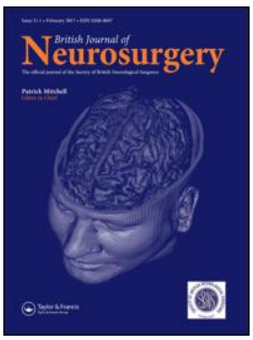

British Journal of Neurosurgery

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ibjn20

Multifocal primary amelanotic meningeal melanomas mimicking lymphoma: a case report and literature review

Yue Cao , Yu-Bo Wang , Xuan-Yu Tan , Yu-He Cui & Gang Zhao

To cite this article: Yue Cao , Yu-Bo Wang , Xuan-Yu Tan , Yu-He Cui & Gang Zhao (2020): Multifocal primary amelanotic meningeal melanomas mimicking lymphoma: a case report and literature review, British Journal of Neurosurgery, DOI: 10.1080/02688697.2020.1834511

To link to this article: https://doi.org/10.1080/02688697.2020.1834511

Published online: 15 Oct 2020.

BRITISH JOURNAL OF NEUROSURGERY
https://doi.org/10.1080/02688697.2020.1834511

Taylor & Francis
Taylor & Francis Group

SHORT REPORT

Multifocal primary amelanotic meningeal melanomas mimicking lymphoma: a case report and literature review

Yue Cao[a,b]*, Yu-Bo Wang[a]*, Xuan-Yu Tan[a,b], Yu-He Cui[a] and Gang Zhao[a]

[a]Neurosurgery, the First Hospital of Jilin University, Changchun, China; [b]Clinical College, Jilin University, Changchun, China

ABSTRACT

Primary meningeal melanoma is a rare type of melanocytic cancer originating from the melanocytes of the leptomeninges. It commonly presents as a solitary mass, and multifocal amelanotic lesions were scarcely reported. Diagnosis of multifocal melanoma is particularly challenging, clinically and diagnostically, especially in the absence of cutaneous nevi and melanin pigment. Surgical biopsy result is the gold standard. In this case study, we present an uncommon case of multifocal primary amelanotic meningeal melanomas mimicking lymphomas in the skull base and near the Sylvian fissure, which serves to provide reference value to the clinical diagnosis. Physicians should be aware of the existence of this special type in the clinical work.

ARTICLE HISTORY
Received 4 February 2020
Revised 27 September 2020
Accepted 6 October 2020

KEYWORDS
Multifocal; amelanotic; primary meningeal melanoma; lymphoma; PET

Introduction

Malignant melanocytic tumors commonly occur in the skin with a high risk of invasion and metastasis. Primary meningeal melanoma (0.5 cases in ten million) is a rare type originating from the melanocytes of the leptomeninges, which has restricted extensive case analyses and has resulted in an inadequacy of systematic diagnostic criteria.[1] The amelanotic variant is more rare called 'amelanotic meningeal melanoma' (AMM). Besides, primary melanoma of the central nervous system (CNS) has generally been observed as isolated nodule, and very few reports of multifocal lesions have been published. Furthermore, similar preoperative symptoms and imaging features to other cerebral tumor types make a challenging diagnosis of primary intracranial melanoma. In this study, we report a case of multifocal primary amelanotic melanomas mimicking lymphoma in the left temporal and right frontal lobes, which were identified by pathological examination and excluded metastases by positron emission tomography (PET). This case provided a new diagnostic direction for multiple lesions.

Case presentation

A 39-year-old women was admitted to our department of neurosurgery with headaches and dizziness accompanied by nausea and vomiting, though her neurological examination proved normal. Preoperative examination and testing were also not found to be abnormal. Magnetic resonance imaging (MRI) revealed two masses. The larger one was in the left temporal lobe and involved the Sylvian fissure. The smaller one was in the right frontal lobe and near the skull base. The larger temporal mass appeared hypo- or hyperintense on T1 weighted imaging (T1WI) and iso- or hyperintense on T2 weighted imaging (T2WI), and the smaller frontal lobe lesion was equisignal on both T1WI and T2WI (Figure 1(A,B)). A cloudlike edema was observed around both masses. Marked enhancement was seen following an injection of gadodiamide (Figure 1(C)). A tentative diagnosis of primary central nervous system lymphoma (PCNSL) was made.

An intracerebral tumor excision of the left temporal lobe was performed. We did not remove the small one, because it was not in the same hemisphere and its position was deep. Surgical resection of it could bring a relatively high risk of mortality and disability. During surgery, a large, non-blackish, vascular firm tumor was observed. It required gross total resection from the surrounding normal brain parenchyma, although it adjoined brain tissue with rich blood supply. The tumor had a close adhesion to the Sylvian fissure. It was later identified to be a malignant melanoma by postoperative pathological examination. The tumor was visualized about 6 cm*4.5 cm*3 cm. The cut surface had a solid, a little tough, white to tan or hazel appearance, with some gelatinous material within (Figure 2). Hematoxylin and Eosin (HE) staining indicated that the tumor penetrated into the brain tissue with high mitotic rate, more than 10/10 HPF (Figure 3). The result of immunohistochemical analysis was as follows (Figure 4): a focal positive reaction for antimelanoma antibody (HMB-45), a positive reaction for S-100 protein and Vimentin; and negative reactions for Cytokeratin (CK), CD56, Lymphocytotoxic Antibody (LCA), and Glial Fibrillary Acidic Protein (GFAP). Proliferation index (Ki-67) was 30% positive (Figure 5). Molecular pathology suggested BRAF∼(V600E) mutation. It was hard to identify whether the lesions were metastatic or not, so a full-body PET scan performed. The smaller remaining tumor on the contralateral side had increased uptake - the highest standardized uptake values (SUV) of 2.6, which indicates

CONTACT Gang Zhao zhaogangjdyy@yeah.net Department of Neurosurgery, the First Hospital of Jilin University, Street Xin-Min 71, Changchun, China
*The first two authors, Yue Cao and Yu-Bo Wang, contributed equally to this work.

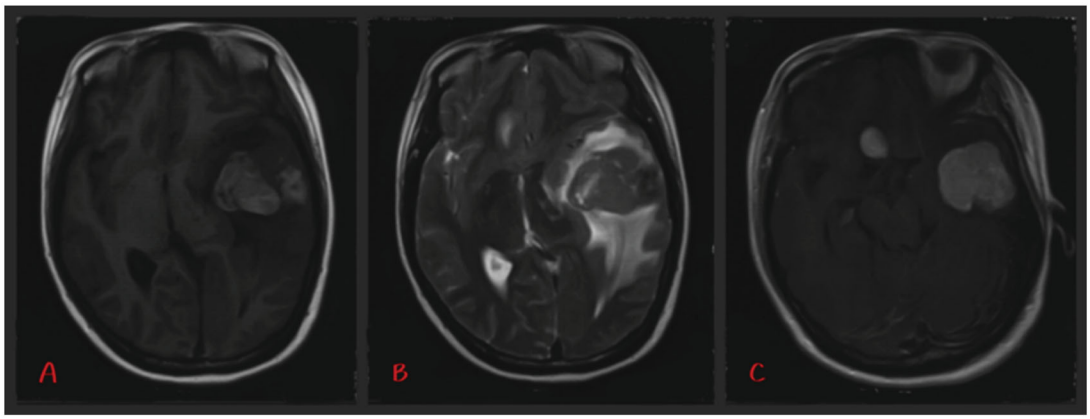

Figure 1. Preoperative brain MRI images. (A, B) Axial view, lesions on T1WI and For Peer Review Only T2WI. (C) Axial view, contrast-enhanced T1W.

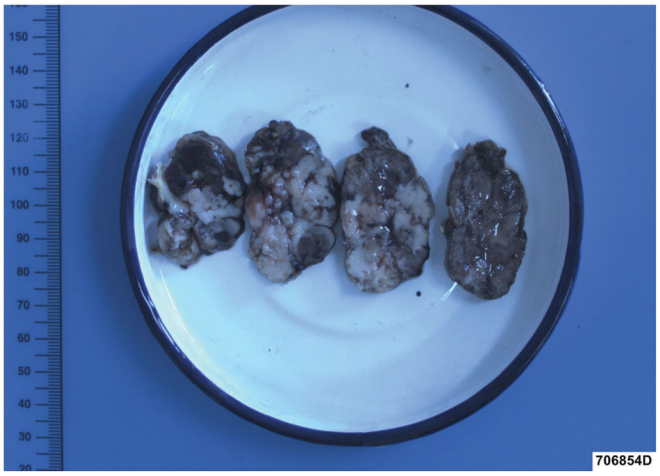

Figure 2. Major gross changes.

a malignant lesion (Figure 6). There was no evidence of melanocytic tumors in any other parts of the body, and no melanism of the skin or mucous membranes was detected. All of these findings justified a diagnosis of multifocal primary melanoma.

Seven days after surgery, the patient was discharged from the hospital without any obvious neurological dysfunction and positive signs of nervous system recovery, but refused further radiochemotherapy. During a follow-up period of 3 months, the patient recovered well without relevant sequelae, and subsequent MRI reexamination did not suggest any recurrences or increase of the tumor in the right frontal lobe (Figure 7).

Literature review and discussion

Primary melanocytic tumors of the CNS derive from leptomeningeal melanocytes, and include four categories according to the behavior of the tumor: melanocytosis, melanomatosis, melanocytoma and melanoma. Primary meningeal melanoma is a rare biologically aggressive tumor that occurs in around 1% of all melanoma cases and 0.07% of all brain tumors.[2–5] Amelanotic meningeal melanoma' (AMM) is an extremely rare type and multiple niduses are more rare . The quantity of melanin pigment in these tumors, as well as the existence of intratumoral hemorrhages, determine their various imaging features. Common treatments including surgical resection, chemotherapy, and radiotherapy could prolong the patient's survival to some extent. This patient had a single BRAF∼(V600E) mutation, which often resulted in faster cell proliferation and more severe tissue infiltration, but also meant the availability of targeting drugs. Unfortunately, the patient in this case refused further treatment for personal reasons. Generally, primary meningeal melanoma is a rare, solitary, intractable disease that is easily misdiagnosed.

In most previous reports, primary meningeal melanoma has appeared as a characteristic solitary mass.[1] However, in this case two lesions were observed, which were eliminated the possibility of metastases by anamnesis and full-body PET scan. Somers et al proposed that an isolated melanoma tended to be primary without evidence of other melanomas detected outside the CNS.[6] Even though one of tumors was not biopsied to confirm its identity, its similar imaging features to the extracted mass suggested both masses were primary melanomas. Primary meningeal melanoma can be multiple which is valued in the diagnosis of intracranial tumors. Multiple lesions appeared mostly in the metastatic tumors, but several evidence showed that our patients had two primary melanomas. Besides, tumor foci in our case were located in different lobes and hemispheres, which were similar to the 'multicentric tumors' in the conception of multiple cerebral glioma. So far, only 5 cases of amelanotic melanomas have been reported in the English literature[7–11] (Table 1). Only one case of them represented multifocal tumors within bilateral frontal cerebral convexities, left occipital lobe, cerebellum, and vermis.[9] Therefore, we should not exclude the possibility of melanoma in the case of multiple niduses without typical melanin signal. Meningeal melanoma should be taken into account when imaging data showed multiple lesions.

In our case, the patient was diagnosed as PCNSL. PCNSL has the feature of multiple foci and always occurs near the lateral ventricle and within the deep white matter in an angiocentric growth pattern.[12] Combining the imaging manifestations with the intraoperative findings, we realized that the two tumors were adjacent to meninges. It is a neglected typical characteristic feature when we made a diagnosis before surgery. Besides, typical intracranial melanoma shows short T1 and T2 signals due to the paramagnetic effects of free radicals within the melanoma.[13,14] Melanin generates an iso-long T1 signal and a moderately long T2 signal. Intratumoral hemorrhaging produces heterogeneous T1 and T2 signals. We consider that non-melanin and minor intratumoral hemorrhage made the nontypical MRI features of

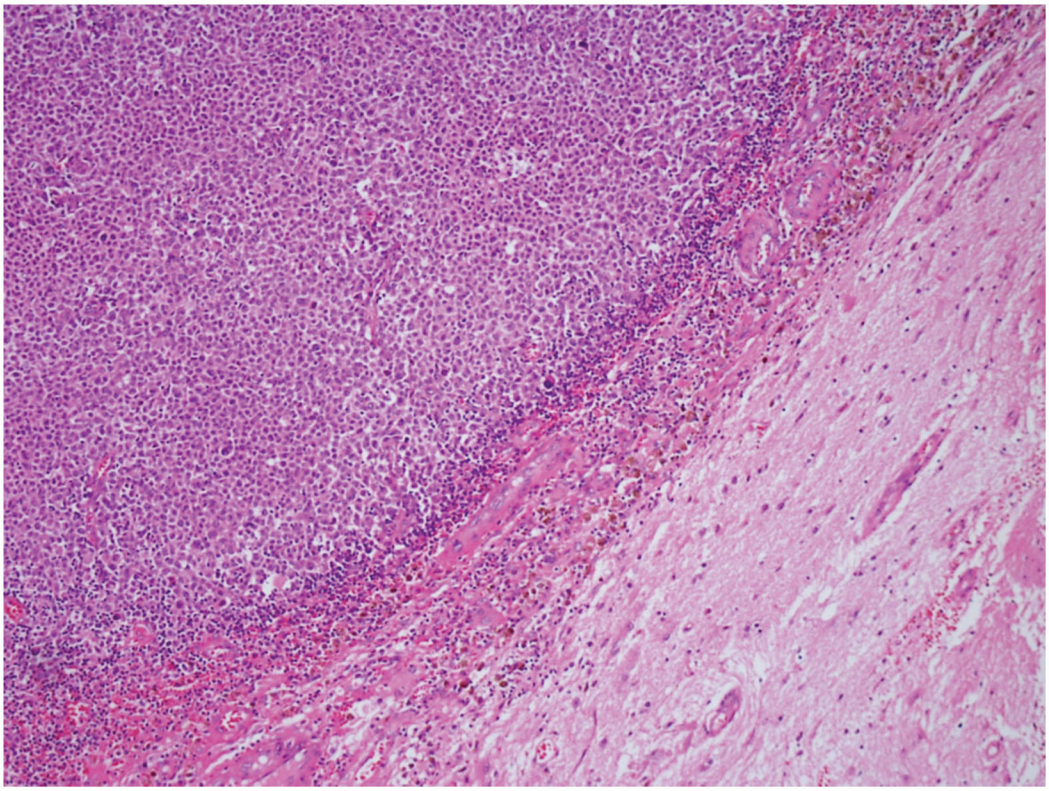

Figure 3. Postoperative histopathology (HE × 100).

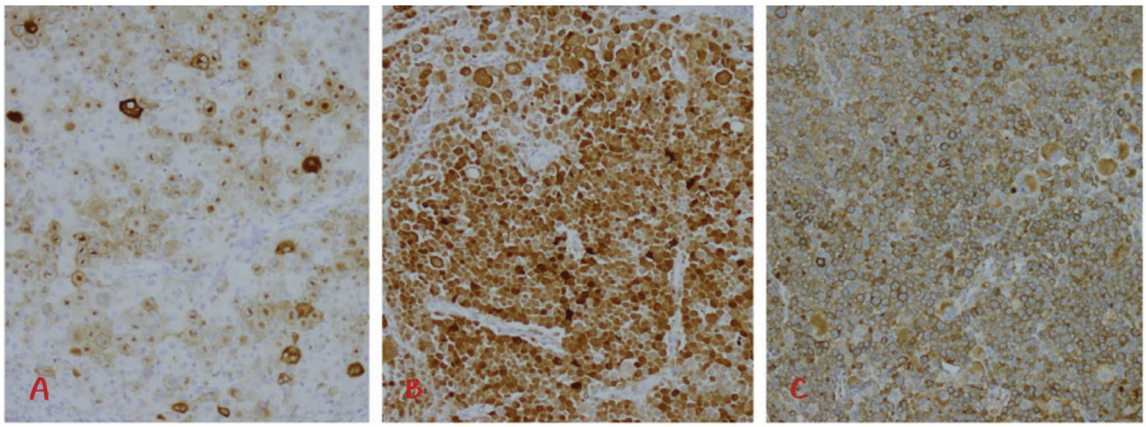

Figure 4. Postoperative immunohistochemical (IHC) examinations (× 400). (A) HMB45 (+). (B) S-100 (+). (C) Vimentin (+).

our patient, which increased the difficulty of diagnosis and led to the misdiagnosis. For the reasons of amelanotic transformation or detergent of the melanoma cells, amelanotic meningeal melanoma occasionally occurs.[8] The lack of melanin will cause the disease being misdiagnosed and often requires surgical biopsy result – the use of stains such as S100 protein and HMB45 to aid in proper identification.[15]

PET plays a significant role in the differentiation between primary tumors and metastases, by ruling out the existence of any melanocytic lesions outside the CNS. In this case, a PET scan was performed after histopathological diagnosis of melanoma, and only the residual tumor in the right frontal lobe presented an intense Fludeoxyglucose (FDG)-uptake nodular shadow. Primary intracranial melanocytic tumor is typically a diagnosis of exclusion, and PET is a valuable imaging tool. Postoperative PET for patients with intracranial melanomas should be performed routinely. In addition, there are apparent differences between primary and metastatic melanomas, especially in life expectancy: the median survival time is only 4.1 months in metastatic cases,[16] while over 17 years can be achieved in patients with primary melanoma.[17] Making an accurate diagnosis is highly significant for prognostic judgement and further treatment.

Conclusion

Primary meningeal melanoma remains a diagnostic and therapeutic challenge in the field of modern neurosurgery. The extent

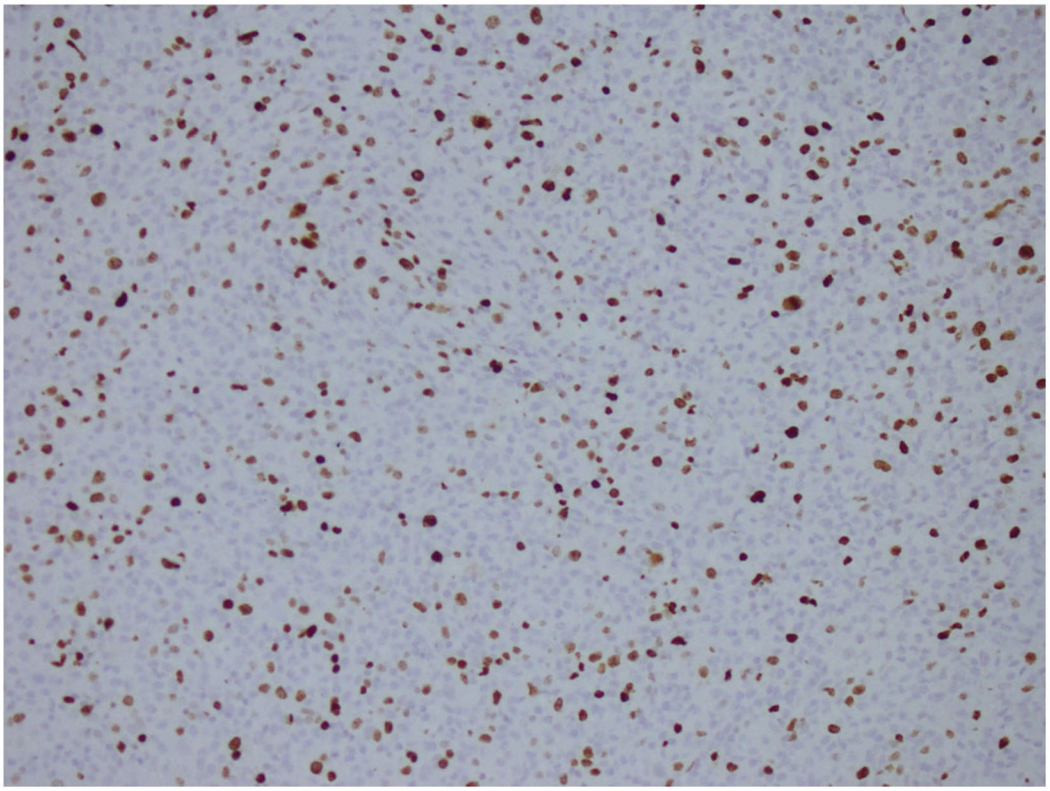

Figure 5. Postoperative immunohistochemical (IHC) examinations (× 400). Ki-67 (30%).

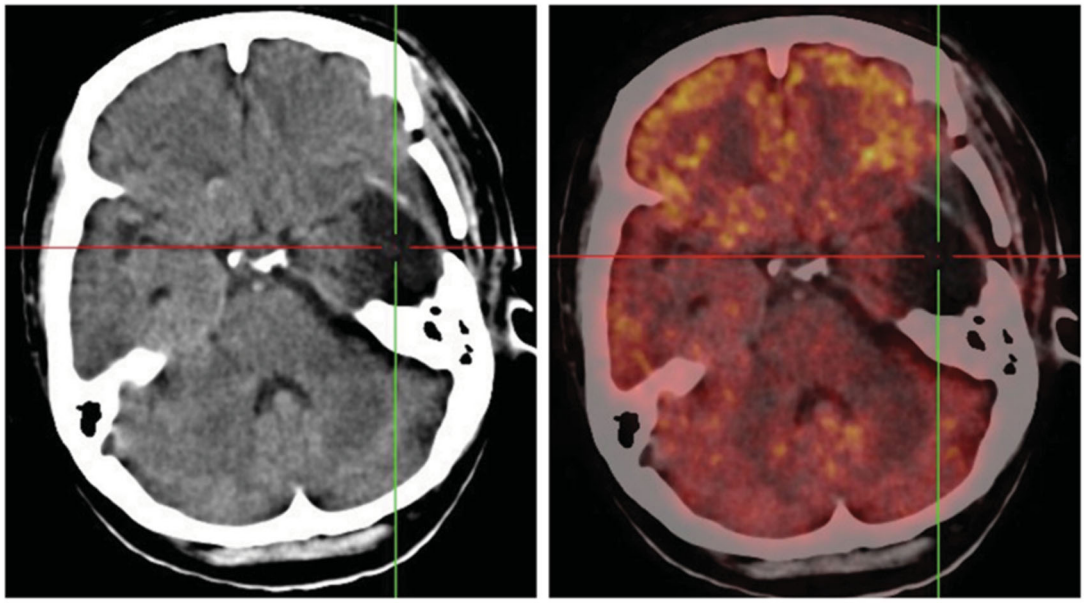

Figure 6. A full-body PET scan only revealed the smaller remaining tumor on the contralateral side had increased uptake – the highest standardized uptake values (SUV) of 2.6, which indicates a malignant lesion.

of surgical resection and the sensitivity to chemoradiotherapy are the key factors to the survival time.[18] Low morbidity rate, as well as poor awareness and vigilance of melanoma contribute to its high misdiagnosis rate. It is important to consider the possibility of melanoma when diagnosing malignant lesions in the skull base or near the Sylvian fissure, although sometimes tumors are amelanotic or multiple. Physicians should be aware of the existence of this special type in the clinical work.

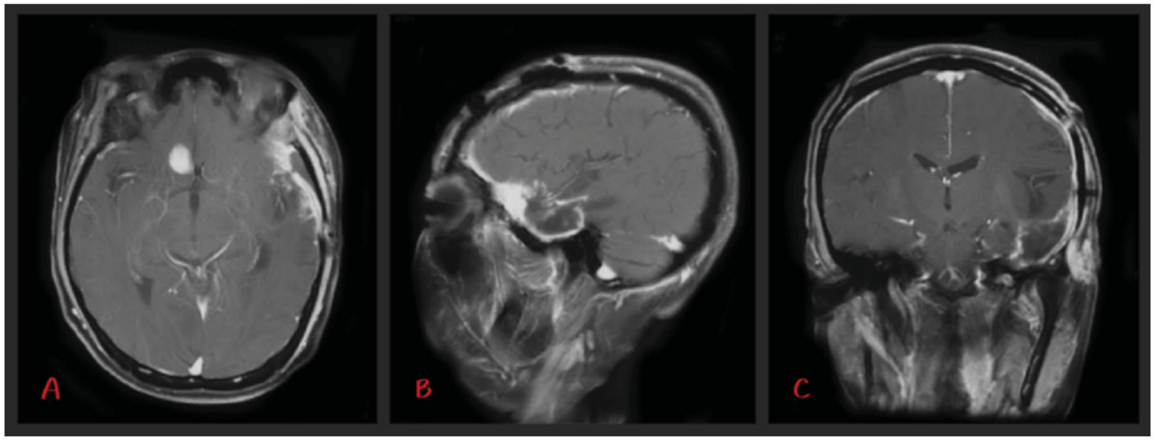

Figure 7. Postoperative brain MRI images. (A) Axial view, contrast-enhanced T1WI. (B) Sagittal view, contrast-enhanced T1WI. (C) Coronal view, contrast-enhanced T1WI.

Table 1. Summary of primary amelanotic meningeal melanomas.

Case	Study	Location	Age	Treatment	*PET*	Ki-67	*Follow-up*
1	Jacob et al.	Pituitary	63	Hypophysectomy + radiotherapy	–	NA	Died
2	Said et al.	Multifocal	60	Biopsy	–	>10%	NA
3	Ma et al.	Right frontal	64	GTR + stereotactic radiosurgery + ipilimumab	Negative	20–30%	5 m
4	Simon et al.	Cerebellum	71	GTR + radio-chemotherapy	–	40%	Died after 8 m
5	Zhang et al.	Cerebellar vermis	26	GTR	–	30%	Died after 10 m

NA: not available; GTR: gross total resection; m: months.

Informed consent statement

Informed written consent was obtained from the patient for publication of this report.

Disclosure statement

The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Liubinas SV, Maartens N, Drummond KJ. Primary melanocytic neoplasms of the central nervous system. *J Clin Neurosci* 2010;17:1227–32.
2. Ma Y, Gui Q, Lang S. Intracranial malignant melanoma: a report of 7 cases. *Oncol Lett* 2015;10:2171–5.
3. Zhao JK, Shao JC, Zhang J. [Primary malignant melanoma of trachea: report of a case]. *Zhonghua bing li xue za zhi = Chinese J Pathol* 2017; 46:865–6.
4. Gempt J, Buchmann N, Grams AE, Zoubaa S. Black brain: transformation of a melanocytoma with diffuse melanocytosis into a primary cerebral melanoma. *J Neurooncol* 2011;102:323–8.
5. Suzuki T, Yasumoto Y, Kumami K, *et al.* Primary pineal melanocytic tumor. Case report. *J Neurosurg* 2001;94:523–7.
6. Somers KE, Almast J, Biemiller RA, Silberstein HJ, Johnson MD, Mohile NA. Diagnosis of primary CNS melanoma with neuroimaging. *J Clin Oncol* 2013;31:e9–11.
7. Zhang S, Wang W, Su X, *et al.* Amelanotic meningeal melanoma with leptomeningeal dissemination: a case report and systematic literature review. *World Neurosurg* 2019;122:229–39.
8. Ma J, Zhang Z, Li S, Chen X, Wang S. Intracranial amelanotic melanoma: a case report with literature review. *World J Surg Onc* 2015;13: 182.
9. Said S, Alkhateeb H, Cooper CJ, *et al.* Primary central nervous system amelanotic melanoma in a Hispanic male: case report. *Polish J Radiol* 2014;79:199–202.
10. Jacob S, Pye E, Hbahbih M, Messios N, Rajabally YA. Rapidly progressive bilateral ophthalmoplegia and enlarging sellar mass caused by amelanotic melanoma. *J Neuro-Ophthalmol* 2006;26:49–50.
11. Mayer S, Mauer UM, Mathieu R, Hackenbroch C, Knupfer J, Schulz C. Primary amelanotic CNS melanoma: case report and literature review. *J Neurol Surg A Cent Eur Neurosurg* 2018;79:96–100.
12. Grommes C, DeAngelis LM. Primary CNS lymphoma. *J Clin Oncol* 2017;35:2410–8.
13. Wadasadawala T, Trivedi S, Gupta T, Epari S, Jalali R. The diagnostic dilemma of primary central nervous system melanoma. *J Clin Neurosci* 2010;17:1014–7.
14. Al-Hadithy N, Al-Nakib K, McGurk S, Quaba A. Primary intracranial melanoma in a child with a giant congenital melanocytic naevus and normal MRI. *BMJ Case Rep* 2013;2013:bcr2013009276.
15. Banerjee SS, Harris M. Morphological and immunophenotypic variations in malignant melanoma. *Histopathology* 2000;36:387–402.
16. Fife KM, Colman MH, Stevens GN, *et al.* Determinants of outcome in melanoma patients with cerebral metastases. *JCO* 2004;22:1293–300.
17. Greco Crasto S, Soffietti R, Bradac GB, Boldorini R. Primitive cerebral melanoma: Case report and review of the literature. *Surg Neurol* 2001; 55:163–8.
18. Chakraborty R, Wieland CN, Comfere NI. Molecular targeted therapies in metastatic melanoma. *Pharmgenomics Pers Med* 2013;6:49–56.