



A rare case of multifocal craniospinal leptomeningeal melanocytoma: A case report and scoping review

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ABSTRACT

Introduction: Leptomeningeal melanocytomas are rare tumours originating from neural crest derived melanocytes. They are usually solitary and presentation with multifocal meningeal melanocytoma is very rare and indicative of potentially more aggressive behaviour. This case report and scoping review sought to evaluate the presentation, and key radiological features that can help differentiate multifocal meningeal melanocytoma from other differentials and provide a discussion of the key management and prognostic points once these tumours are diagnosed.

Case presentation: A 26 year old male presented with neck pain radiating to both shoulders and subjective weakness in left shoulder movement. MRI demonstrated a large enhancing C2–C3 intradural-extramedullary lesion with further lesions at the T7/T8 level, left cerebellopontine angle and midline suprachiasmatic region. Whilst the imaging appearances were initially thought to be indicative of a phacomatosis such as NF2-related schwannomatosis, surgical excision of the cervical tumour confirmed a melanocytic tumour of leptomeningeal origin, consistent with multifocal meningeal melanocytoma. Patient made a good post-operative recovery and remains under half yearly radiological surveillance, with repeat MRI 6 months after surgery demonstrating subtle growth of the untreated intracranial and spinal lesions.

Literature review and conclusions: This is the first description, to our knowledge, of a multifocal meningeal melanocytoma associated with both cerebellopontine angle and suprasellar lesions. This case and included scoping review highlight the need to consider this rare diagnosis whenever multifocal craniospinal lesions are encountered, and the need to consider aggressive management through surgical resection and adjuvant craniospinal radiotherapy once these tumours are diagnosed.

1. Introduction

Meningeal melanocytomas are rare, pigmented tumours that originate from neural crest derived leptomeningeal melanocytes within the central nervous system (CNS) (Yang et al., 2016; Turhan et al., 2004). They account for only 0.06–0.1% of all CNS tumours, and represent one of the four primary melanocytic CNS tumours, along with meningeal melanoma and the diffuse meningeal melanocytic neoplasms: meningeal melanocytosis and meningeal melanomatosis (Louis et al., 2021; WHO Classification of Tumours Editorial Board. Central nervous system

tumours, 2021). Meningeal melanocytomas can occur anywhere along the neuroaxis but are most commonly found in regions of melanocyte concentration such as around the foramen magnum, the cervical and thoracic spine, and within the posterior cranial fossa adjacent to cranial nerve nuclei (Küsters-Vandeveldt et al., 2015; Czarnecki et al., 1997). Within the spine they most commonly occur as an intradural-extramedullary tumour, but can also arise as extradural and rarely intramedullary tumours (Louis et al., 2021; Czarnecki et al., 1997; O'Brien et al., 2006).

Under the World Health Organization (WHO) classification they are

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generally considered as a benign, histological grade I, well differentiated tumour but leptomeningeal spread or infiltrative growth secondary to malignant transformation has been reported (Córdoba et al., 1989; Wang et al., 2007, 2011; Bydon et al., 2003; Kim et al., 2013; Perrini et al., 2010; Uozumi et al., 2003). Primary meningeal melanocytomas usually arise as solitary lesions and primary multifocal meningeal melanocytoma is very rare, and may be indicative of a more aggressive clinical course (Yang et al., 2016; Ali et al., 2009). Herein we present the case of a young male who presented with primary multifocal leptomeningeal melanocytoma with both multiple spinal and cranial lesions. Through this case and an included scoping literature review, we provide an overview of the presentation and salient radiological features that can help differentiate this rare pathological presentation from other differentials, and a discussion of the key management and prognostic points relating to multifocal melanocytoma once diagnosed.

2. Case presentation

A previously fit and well 26 yr. old male presented to our neurosurgical department with an approximately 14-month history of axial neck pain radiating to both shoulders, and weakness in left shoulder movement. On examination there were no stigmata indicative of a phacomatosis or neurocutaneous syndrome (including no nevus of Ota (Hino et al., 2005)). Subsequent MRI demonstrated a large T1 hyperintense C2–C3 intradural-extramedullary lesion anterior to the cord (Fig. 1) with a further T1 hyperintense lesion at the T7/T8 level. Within the brain, MR imaging demonstrated additional T1 hyper- and T2 hypointense lesions in the left cerebellopontine angle (CPA) and midline suprachiasmatic/suprasellar regions, with both lesions demonstrating strong heterogeneous enhancement on T1-weighted post-contrast imaging. Subsequent CT imaging of the body did not reveal any significant systemic pathology and based on the patient's age and MRI appearances of multiple enhancing lesions a presumptive diagnosis of NF2-related schwannomatosis (neurofibromatosis type II) was suspected.

Given the left upper limb weakness, surgery was performed, and the patient subsequently underwent a C1–C3 laminoplasty and resection of the intradural cervical tumour with neuromonitoring. Intraoperatively a dark brown, haemorrhagic tumour was encountered and at the end of surgery a complete macroscopic resection was achieved, with no residual tumour evident on post-operative MRI (Fig. 2). Histological analysis

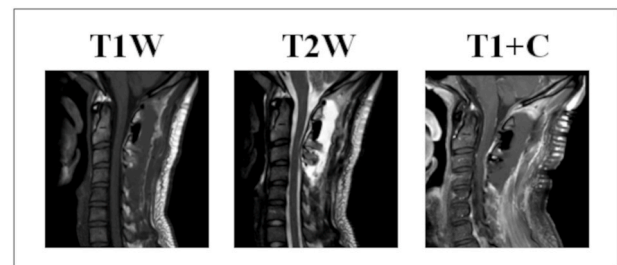


Fig. 2. Post-operative MRI spine imaging

Sagittal T2-weighted and T1-weighted images with and without contrast shown. Status post C1–C3 laminoplasty and resection of the intradural cervical tumour. Note that there has been complete macroscopic resection of the C2/3 tumour with no residual tumour evident on post-operative MR imaging. T1W = T1-weighted; T2W = T2-weighted; T1+C = Post-contrast T1-weighted.

of resected tumour revealed sheets of loosely cohesive epithelioid cells with large pleomorphic, often grooved nuclei, prominent nucleoli, and variable amounts of fine dusky brown cytoplasmic pigmentation (Fig. 3). Ki67 proliferation index was ~5% with no microscopic evidence of necrosis and inconspicuous mitotic activity. Cellular staining was strongly positive for the melanocyte markers HMB (Human Melanoma Black) 45 and Melan-A (Fig. 3), and the neural lineage markers S100 and SOX10. BRAF^{V600E} mutation, a marker of cutaneous melanoma, was not, however, present (Ottaviano et al., 2021). Immunohistochemical staining for PRAME (Preferentially expressed Antigen in Melanoma), a melanoma associated antigen expressed in malignant melanoma but not benign melanocytic proliferations, was also negative (Lezcano et al., 2018; Turner et al., 2024; Kaczorowski et al., 2022; Lang-Orsini et al., 2021). Overall histological appearances and the absence of a BRAF^{V600E} mutation were thought to favour a melanocytic tumour of CNS/leptomeningeal origin, which in the presence of multiple extra-axial lesions could indicate multifocal meningeal melanocytoma or less likely diffuse meningeal melanocytosis/melanomatosis. The patient made a good post-operative recovery from the surgery and was discharged home on post-operative day 4. The patient remained well at last clinical follow up but repeat MRI neuroaxis 6 months after surgery did show very subtle growth of the two untreated intracranial lesions and spinal lesion. The patient remains under half yearly radiological

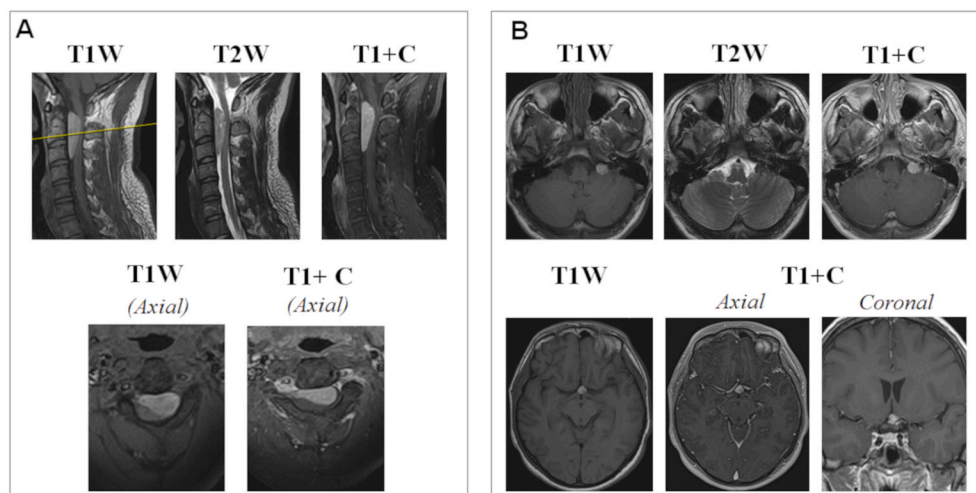


Fig. 1. Pre-operative MRI imaging. A: Selected pre-operative sagittal (top row) and axial (bottom row) MRI spine images demonstrating the left sided intradural-extramedullary tumour at the C2/3 level. Note the hyperintensity on non-contrast T1W imaging, isointensity on T2-weighted imaging and enhancement on post-contrast T1W imaging. Horizontal line on sagittal images denotes the location of axial imaging. B: Selected axial and coronal MRI brain images demonstrating T1 hyperintense lesions located within the left cerebellopontine angle (top row) and midline suprasellar region (bottom row). Note for both lesions the hyperintensity on non-contrast T1W imaging, hypointensity on T2-weighted imaging, and enhancement on post-contrast T1W imaging. T1W = T1-weighted; T2W = T2-weighted; T1+C = Post-contrast T1-weighted.

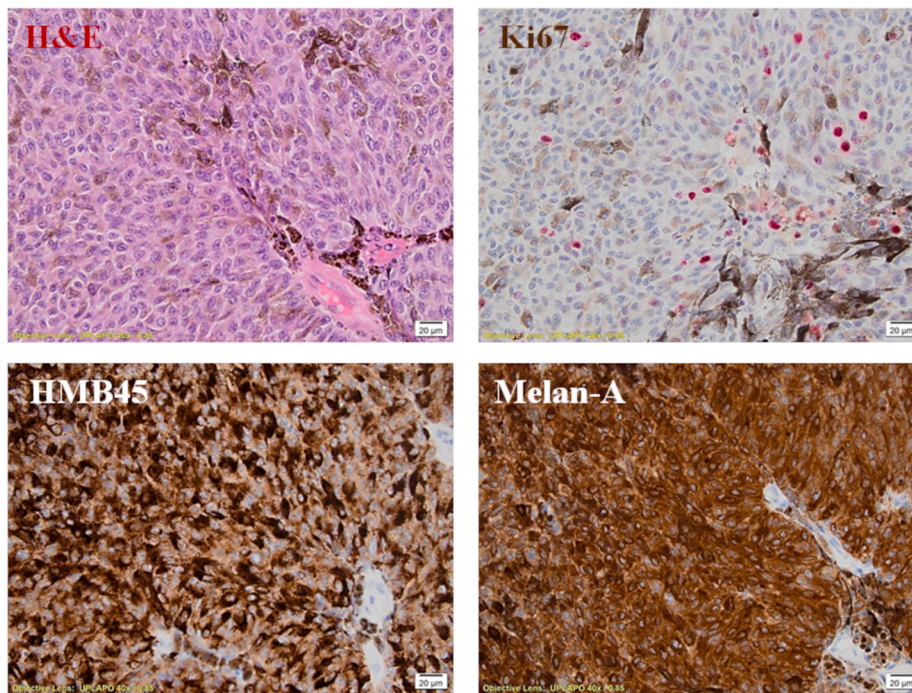


Fig. 3. Photomicrographs of stained tumour sections

Clockwise from top left. Top left: Haematoxylin and eosin (H&E, $\times 40$ objective)–stained sections show sheets of epithelioid cells with large pleomorphic nuclei demonstrating prominent nucleoli and grooving. Fine, dusty, cytoplasmic pigment dark granules are present in many cells. Mitotic activity is inconspicuous and there is no necrosis. Top right: Ki67 immuno-proliferation marker (Vectared kit, $\times 40$ objective) shows some proliferative activity ($\sim 5\%$) but much lower than would be expected for metastatic cutaneous melanoma. Bottom: Human Melanoma Black-45 (HMB45) and Melan-A (Vectastain kit, DAB chromogen, $\times 40$ objective). Melanocyte immuno-markers demonstrate strong tumour cell staining, confirming melanocytic cell lineage.

surveillance with MRI with a plan for craniospinal radiotherapy in the event of significant or symptomatic tumour growth.

3. Literature review and discussion

Primary melanocytomas are usually solitary lesions, and primary multifocal meningeal melanocytoma is very rare; this being to our knowledge the first reported case of multifocal meningeal melanocytoma from the UK, and one of only eight previously reported cases in the literature. Using the search terms ‘central nervous system’, ‘melanocytoma’, ‘meningeal’ ‘multifocal’, and ‘tumour’ we performed a literature search of previous multifocal meningeal melanocytoma cases published on PubMed, Google Scholar, and Science Direct database. These results were then reported using the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) protocol guidelines (Tricco et al., 2018). Citations within derived articles were used to identify additional articles for screening and all identified articles were assessed for suitability in the scoping review. Published case reports or series written in English language and evaluating patients with primary multifocal meningeal melanocytoma were included. Articles concerning patients with either solitary tumours, non-CNS cutaneous melanosis or non-melanocytoma pathologies such as meningeal melanoma or diffuse meningeal melanocytosis/melanomatosis were, however, excluded. A total of seven previous articles met the inclusion criteria and the following data items were extracted from included articles if available and summarised in Table 1: patient demographics (age, sex), symptomatic presentation and anatomical location, tumour radiological and histological features, management strategy, and patient outcome.

3.1. Symptomatic presentation and anatomical location

In all previously reported seven cases of primary multifocal

meningeal melanocytoma there was spinal involvement by at least one tumour; and the usual presentation of multifocal melanocytoma, such as in our case, was with back and/or limb pain with or without weakness. In three previous cases (Ali et al., 2009; Merciadri et al., 2011; Franken et al., 2009), there was associated cranial involvement, and in two such cases the patients presented initially with headache and nausea, features absent in our case. Like solitary or sporadic tumours, cranial involvement most involved the posterior fossa, CPA, and cerebellum, but our case is unique in being the first description of a multifocal spinal melanocytoma associated with both posterior fossa and suprasellar lesions.

3.2. Radiological features

On pre-operative imaging meningeal melanocytoma can often be mistaken for more common pathologies such as meningioma, schwannoma, cavernous malformation and hypervascular metastatic tumours (Küsters-Vandeveldt et al., 2015; Bakan et al., 2015; Moser et al., 2005) (Yang et al., 2016). In the presented case, the multifocal tumours within the CPA and spine were initially diagnosed as multiple meningioma and a presumptive diagnosis of NF2-related schwannomatosis (neurofibromatosis type II) made. Earlier reported cases have similarly misdiagnosed both multifocal meningeal melanocytoma (Yang et al., 2016; Ali et al., 2009) and meningeal melanomatosis (Lang-Orsini et al., 2021) as neurofibromatosis, and whenever multiple spinal tumours are encountered, with or without cranial involvement, multifocal melanocytoma should be considered in the differential. The paramagnetic melanin content within melanocytic tumours shortens T1 and T2 relaxation times resulting in characteristic hyper- and hypointensity on T1- and T2-weighted imaging respectively (Hou et al., 2012; Wang et al., 2013). Whereas the differential diagnosis of spinal meningeal melanocytoma on imaging also includes intermediate-grade melanocytoma and malignant melanoma, malignant melanoma often shows haemorrhage and a more heterogeneous imaging pattern when compared to

Table 1
Previous reported cases of primary multifocal melanocytoma within the CNS.

Author	Year	Age, Sex	Presenting symptoms	Radiological features	Pathology	Management	Outcome
Shownkeen et al	2002	38, M	Neck pain with bilateral arm pain; upper limb paraesthesia. Symptomatic worsening after road traffic collision.	-Intradural-extramedullary lesion at C3–C4 which displayed T1 isointensity, T2 hypointensity, and lobular enhancement on post-contrast imaging. - Two satellite intradural-extramedullary lesions at the C4 and C5 levels.	Melanocytoma Ki67 < 2%	Surgical resection Extent of resection N.R	N.R
Ali et al	2009	31, M	Headache with vomiting; hearing impairment.	-Diffuse leptomeningeal hyperpigmentation. -Bilateral cerebellopontine angle lesions. -Intradural-extramedullary lesion at the T5–T6 level.	Melanocytoma (spine) Low MIB-1	GTR	Died within a few weeks.
Franken et al	2009	26, M	Headache with vomiting.	-Two separate lesions in the posterior fossa subarachnoid space (foramen magnum and infratentorial supracerebellar). Both lesions displayed T1 hyperintensity and T2 hypointensity with post-contrast enhancement. -Two lesions in the spinal canal at the L3–L4 levels.	Melanocytoma Low mitotic activity	GTR of the two intracranial tumours. Craniospinal irradiation.	No progression or recurrence at 1.5yrs.
Reddy et al	2012	43, F	Neck pain.	-Intradural-extramedullary lesion at the C1–C2 level with T1 hyperintensity, T2 hypointensity, and homogenous post-contrast enhancement. -Satellite nodule adjacent to lower pole of tumour.	Melanocytoma Ki67 < 1%	GTR of tumour and nodule	No progression or recurrence at 6 months.
Merciadri et al	2011	68, M	Back pain; lower extremity weakness.	-Intradural-extramedullary dumbbell-shaped lesion at the T12–L1 level that displayed T1 hyperintensity, slight T2 hyperintensity, and intense homogenous post-contrast enhancement. -Three infratentorial lesions: left cerebellopontine angle, right cerebellar tonsil, and left vermis.	Melanocytoma Mitotic activity extremely low	GTR of the spinal tumour. Stereotactic external beam irradiation to each intracranial lesion.	No progression or recurrence at 12 months.
Foit et al	2013	43, M	Left neck and shoulder pain; left-sided cephalalgia; paraesthesia of the left hand.	-Diffuse leptomeningeal hyperpigmentation. -Intradural-extramedullary lesion at the C2–C3 level with extradural extension. -Intradural-extramedullary lesion at the T1–T2 level. -Both lesions displayed T1 hyperintensity and T2 hypointensity with homogenous post-contrast enhancement.	C2–C3 lesion: Melanocytoma, Mib1 1 % T1–T2 lesion: intermediate-grade melanocytoma due to presence of necrosis. Mib1-index 3 %	Both lesions partially resected. Stereotactic external beam irradiation to both tumour locations.	No progression or recurrence at 18 months.
Yang et al	2016	41, F	Pain in the left lumbosacral region and radiating pain to the left lower extremity with numbness.	-Scattered multifocal nodules in the thoracolumbar spine with homogenous T1 hyperintensity, homogenous T2 hypointensity, and homogenous post contrast enhancement. -Large extradural mass at the T12–L1 vertebral level with other intradural-extramedullary masses -Diffuse leptomeningeal enhancement.	Melanocytoma Ki-67 4%	GTR of the two largest masses.	No progression or recurrence for 18 months. 18 months after surgery, presented with cough and dysphagia and lapsed into a coma. Brain MRI demonstrated multiple nodules in the posterior fossa thought to represent intracranial metastasis.
Lewis et al	2023	26, M	Neck pain radiating to both shoulders and subjective weakness in left shoulder movement.	-C2–C3 intradural-extramedullary lesion anterior to the cord with T1 hyperintensity, T2 hypointensity, and post-contrast enhancement. -Additional T1 hyperintense enhancing lesion at the T7–T8 level. -Lesions in the left cerebellopontine angle and midline suprachiasmatic regions.	Melanocytoma Ki-67 5%	GTR of the C2–3 spinal lesion.	Slight interval progression in untreated lesions at 3 months.

GTR = Gross total resection; N.R = Not reported.

melanocytoma (Yang et al., 2016; Hou et al., 2012). Other less common non-melanocytic pathologies can also be differentiated based on their imaging characteristics. Neurofibromas for example often show high rather than low signal intensity on T2 weighted images, whereas primary CNS lymphoma usually lacks the high signal on T1 weighted images seen with melanocytic tumours (Yang et al., 2016; Kraft Roverea et al., 2014). Non-neoplastic conditions such as subacute subdural and meningitis can also mimic these tumours but can be differentiated based on patient's history and presentation (Yang et al., 2016; Córdoba et al., 1989).

3.3. Histological features

Whilst pre-operative imaging can guide towards the diagnosis, a definitive diagnosis of melanocytoma often still depends on obtaining tissue with pathological and immunohistochemical analyses. Immunohistochemistry analysis of melanocytic tumours often show positive staining for: melanocyte markers such as HMB-45 and Melan-A; neural lineage markers such as S-100 protein; and vimentin (predominate cytoskeleton intermediate filament in mesenchymal cells). Staining for glial fibrillary acidic protein, epithelial membrane antigen, and synaptophysin is, however, usually negative (Gonçalves et al., 2002; Nakahara et al., 2010; Painter et al., 2000; Litofsky et al., 1992). Electron microscopy of tumour cells demonstrates melanocytic differentiation with melanosomes in various stages of maturity and the presence of cytoplasmic dendritic processes (Louis et al., 2016; Padilla-Vázquez et al., 2017). Both melanocytoma and melanoma can test positive for HMB-45, Melan-A, MITF (Microphthalmia-associated transcription factor) and S-100 protein. Vimentin, however, is only rarely present in malignant melanoma; and crucially unlike cutaneous melanoma, which display BRAF^{V600E} mutations (present in 40–50% of cutaneous melanomas and their metastases), CNS derived melanocytic lesions have no such mutation (Ottaviano et al., 2021; Painter et al., 2000; Padilla-Vázquez et al., 2017; Davies et al., 2002; Ribas and Flaherty, 2011). A low proliferation index (Ki-67, <2%) and the absence of nuclear atypia, mitotic figures, necrosis, and microvascular invasion/bleeding, can also further help distinguish melanocytoma from intermediate melanocytic neoplastic lesions and malignant melanoma, which often has a Ki67 index >6% (Yang et al., 2016; Reddy et al., 2012). In addition, immunohistochemical staining for PRAME, which was negative in our case, may also be helpful in differentiating malignant melanoma and meningeal melanomatosis from more benign melanocytic proliferations (Lezcano et al., 2018; Turner et al., 2024; Kaczorowski et al., 2022; Lang-Orsini et al., 2021).

An important differential diagnosis to consider, and which was initially considered in this case is that of diffuse meningeal melanocytosis and its more aggressive form meningeal melanomatosis. Compared to primary melanocytoma which presents as solitary or multifocal discrete lesions, these conditions represent diffuse, extensive proliferation of melanocytic cells throughout the leptomeninges, with frequent extension into the perivascular spaces; and in the case of diffuse melanomatosis direct invasion into the brain parenchyma itself (Painter et al., 2000; Demirci et al., 1995). Diffuse melanocytosis/melanomatosis more frequently affects children with affected individuals often presenting with hydrocephalus secondary to obstructed CSF flow or decreased absorption, with many patients requiring long term CSF diversion through shunting (Painter et al., 2000; Demirci et al., 1995; Baumgartner et al., 2021). Diffuse melanocytosis/melanomatosis may also be associated with cutaneous benign pigmented nevi in a rare nonfamilial disorder known as neurocutaneous melanosis (Painter et al., 2000; Demirci et al., 1995; Vanzielegem et al., 1999), but rare reports of isolated or *forme fruste* leptomeningeal melanocytosis without cutaneous manifestations are also documented (Baumgartner et al., 2021; Noronha and Rocha, 2019). Compared to primary melanocytoma and diffuse melanocytosis, diffuse meningeal melanomatosis is characterised by cellular atypia, necrosis and a high mitotic rate and often presents a

more aggressive clinical course. Indeed case series have demonstrated a median overall survival of only 4 months following diagnosis for primary multiple melanomatosis (Baumgartner et al., 2021), and that genetically both diffuse melanocytosis and melanomatosis show some overlap with the *NRAS* mutations seen in cutaneous malignant melanoma (Baumgartner et al., 2021).

3.4. Operative and non-operative management

Despite the initially benign histopathological features of primary melanocytomas, malignant progression with infiltrative growth or leptomeningeal spread has been reported (Córdoba et al., 1989; Wang et al., 2007, 2011; Bydon et al., 2003; Kim et al., 2013). Many authors therefore advise gross total resection (GTR) for solitary melanocytoma, as incomplete removal carries a risk of recurrence or transformation to malignant melanoma (Turhan et al., 2004; Córdoba et al., 1989; Bydon et al., 2003; Perrini et al., 2010; Clarke et al., 1998; Rades et al., 2001). Rades et al., for example, in a series of unifocal meningeal melanocytoma treated with surgery and adjuvant radiotherapy reported a 5 year survival rate of 84% in patients undergoing complete excision (78% patients) compared to only 40% in patients undergoing partial excision (Rades and Schild, 2006). Data on outcomes following surgery for primary multifocal melanocytoma is scarce given the rarity of this condition, but in cases of multifocal disease, it is reasonable to recommend that GTR of the largest lesion or lesions should be attempted. In none of the previously reported multifocal melanocytoma cases, were features consistent with malignant transformation found (Ki67 > 6%, nuclear atypia, high mitotic activity). Foit et al., however, reported non-uniformity or heterogeneity across lesions with differing pathological types and proliferation indices from different tissue samples (Foit et al., 2013).

Many authors recommend that even in the absence of malignant pathological features multifocal meningeal melanocytoma should be considered a distinct pathological entity with a more aggressive clinical course and poorer prognosis (Ali et al., 2009), and a more aggressive treatment strategy is therefore recommended (Yang et al., 2016). Due to the rarity of melanocytoma the role of adjuvant radiotherapy in sporadic and multifocal cases is, however, unknown. In our described case there was subtle growth of the untreated intracranial and spinal lesions at 6 months post-surgery. Given the young age of the patient, however, and the fact that he remained well at last clinic follow up we elected to not undertake any craniospinal radiotherapy unless there is significant or symptomatic tumour growth. Earlier case reports have shown that post-operative stereotactic radiosurgery or high-dose radiotherapy (>45 Gy) may help control tumour growth and to improve prognosis after partial or complete resection of these tumours (Mericiadri et al., 2011; Rades et al., 2001, 2004; Rades and Schild, 2006; Foit et al., 2013) but the role of radiotherapy in the management of meningeal melanocytoma, requires larger dedicated studies with long-term follow up.

3.5. Patient outcome

Given the rarity of this condition, data on outcomes following surgery for multifocal melanocytoma is scarce. Among the six previously reported cases with detailed follow-up and treatment data, three were treated with GTR alone (Yang et al., 2016; Ali et al., 2009; Reddy et al., 2012), and the other three were treated with surgery followed by radiotherapy (Mericiadri et al., 2011; Franken et al., 2009; Foit et al., 2013). A limitation of the available data is that for all cases the reported follow-up period is short (several weeks to 18 months). Two patients reportedly died during follow-up (Yang et al., 2016; Ali et al., 2009), with no progression or recurrence of the tumours noted in four cases during the short follow up period (Mericiadri et al., 2011; Franken et al., 2009; Reddy et al., 2012; Foit et al., 2013). In one case by Yang et al., the patient experienced a recurrence 18 months after surgery for a T12–L1 extradural melanocytoma with intermediate proliferation rate (Ki67

4%), with the development of multiple enhancing nodules (presumed metastases) within the posterior fossa. In a second case by Ali et al. (2009), the patient presented with bilateral CPA and spinal lesions and diffuse associated leptomeningeal hyperpigmentation, and died within a few weeks of surgery. Diffuse leptomeningeal hyperpigmentation was reported in two cases of multifocal melanocytoma (Ali et al., 2009; Foit et al., 2013) and has also been reported rarely in cases of solitary meningeal melanocytoma (Bydon et al., 2003; Kim et al., 2013). Similar to multifocal tumours at presentation, diffuse leptomeningeal hyperpigmentation is thought to be a negative prognostic sign and may show some overlap with diffuse melanomatosis. Earlier case reports for example of a solitary intraspinal melanocytoma with craniospinal leptomeningeal spread have displayed an aggressive clinical course and death within 2 years of diagnosis (Bydon et al., 2003; Kim et al., 2013).

4. Limitations and conclusions

Within this report we have presented the first description of a multifocal craniospinal melanocytoma associated with spinal, posterior fossa and suprasellar lesions. Although multifocal craniospinal melanocytoma is rare with only seven previously reported cases in the literature, this case and scoping literature review highlights that whenever multifocal cranial and spinal lesions are seen multifocal meningeal melanocytoma should be considered within the differential. The growth pattern of these tumours can vary but compared to solitary tumours multifocal meningeal melanocytoma can display a more aggressive growth pattern. Once diagnosed aggressive management through surgical resection should therefore be undertaken, and in cases where there is progressive or symptomatic further tumour growth adjuvant craniospinal radiotherapy should be considered.

Disclosure of interest

No funding was received for this study and the authors report there are no competing interests to declare. All authors have contributed to the article and have approved the final article.

Ethical approval

Individual informed consent has been obtained for writing the case and publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Ali, Y., Rahme, R., Moussa, R., Abadjian, G., Menassa-Moussa, L., Samaha, E., 2009. Multifocal meningeal melanocytoma: a new pathological entity or the result of leptomeningeal seeding? *J. Neurosurg.* 111, 488–491. <https://doi.org/10.3171/2009.3.JNS081096>.
- Bakan, S., Kayadibi, Y., Ersen, E., Vatankulu, B., Ustundag, N., Hasiloglu, Z.I., 2015. Primary psammomatous melanotic schwannoma of the spine. *Ann. Thorac. Surg.* 99, e141–e143. <https://doi.org/10.1016/j.athoracsur.2015.02.060>.
- Baumgartner, A., Stepien, N., Mayr, L., Madlener, S., Dorfer, C., Schmook, M.T., Traub-Weidinger, T., Lötsch-Gojo, D., Kirchhofer, D., Reisinger, D., Hedrich, C., Arshad, S., Irshik, S., Boztug, H., Engstler, G., Bernkopf, M., Rifatbegovic, F., Höller, C., Slavc, I., Berger, W., Müllauer, L., Haberler, C., Azizi, A.A., Peyrl, A., Gojo, J., 2021. Novel insights into diagnosis, biology and treatment of primary diffuse leptomeningeal melanomatosis. *J. Personalized Med.* 11 <https://doi.org/10.3390/jpm11040292>.
- Bydon, A., Gutierrez, J.A., Mahmood, A., 2003. Meningeal melanocytoma: an aggressive course for a benign tumor. *J. Neuro Oncol.* 64, 259–263. <https://doi.org/10.1023/a:1025628802228>.
- Clarke, D.B., Leblanc, R., Bertrand, G., Quartey, G.R., Snipes, G.J., 1998. Meningeal melanocytoma. Report of a case and a historical comparison. *J. Neurosurg.* 88, 116–121. <https://doi.org/10.3171/jns.1998.88.1.0116>.

- Córdoba, A., Tuñón, T., Vázquez, J.J., 1989. [Meningeal melanocytoma. Presentation of a case and review of the literature]. *Arch. Neurobiol.* 52, 93–99.
- Czarnecki, E.J., Silbergleit, R., Gutierrez, J.A., 1997. MR of spinal meningeal melanocytoma. *AJNR. Am. J. Neuroradiol.* 18, 180–182.
- Davies, H., Bignell, G.R., Cox, C., Stephens, P., Edkins, S., Clegg, S., Teague, J., Woffendin, H., Garnett, M.J., Bottomley, W., Davis, N., Dicks, E., Ewing, R., Floyd, Y., Gray, K., Hall, S., Hawes, R., Hughes, J., Kosmidou, V., Menzies, A., Mould, C., Parker, A., Stevens, C., Watt, S., Hooper, S., Wilson, R., Jayatilake, H., Gusterson, B.A., Cooper, C., Shipley, J., Hargrave, D., Pritchard-Jones, K., Maitland, N., Chenevix-Trench, G., Riggins, G.J., Bigner, D.D., Palmieri, G., Cossu, A., Flanagan, A., Nicholson, A., Ho, J.W.C., Leung, S.Y., Yuen, S.T., Weber, B.L., Seigler, H.F., Darrow, T.L., Paterson, H., Marais, R., Marshall, C.J., Wooster, R., Stratton, M.R., Futreal, P.A., 2002. Mutations of the BRAF gene in human cancer. *Nature* 417, 949–954. <https://doi.org/10.1038/nature00766>.
- Demirci, A., Kawamura, Y., Sze, G., Duncan, C., 1995. MR of parenchymal neurocutaneous melanosis. *AJNR. Am. J. Neuroradiol.* 16, 603–606.
- Foit, N.A., Neidert, M.C., Woernle, C.M., Rushing, E.J., Krayenbühl, N., 2013. Bifocal extra- and intradural melanocytoma of the spine: case report and literature review. *Eur. Spine J. Off. Publ. Eur. Spine Soc. Eur. Spinal Deform. Soc. Eur. Sect. Cerv. Spine Res. Soc.* 22 (Suppl. 3), S521–S525. <https://doi.org/10.1007/s00586-013-2773-x>.
- Franken, S.P.G., Setz-Pels, W., Smink-Bol, M., Gijtenbeek, J.M.M., Nanda, D., Van Der Maazen, R.W.M., Van Der Vliet, T., Bussink, J., 2009. Unusual case of bifocal leptomeningeal melanocytoma in the posterior fossa with seeding in the spinal canal. *Br. J. Radiol.* 82, e182–e188. <https://doi.org/10.1259/bjr/30756805>.
- Gonçalves, J., Díaz, P., Subhi-Issa, I., Maillo, A., Blanco, A., 2002. [Spinal meningeal melanocytoma simulating neurinoma: case report]. *Neurocirugía (Astur)* 13, 393–396. [https://doi.org/10.1016/s1130-1473\(02\)70595-2](https://doi.org/10.1016/s1130-1473(02)70595-2).
- Hino, K., Nagane, M., Fujioka, Y., Shiokawa, Y., 2005. Meningeal melanocytoma associated with ipsilateral nevus of Ota presenting as intracerebral hemorrhage: case report. *Neurosurgery* 56, E1376. <https://doi.org/10.1227/01.neu.0000159716.45457.bc>; discussion E1376.
- Hou, G.Q., Sun, J.C., Zhang, X.J., Shen, B.X., Zhu, X.J., Liang, L., Zhang, X.L., 2012. MR imaging findings of the intraspinal meningeal melanocytoma: correlation with histopathologic findings. *AJNR. Am. J. Neuroradiol.* 33, 1525–1529. <https://doi.org/10.3174/ajnr.A2987>.
- Kaczorowski, M., Chlopek, M., Kruczak, A., Ryś, J., Lasota, J., Miettinen, M., 2022. PRAME expression in cancer. A systematic immunohistochemical study of >5800 epithelial and nonepithelial tumors. *Am. J. Surg. Pathol.* 46, 1467–1476. <https://doi.org/10.1097/PAS.0000000000001944>.
- Kim, O.H., Kim, S.J., Choo, H.J., Lee, S.J., Lee, I.S., Kim, J.Y., Kim, H., 2013. Spinal meningeal melanocytoma with benign histology showing leptomeningeal spread: case report. *Korean J. Radiol.* 14, 470–476. <https://doi.org/10.3348/kjr.2013.14.3.470>.
- Kraft Roverea, R., Dagnonia, C., Gomes de Oliveiraa, G., Sapellia, J., 2014. Meningeal melanocytoma: case report and literature review. *Bol. Asoc. Med. P. R.* 106, 30–32.
- Küsters-Vandeveldel, H.V.N., Küsters, B., van Engen-van Grunsvan, A.C.H., Groenen, P.J.T.A., Wesseling, P., Blokx, W.A.M., 2015. Primary melanocytic tumors of the central nervous system: a review with focus on molecular aspects. *Brain Pathol.* 25, 209–226. <https://doi.org/10.1111/bpa.12241>.
- Lang-Orsini, M., Wu, J., Heilman, C.B., Kravtsova, A., Weinstein, G., Madan, N., Arkun, K., 2021. Primary meningeal melanoma masquerading as neurofibromatosis type 2: illustrative case. *J. Neurosurgery. Case Lessons.* 2 <https://doi.org/10.3171/CASE21444>. CASE21444.
- Lezcano, C., Jungbluth, A.A., Nehal, K.S., Hollmann, T.J., Busam, K.J., 2018. PRAME expression in melanocytic tumors. *Am. J. Surg. Pathol.* 42, 1456–1465. <https://doi.org/10.1097/PAS.0000000000001134>.
- Litofsky, N.S., Zee, C.S., Breeze, R.E., Chandrasoma, P.T., 1992. Meningeal melanocytoma: diagnostic criteria for a rare lesion. *Neurosurgery* 31, 945–948. <https://doi.org/10.1227/00006123-199211000-00019>.
- Louis, D.N., Perry, A., Reifenberger, G., von Deimling, A., Figarella-Branger, D., Cavenee, W.K., Ohgaki, H., Wiestler, O.D., Kleihues, P., Ellison, D.W., 2016. The 2016 World Health organization classification of tumors of the central nervous system: a summary. *Acta Neuropathol.* 131, 803–820. <https://doi.org/10.1007/s00401-016-1545-1>.
- Louis, D.N., Perry, A., Wesseling, P., Brat, D.J., Cree, I.A., Figarella-Branger, D., Hawkins, C., Ng, H.K., Pfister, S.M., Reifenberger, G., Soffiatti, R., von Deimling, A., Ellison, D.W., 2021. The 2021 WHO classification of tumors of the central nervous system: a summary. *Neuro Oncol.* 23, 1231–1251. <https://doi.org/10.1093/neuroonc/noab106>.
- Merciadri, P., Secci, F., Sbaffi, P.F., Zona, G., 2011. Multifocal meningeal melanocytoma of the conus medullaris. *Acta Neurochir.* 153, 2283–2285. <https://doi.org/10.1007/s00701-011-1143-x>.
- Moser, T., Nogueira, T.S., Fakhoury, W., Pflieger, N., Neuville, A., Kehri, P., Beltechi, R., Serban, A., Silvestre, R., Dietemann, J.L., 2005. [Primary meningeal intermediate grade melanocytic neoplasm: case report with radiologic-pathologic correlation]. *J. Neuroradiol. = J. Neuroradiol.* 32, 59–62. [https://doi.org/10.1016/s0150-9861\(05\)83024-x](https://doi.org/10.1016/s0150-9861(05)83024-x).
- Nakahara, K., Morota, N., Ihara, S., Oka, H., Matsuoka, K., Nakagawa, A., 2010. Meningeal melanocytoma extruded from the skull of a neonate—case report. *Neurol. Med.-Chir.* 50, 240–242. <https://doi.org/10.2176/nmc.50.240>.
- Noronha, C., Rocha, L., 2019. Meningeal melanocytoma: a challenging diagnosis. *Lancet Oncol.* 20, e343. [https://doi.org/10.1016/S1470-2045\(19\)30298-0](https://doi.org/10.1016/S1470-2045(19)30298-0).
- Ottaviano, M., Giunta, E.F., Tortora, M., Curvietto, M., Attademo, L., Bosso, D., Cardalesi, C., Rosanova, M., De Placido, P., Pietrolungo, E., Riccio, V., Mucci, B., Parola, S., Vitale, M.G., Palmieri, G., Daniele, B., Simeone, E., Youth, O.B.O.S., 2021.

- BRAF gene and melanoma: back to the future. *Int. J. Mol. Sci.* 22 <https://doi.org/10.3390/ijms22073474>.
- O'Brien, D.F., Crooks, D., Mallucci, C., Javadpour, M., Williams, D., du Plessis, D., Broome, J., Foy, P., Pizer, B., 2006. Meningeal melanocytoma., *child's nerv. Syst. ChNS off. J. Int. Soc. Pediatr. Neurosurg.* 22, 556–561. <https://doi.org/10.1007/s00381-005-0019-x>.
- Padilla-Vázquez, F., Escobar-de la Garma, V.H., Ayala-Arcipreste, A., Mendizábal-Guerra, R., Cuesta-Mejía, T., 2017. [Melanocytoma and meningeal melanocytosis, similar but different lesions]. *Cir. Cir.* 85, 273–278. <https://doi.org/10.1016/j.circir.2016.11.006>.
- Painter, T.J., Chaljub, G., Sethi, R., Singh, H., Gelman, B., 2000. Intracranial and intraspinal meningeal melanocytosis. *AJNR. Am. J. Neuroradiol.* 21, 1349–1353.
- Perrini, P., Caniglia, M., Pieroni, M., Castagna, M., Parenti, G.F., 2010. Malignant transformation of intramedullary melanocytoma: case report. *Neurosurgery* 67, E867–E869. <https://doi.org/10.1227/01.NEU.0000372919.96651.34> discussion E869.
- Rades, D., Schild, S.E., 2006. Dose-response relationship for fractionated irradiation in the treatment of spinal meningeal melanocytomas: a review of the literature. *J. Neuro Oncol.* 77, 311–314. <https://doi.org/10.1007/s11060-005-9048-2>.
- Rades, D., Heidenreich, F., Tatagiba, M., Brandis, A., Karstens, J.H., 2001. Therapeutic options for meningeal melanocytoma. Case report. *J. Neurosurg.* 95, 225–231. <https://doi.org/10.3171/spi.2001.95.2.0225>.
- Rades, D., Schild, S.E., Tatagiba, M., Molina, H.A., Alberti, W., 2004. Therapy of meningeal melanocytomas. *Cancer* 100, 2442–2447. <https://doi.org/10.1002/cncr.20296>.
- Reddy, R., Krishna, V., Sahu, B.P., Uppin, M., Sundaram, C., 2012. Multifocal spinal meningeal melanocytoma: an illustrated case review. *Turk. Neurosurg.* 22, 791–794. <https://doi.org/10.5137/1019-5149.JTN.4322-11.1>.
- Ribas, A., Flaherty, K.T., 2011. BRAF targeted therapy changes the treatment paradigm in melanoma. *Nat. Rev. Clin. Oncol.* 8, 426–433. <https://doi.org/10.1038/nrclinonc.2011.69>.
- Tricco, A.C., Lillie, E., Zarin, W., O'Brien, K.K., Colquhoun, H., Levac, D., Moher, D., Peters, M.D.J., Horsley, T., Weeks, L., Hempel, S., Akl, E.A., Chang, C., McGowan, J., Stewart, L., Hartling, L., Aldcroft, A., Wilson, M.G., Garrity, C., Lewin, S., Godfrey, C.M., Macdonald, M.T., V Langlois, E., Soares-Weiser, K., Moriarty, J., Clifford, T., Tunçalp, Ö., Straus, S.E., 2018. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann. Intern. Med.* 169, 467–473. <https://doi.org/10.7326/M18-0850>.
- Turhan, T., Oner, K., Yurtseven, T., Akalin, T., Ovul, I., 2004. Spinal meningeal melanocytoma. Report of two cases and review of the literature. *J. Neurosurg.* 100, 287–290.
- Turner, N., Ko, C.J., McNiff, J.M., Galan, A., 2024. Pitfalls of PRAME immunohistochemistry in a large series of melanocytic and nonmelanocytic lesions with literature review. *Am. J. Dermatopathol.* 46, 21–30. <https://doi.org/10.1097/DAD.0000000000002584>.
- Uozumi, Y., Kawano, T., Kawaguchi, T., Kaneko, Y., Ooasa, T., Ogasawara, S., Yoshida, H., Yoshida, T., 2003. Malignant transformation of meningeal melanocytoma: a case report. *Brain Tumor Pathol.* 20, 21–25. <https://doi.org/10.1007/BF02478943>.
- Vanzieleghem, B.D., Lemmerling, M.M., Van Coster, R.N., 1999. Neurocutaneous melanosis presenting with intracranial amelanotic melanoma. *AJNR. Am. J. Neuroradiol.* 20, 457–460.
- Wang, F., Li, X., Chen, L., Pu, X., 2007. Malignant transformation of spinal meningeal melanocytoma. Case report and review of the literature. *J. Neurosurg. Spine* 6, 451–454. <https://doi.org/10.3171/spi.2007.6.5.451>.
- Wang, F., Qiao, G., Lou, X., Song, X., Chen, W., 2011. Malignant transformation of intracranial meningeal melanocytoma. Case report and review of the literature. *Neuropathology* 31, 414–420. <https://doi.org/10.1111/j.1440-1789.2010.01160.x>.
- Wang, H., Zhang, S., Wu, C., Zhang, Z., Qin, T., 2013. Melanocytomas of the central nervous system: a clinicopathological and molecular study. *Eur. J. Clin. Invest.* 43, 809–815. <https://doi.org/10.1111/eci.12109>.
- WHO Classification of Tumours Editorial Board. Central nervous system tumours, 2021, 5, 6. WHO Classification of Tumours Series. International Agency for Research on Cancer, Lyon (France). n.d.
- Yang, C., Fang, J., Li, G., Yang, J., Xu, Y., 2016. Primary scattered multifocal melanocytomas in spinal canal mimicking neurofibromatosis. *Spine J.* 16, e553–e559. <https://doi.org/10.1016/j.spinee.2016.03.007>.