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CASE REPORT Open Access

Primary intracranial malignant melanoma in an adolescent female: a case report

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Abstract

Background Primary central nervous system melanoma is an extremely rare entity and even rarer in children and adolescents as compared to adults. It is often difficult to consider a diagnosis of intracranial melanoma pre-operatively without any clinical evidence of neurocutaneous melanosis.

Case presentation Herein, a case of primary melanoma of the brain is reported in a 17-year-old female who presented with headache, vomiting, and focal neurological deficit in the form of left-sided facial palsy and limb weakness. A contrast-enhanced computed tomography of head was performed which revealed a heterogeneously hyperattenuating mass lesion at left gangliocapsular region showing peripheral enhancement with internal non-enhancing cystic component. The patient underwent left frontotemporal craniotomy. The diagnosis was made on histopathological examination, which showed an invasive tumor comprising of epithelioid to spindled cells arranged in sheets, nests, and singly scattered. The special stains and immunohistochemical markers proved very helpful in establishing the diagnosis.

Conclusions The case highlights the uncommon occurrence of primary intracranial melanoma in the pediatric age group, the perplexing histological features, and the rapid and fatal course.

Keywords Case report, Melanoma, Primary intracranial melanoma, Pediatric

Background

Malignant melanoma arises from the specialized pigmented cells called melanocytes, which are derived from the neural crest, and have aggressive behavior. They arise most often in the skin. However, they can occur at any sites, including the uvea, mucosal surface, leptomeninges and visceral organs [1]. Primary intracranial melanoma, though uncommon, are reported chiefly in the adult population and have a predilection toward the cerebral lobes, posterior fossa and pineal region [2]. In children, it is even more rarer and observed in association with congenital melanocytic nevi or neurocutaneous melanosis [3]. Herein, we describe a case of primary intracranial malignant melanoma (PIMM) in a young adolescent female with no known extracranial primary tumor.

Case presentation

A 17-year-old female patient presented to the outpatient department with headache and vomiting for three months associated with acute onset left-sided facial palsy. The patient had no visual complaints, seizures or loss of consciousness. There was no significant past medical or family history. On examination, her vitals were stable. Neurological examination showed normal flexor plantar reflex of both limbs and a Glasgow coma scale of 15/15. Complete blood count was within normal limits. Patient

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underwent a contrast-enhanced computed tomography of brain (shown in Fig. 1a) which showed a large lobulated solid-cystic heterogeneously hyperattenuating mass lesion at the left gangliocapsular region. The post-contrast scan (shown in Fig. 1b) showed moderate enhancement of the solid component of the tumor with mild peripheral wall enhancement. MRI was performed for further characterization. The axial T2 (shown in Fig. 1c) and T1 (shown in Fig. 1d) images demonstrate the solid-cystic nature of the lesion, the cystic component showing hypointense signal on T2 and hyperintense signal on T1 with fluid–fluid level (white arrows). The solid component of the lesion shows heterogeneous signal on both T2 and T1 images. The susceptibility-weighted image showed extensive blooming and does not restrict on the diffusion image. Considering the hypointense

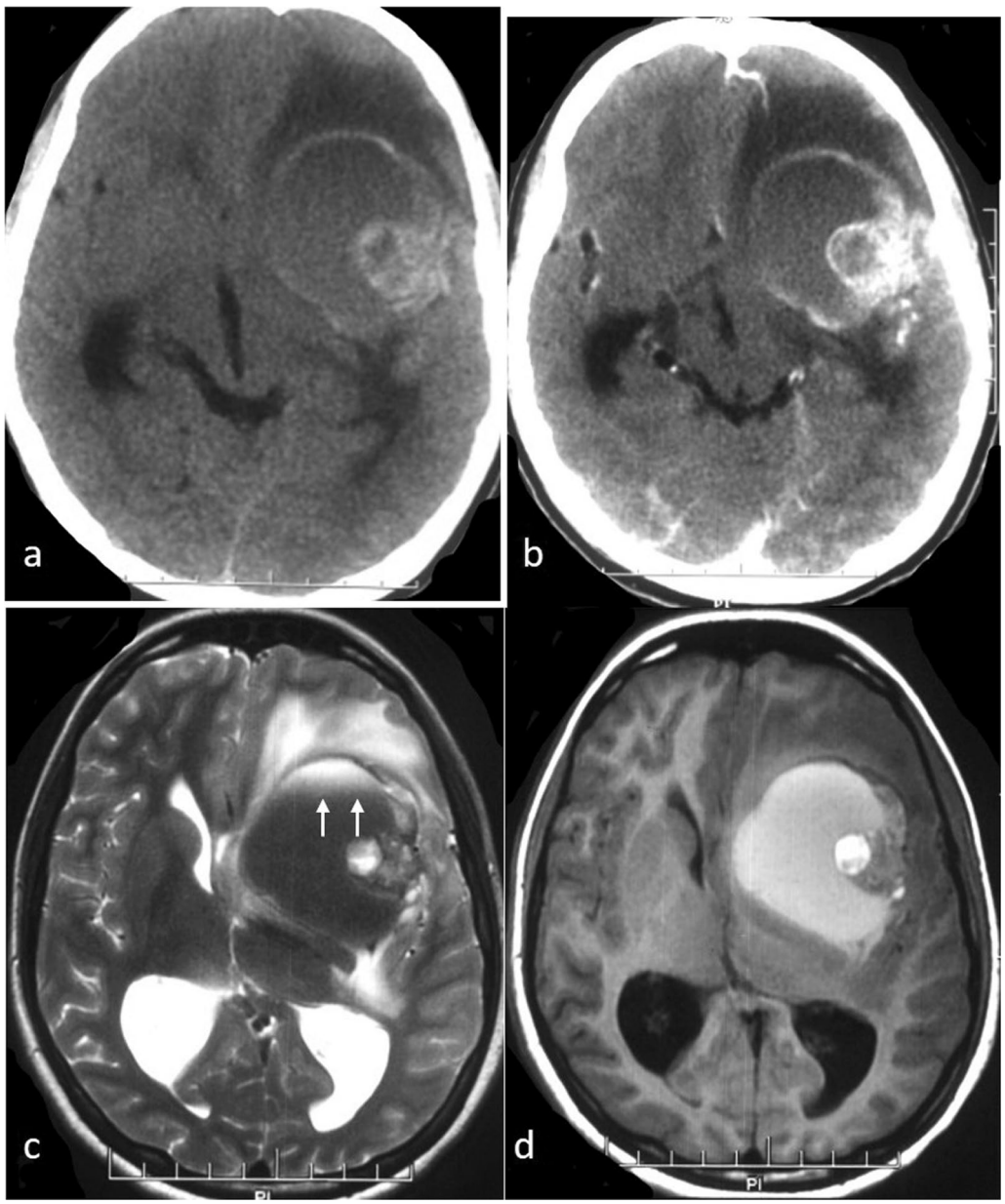

Fig. 1 The axial plain (**a**) and contrast CT head (**b**) reveals heterogeneous hyperattenuating mass at left gangliocapsular region with moderate perilesional edema and showed moderate post-contrast enhancement with internal non-enhancing cystic component. The axial T2 (**c**) and T1 (**d**) images demonstrate the solid-cystic nature of the lesion, the cystic component showing hypointense signal on T2 and hyperintense signal on T1 with fluid–fluid level (white arrows). The solid component of the lesion shows heterogeneous signal on both T2 and T1 images

signal on T2 and a hyperintense signal on T1 images, a possibility of left basal ganglia diffuse glioma with internal hemorrhage or primary cerebral melanoma was considered. The patient underwent left frontotemporal craniotomy. Intraoperatively, a soft, highly vascular, blackish and intra-axial lesion in the left gangliocapsular region was identified. The lesion was excised and sent for histopathology.

Gross examination showed multiple hemorrhagic to gray white soft tissue pieces. Microscopic examination showed brain parenchyma with an invasive tumor comprising of epithelioid to spindled cells arranged in sheets, nests, and singly scattered. The tumor cells showed moderate nuclear pleomorphism and had eccentric to central nuclei, coarse chromatin, prominent nucleoli and moderate amount of well-defined eosinophilic granular cytoplasm. Few intranuclear inclusions were also noted. Several of these cells contained intracytoplasmic pigment, which was coarse black granules and obscuring the nuclear details, as well. Frequent mitotic activity was seen. Several multinucleated bizarre cells were seen along with areas of necrosis and hemorrhage. Many hemosiderophages were also noted (shown in Fig. 2a–d). A differential diagnosis of metastatic epithelial malignancy, germ cell tumor, hematological malignancies and melanoma was considered based on morphological findings. Thereafter, a panel of immunohistochemical markers comprising CK, CD45, synaptophysin, SALL4, human melanoma black-45 (HMB-45) antibody and SRY-related HMG-box 10 (SOX10) were applied (shown in Fig. 3a, b). Tumor cells showed strong expression of HMB-45 and SOX10, while they were negative for CK, CD45, synaptophysin and SALL4. The possibility of meningioma was not considered as the lesion was intra-axial, and no dural attachment was noted. The possibility of glioma was ruled out based on morphological features and the absence of fibrillary background.

A final diagnosis of malignant melanoma was considered. A detailed examination to look for foci of a melanocytic lesion at any extracranial site was done. On dermatological examination, a few small-sized nevi ranging in size from 0.2 to 0.5 cm with regular borders were noted on the face and neck with an occasional nevus in the axillary region. These lesions were present clinically for several years and did not show any increase in size or any change in shape. Ultrasonography of abdomen and neck revealed no evidence of melanoma. Hence, a diagnosis of primary intracranial melanoma was rendered,

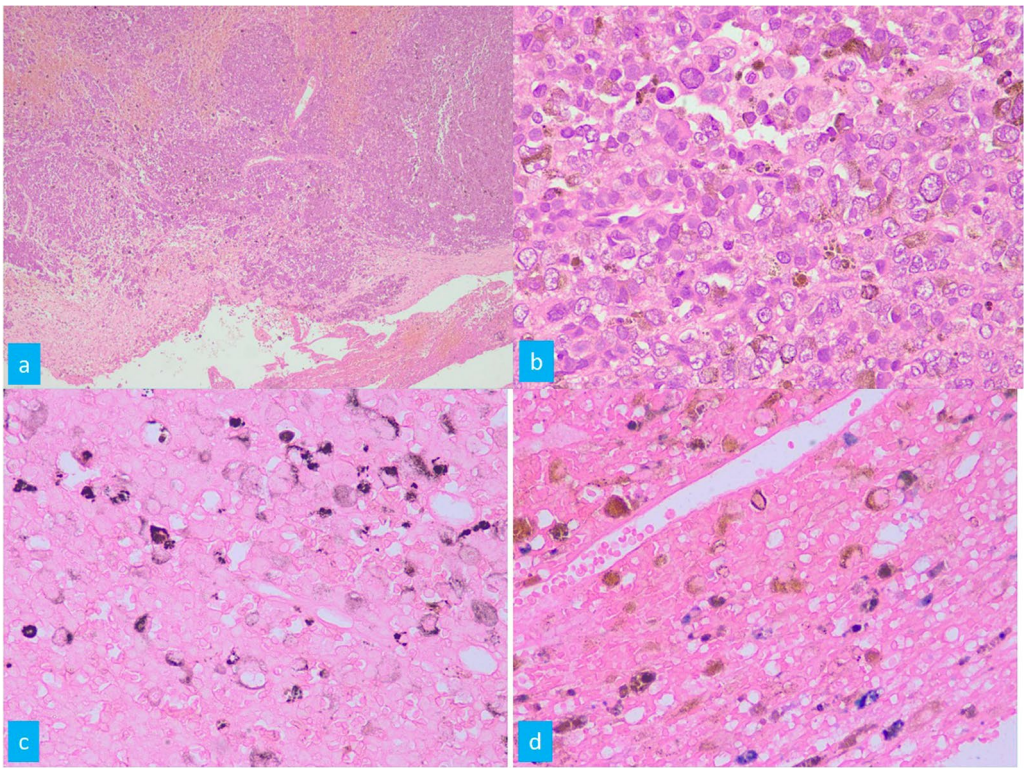

Fig. 2 **a** Histopathological examination shows a melanocytic tumor arranged in dyscohesive solid sheets and infiltrating into the glial tissue. **b** The tumor cells are large polygonal cells with powdery chromatin, prominent nucleoli and moderate amount of cytoplasm, which often contain pigment. **c** Schmorl's stain highlights the intracytoplasmic melanin pigment. **d** Perls stain shows scattered hemosiderin laden cells

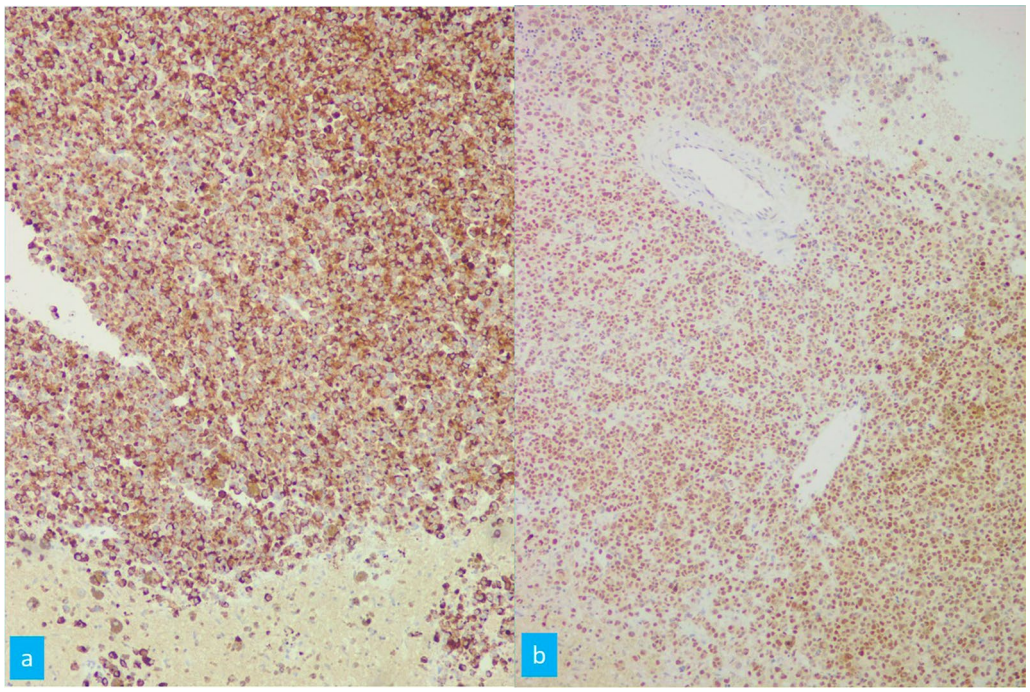

Fig. 3 The tumor cells show strong cytoplasmic expression of HMB-45 (**a**) and strong nuclear expression of SOX10 (**b**)

and the patient was referred to the oncology department for adjuvant treatment.

On follow-up, the patient presented with headache and swelling over the previous operative site. NCCT brain revealed extradural collection over the left frontotemporal craniotomy region and hydrocephalus. Therapeutic lumbar puncture and ventriculoperitoneal shunting were done. On a repeat follow-up after two weeks, the NCCT brain showed subdural hygroma due to shunt overdrainage. The relatives of the patient declined any further treatment. Unfortunately, the patient succumbed to the illness after one month before any adjuvant therapy was initiated.

Discussion

Melanoma in adolescents or children is uncommon and accounts for approximately 3–4% of all malignancies in childhood [4]. However, an increasing incidence has been recorded over the recent three decades, particularly in the adolescent age group (≥15 years). A retrospective study described 13 cases of pediatric melanoma (3–21 years) over a period of 13 years, of which 9 cases had been documented in patients ≥15 years of age [5].

Intracranial malignant melanomas are uncommon and can occur either as primary form or as metastasis. Metastatic melanomas are the third commonest intracranial metastatic tumors in adults. Nevertheless, PIMMs are rare, with an estimated 250 cases described in English literature [6]. PIMMs comprise only 0.07% of total intracranial malignancies [7]. The first case of primary intracranial melanoma was first described by Ogle in 1899 [8]. PIMMs are described chiefly in adults with a peak incidence in the 4th-5th decades [6]. It is extremely rare in the adolescent age group. Since 2001, only 8 cases of PIMMs in patients less than 20 years of age have been described in the literature (Table 1) [9–16].

Clinically, these cases present with headache, focal neurological deficits, seizures, mental state alteration and intracranial hypertension. On CT scan, hyperdense lesions with moderate post-contrast enhancement are seen. On MRI, these lesions show hyperintensity on T1-weighted images and hypointensity on T2 images. This is because of the paramagnetic effects of melanin [11]. Increased propensity to intratumoral bleed is seen in melanomas, often resulting in diagnostic confusion with hemorrhage and vascular neoplasms such as metastatic renal cell carcinoma on radiological imaging.

Histologically, primary central nervous system (CNS) melanomas share similar features to melanomas at other sites. Microscopic findings reveal a highly cellular tumor arranged in solid sheets of dyscohesive large epithelioid to spindled cells. Immunohistochemistry is often required for confirmation of diagnosis, particularly in teenagers where these lesions are very uncommon. The differential diagnosis for these tumors includes metastatic melanomas that are far more

Table 1 Primary intracranial malignant melanoma cases described in childhood and adolescent age group

No	Authors/year	Age/sex	Clinical features	Location	Treatment	Outcome
1	Lim et al./2023 [10]	15/M	Headaches, vomiting and photophobia	Right frontal lobe	Surgery + CT + RT	Died at 8 months
2	Otero-soto et al./2021 [9]	17/M	tonic–clonic seizures	Right frontal parafalcine	Surgery + CT + RT	Died
3	Sivaraju et al./2018 [11]	16/M	Headache, vomiting, left upper and lower limb weakness	Right parietal region	Surgery + RT	Died at 9 months
4	Mondal S et al./2017 [12]	11/F	Headache, vomiting, ataxia	left occipital region	Surgery + RT	Disease free at 24 months
5	Balakrishnan et al./2015 [13]	16/M	Headache, seizure, blurring of vision, vertigo	Temporal lobe	Surgery + CT + RT	Died at 7 months
6	Chen et al./2013 [14]	16/M	Headache, impaired vision	Frontotemporal	Surgery + CT + RT	Died at 6 months
7	Son et al./2003 [15]	12/M	Headache	Parietal-Falx	Surgery + RT	Died at 25 months
8	Desai et al./2001 [16]	17/F	Headache, vomiting, diplopia	Cerebello-pontine angle	Surgery + RT	Alive at 12 months

CT Chemotherapy; *F* female; *M* male; and *RT* radiotherapy

common than primary CNS melanomas. The diagnosis of these primary CNS melanomas can only be made by excluding any evidence of melanomas arising from the site other than CNS. This can be done by detailed clinical examination, including dermatological, ophthalmological and radiological examination. The other primary tumors of CNS that can produce melanin pigment include uncommon variants of schwannoma, medulloblastoma, meningioma and gliomas. These entities can be easily differentiated by imaging and pathological features.

Until recently, the molecular pathogenesis of intracranial melanomas was largely unknown in comparison with melanomas arising outside CNS due to the rarity of these neoplasms. Studies have shown that PIMMs have different molecular profile compared to the melanomas arising in the cutaneous sites. The genetic abnormalities of PIMMs resemble those of the uveal melanomas and include mutation in GNAQ and GNA11 genes. In addition, NRAS gene mutation is described in PIMMs of pediatric age group [17].

To date, there is no consensus regarding treatment for PIMMs. Usually, surgery is the preferred treatment for the patients, while there is no clear benefit of radiotherapy or chemotherapy [7]. Arai et al. [6], in their review of 49 cases of PIMMs, concluded that gross resection is the most effective treatment. Currently, available adjuvant therapy has no significant role in increasing survival as of now. Primary CNS melanoma has a better prognosis than metastatic malignant melanoma. Man et al., in a study of 84 primary CNS melanomas, concluded that age is an important predictor of prognosis and pediatric age group patients usually have the worst prognosis. Median survival in the pediatric, adult and elderly population is approximately 3, 17 and 16 months, respectively [18].

Conclusion

The primary CNS melanoma is a rare entity, especially in the pediatric and adolescent age group. The diagnosis of intracranial melanoma is often challenging due to a lack of specific clinical and radiological imaging findings. It remains a complex diagnosis on radiological imaging and needs exclusion of commoner entities. Histopathology, along with the use of immunohistochemistry, aids in establishing the diagnosis of these lesions. The present case highlights the difficulties faced in management of this rare neoplasm and adds to the limited pool of literature for primary intracranial malignant melanoma. A multidisciplinary neuro-oncology tumor board comprising of neurosurgeons, radiologists, dermatologists, pathologists and oncologist should be formed to effectively manage such rare entity.

Abbreviations

CNS	Central nervous system
CT	Computed tomography
HMB-45	Human melanoma black-45
MRI	Magnetic resonance imaging
PIMM	Primary intracranial malignant melanoma
SOX10	SRY-related HMG-box 10

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Author contributions

VV, PS and PAE assisted in pathology analysis, critically reviewed the literature and drafted the manuscript. ST provided the radiological findings of the case. JSG and DKJ managed the patient and provided the intra-operative details. All authors have read and approved the manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate
The Institutional Review Board of the All India Institute of Medical Sciences (AIIMS), Jodhpur, does not mandate the ethical approval for publication of individual case study.

Consent for publication
The written informed consent to publish the images and clinical details of the patient was obtained from study participant's parents. The consent will be made available on the request of the editor.

Competing interests
The authors declare that they have no competing interests.

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