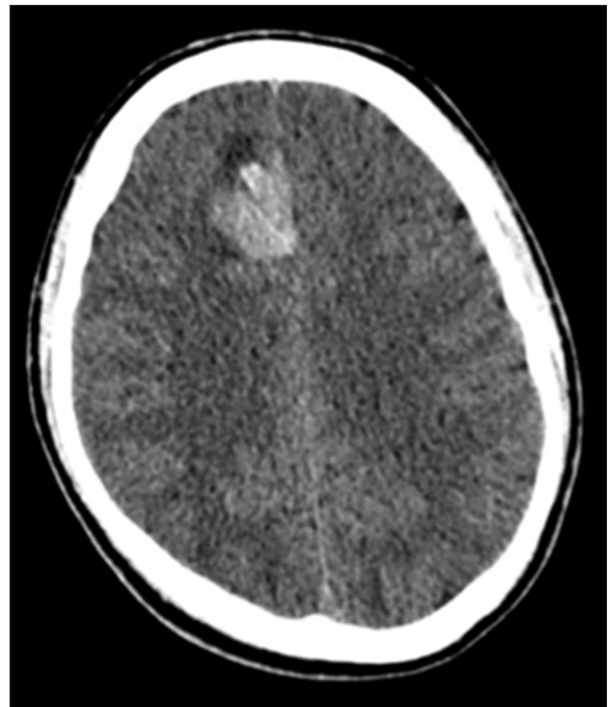


Figure 1. An axial computed tomography scan of the head without intravenous contrast shows a hyperdense right frontal parafalcine lesion with decreased attenuation in the periphery, suggestive of edema.

seizures without focal neurologic deficits [4]. Results of initial laboratory tests were within normal limits for the patient's age.

On admission, an initial non-contrast computed tomography (CT) scan of the head (**Figure 1**) revealed a hyperdense right frontal superior parafalcine lesion with associated peripheral edema. Subsequent pre-contrast brain MRI further characterized a lobulated extra-axial parafalcine lesion, which was in very close apposition to the dura. This mass had intrinsic T1 hyperintensity (**Figures 2A, 2B, 3A**), few punctate foci of susceptibility artifact within the lesion on gradient recalled echo (GRE) sequences (**Figure 3C**), and mild adjacent vasogenic edema (**Figure 2C**). After administration of intravenous gadolinium, the lesion displayed increased T1 signal intensity (**Figure 3B**) and a combination of contrast enhancement and inherent T1 shortening. Moreover, a whole-spine contrast-enhanced MRI showed no metastasis to the spine. Further evaluation included a lumbar puncture, which showed no evidence of malignant cells.

The differential diagnosis, based mainly on imaging findings, included parafalcine meningioma, specifically with hemorrhagic products, in view of the high T1 signal and susceptibility artifact, as well as high-grade hemorrhagic glioma. Neurosurgical management included gross mass resection, which was achieved with a right frontal craniotomy approach.

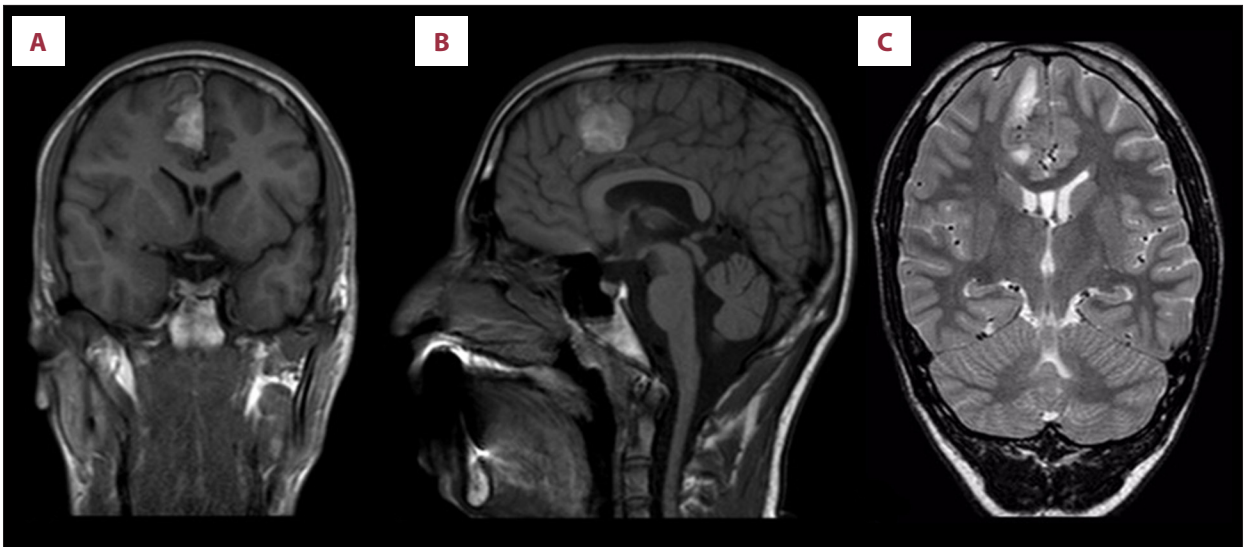


Figure 2. (A) Coronal and (B) sagittal non-contrast T1-weighted sequences show a right parafalcine T1 hyperintense lesion. (C) A coronal T2-weighted sequence shows a lesion that is isointense to gray matter with mild adjacent vasogenic edema.

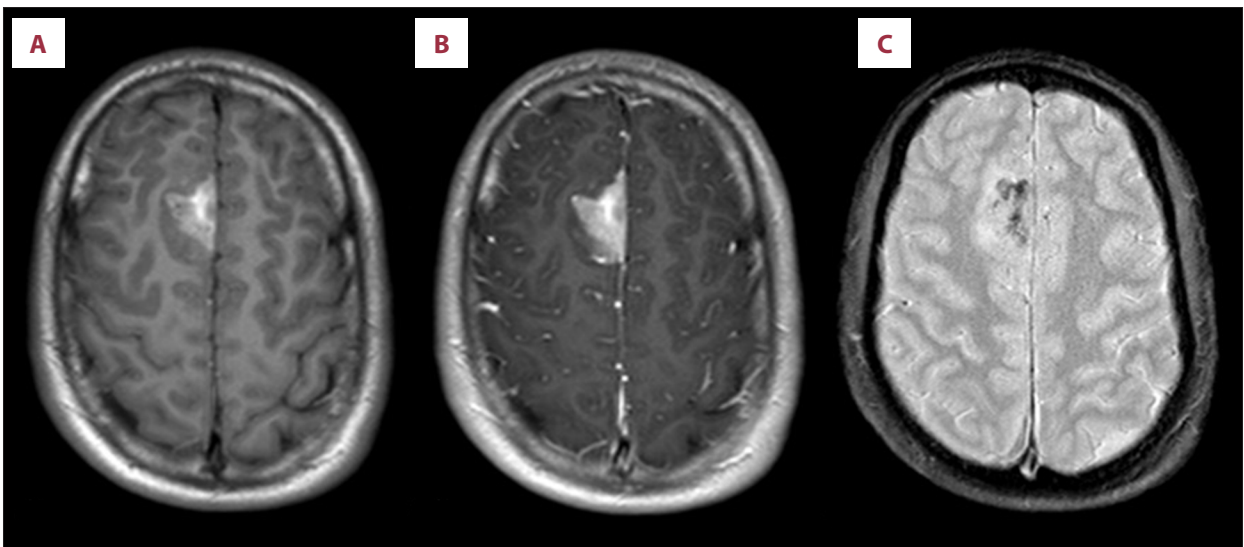


Figure 3. (A) An axial pre-contrast T1-weighted sequence shows a right frontal, extra-axial, intrinsically T1-hyperintense lesion. (B) A post-contrast T1-weighted sequence shows a combination of intrinsic T1 hyperintensity and contrast enhancement. (C) An axial gradient recalled echo susceptibility-weighted sequence shows foci of susceptibility along the anteromedial portions of the lesion, which correlates with blood products. Note that areas of susceptibility do not correlate with areas of intrinsic T1 hyperintensity, indicating that the mass contains both melanocytic components and blood products.

On intraoperative examination and resection, the mass was located in the right frontal lobe and was firm and dark brown, with blood clots (**Figure 4**).

Histopathologic analysis on hematoxylin & eosin staining showed nests of melanocytes next to normal brain tissue (**Figure 5A**). On magnification (40×), the sheets of malignant melanocytes with prominent eosinophilic nucleoli and dense pigment were readily visible (**Figure 5B**). A positive immunoreaction was elicited after staining strongly with HMB45 (red

chromophore), confirming that the lesion was a malignant melanoma (**Figure 5C**). It also demonstrated strong, diffuse staining with Melan A and up to 10% of the neoplastic cells were Ki67-positive. No BRAF V600E mutation was present. A follow-up postoperative brain MRI showed nothing that suggested the presence of residual tumor.

The patient had an approximately 1-cm plaque with regular pigmentation on his lower back that was negative for malignant cells (final pathologic diagnosis unavailable because testing

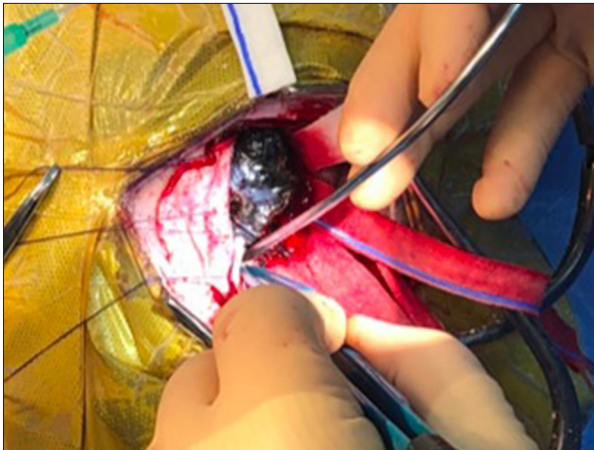


Figure 4. An intraoperative photograph taken during excision of the mass by a neurosurgeon shows a dark, firm, pigmented mass with a dural attachment, which was resected.

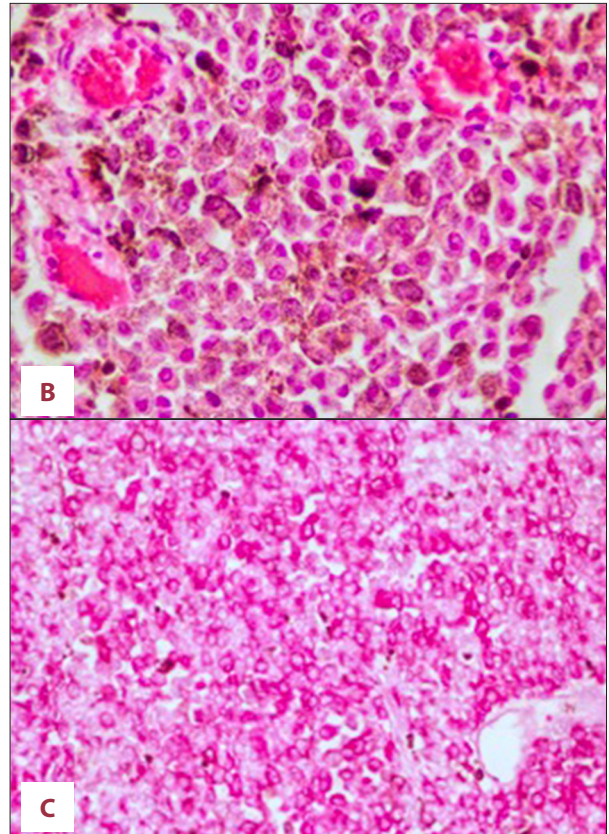
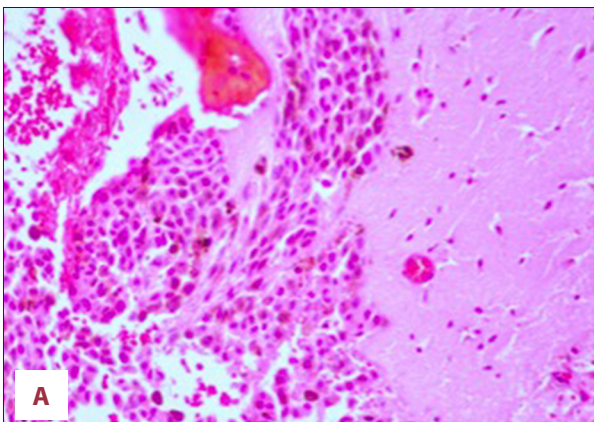


Figure 5. (A) Hematoxylin & eosin (H&E) staining (magnification 20×) shows nests of melanoma cells (left) next to normal brain tissue (right). (B) H&E staining (magnification 40×) shows sheets of malignant melanocytes with prominent eosinophilic nucleoli and dense melanin pigmentation. (C) Magnification (magnification 20×) shows a positive cytoplasmic immunoreaction to HMB45 (red chromophore).

was performed at a community laboratory) and no evidence of retinal lesions was found on ophthalmologic evaluation. Both whole-body bone scintigraphy and positron emission tomography-CT were negative. The patient was diagnosed with primary brain melanoma based on histopathologic analysis and after exclusion of an alternate site of the primary tumor. He received 5 radiosurgery treatments and was started on pembrolizumab, which was later changed to nivolumab and ipilimumab after positive malignant cells were found in his cerebrospinal fluid. Thirteen months after diagnosis, he returned to the Emergency Department complaining of increased abdominal girth and constipation. A CT scan of his abdomen and pelvis was remarkable for extensive metastasis to the omentum. Palliative care was provided and he died soon thereafter of disease progression.

Discussion

Primary brain melanoma is a rare diagnosis with a small number of reports in the literature; it accounts for .005 cases per

100,000 patients and approximately 0.1% of all brain tumors [5]. Moreover, as previously stated, the incidence of melanoma in the pediatric population is even lower. CT findings can be indeterminate and inconclusive if there is no clear history of melanosis, neurocutaneous disorder, or primary cutaneous melanoma. In the pediatric population, most cases are associated with cutaneous melanosis and giant congenital nevus [3].

Melanin in the brain, as in the rest of the body, results in T1 and T2 shortening, which translate as hyperintensity and hypointensity, respectively [6]. The presence of hemorrhage within the lesion may contribute to the high signal on T1, which can be distinguished by using susceptibility-weighted sequences that would reflect the presence of hemosiderin in the mass. Typical features on MRI and CT, both of which are part of the full imaging work-up for patients with suspected brain melanoma, are heterogeneity and avid contrast enhancement. Although the MRI characteristics may overlap with those of hemorrhagic

meningioma, the areas of intrinsic T1 hyperintensity in melanoma do not always correlate with corresponding susceptibility artifact on GRE sequences. Moreover, these two entities may be completely indistinguishable based on their imaging appearance; therefore, a multidisciplinary approach is essential. On gross pathology, melanomas are firm and darkly pigmented, dural-based masses, while hemorrhagic tumors tend to have a beefy red appearance, owing to coagulated blood products. Ultimately, immunohistochemistry provides the final diagnosis, with specific neural markers including MelanA, S100, and HMB45. Notably, presence of Ki67 in about 8% of cells is specific for melanoma. Because primary brain melanoma is so rare, the diagnosis can be made after dermatologic and ophthalmologic evaluations have been performed and a melanoma in the skin or eye globes has been confidently excluded.

When a lesion that exhibits the previously described imaging characteristics is encountered, the possibility of a metastatic lesion from an occult melanoma in another part of the body should be entertained and excluded. Metastatic melanocytic lesions of the CNS are by far the most common source of a pigmented lesion found in the brain and management and prognosis in these cases varies significantly from that for a primary melanin-containing lesion [7]. The primary treatment for local intraparenchymal melanoma is complete resection with or without radiotherapy, often with good survival [8]. As mentioned earlier, melanocytes are normally found in the leptomeninges, especially in the ventral aspect of the medulla oblongata and the base of the brain. Therefore, the presence of a melanoma at these sites is the most frequent presentation of this entity and likely arises from abnormal leptomeningeal melanocytes. Another important consideration is the possibility of lesions that may undergo melanization, such as schwannomas, gliomas [7], and melanocytic meningiomas, as well as meningeal melanocytosis, which is benign. Of the few reported cases of primary brain melanoma in the literature, the vast majority have been in adults.

The prognosis also varies and there have been mixed outcomes reported in the literature as well as use of different treatment regimens. The mainstays of treatment for intraparenchymal melanotic tumors are complete resection and postoperative chemoradiotherapy, which result in a survival of up to 17 years in adults [2]. In contrast, the prognosis is poor in pediatric patients, with a median survival of 8 months after presentation [8]. The importance of recognizing this entity as

part of our diagnostic repertoire is that the outcome also varies when compared to metastatic melanoma, which carries a survival rate of 5 to 6 months [2].

While some patients with primary brain melanoma have satisfactory responses to therapy, most develop recurrence or metastatic disease, as was the case in the present report. Our patient went on to develop tumor recurrence and extensive intra-abdominal metastatic disease despite surgical and medical treatment.

Conclusions

As previously stated, diagnosing a primary intracranial melanoma with imaging alone is virtually impossible if clinical data and findings from a thorough physical examination are not available. Nonetheless, the gross macroscopic appearance may help both the neurosurgeon and the pathologist to narrow a preliminary diagnosis. The present case demonstrates the diagnostic conundrum of this entity in the setting of a pediatric patient and it is so rare that other, more common diagnoses are ranked higher in the differential to account for the imaging findings. Only after in-depth collaboration between the radiologists, dermatologists, ophthalmologists, pathologists, and neurosurgeons can the diagnosis be made and an adequate treatment plan offered to the patient. Intracranial primary malignant melanoma remains a complex radiological diagnosis that relies on the exclusion of other potential, more common entities and an optimal multidisciplinary approach. Familiarization with the clinical presentation and imaging manifestations of this rare entity is key for any radiologist interpreting neuroimaging cases.

Acknowledgments

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Conflicts of Interest

None.

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