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Spinal melanotic ependymoma: A case report and review of literature

Stefan L. Leber[a,b,d], Klaus A. Leber[c], Johannes Haybaeck[a,d,e,f,g,*]

[a] Department of Neuropathology, Diagnostic & Research Center for Molecular BioMedicine, Institute of Pathology, Medical University of Graz, Austria
[b] Department of Neuro-, Vascular-, and Interventional Radiology, Medical University of Graz, Austria
[c] Department of Neurosurgery, Medical University of Graz, Austria
[d] Department of Pathology, Medical Faculty, Otto-von-Guericke University Magdeburg, Germany
[e] Department of Pathology, Neuropathology, and Molecular Pathology, Medical University of Innsbruck, Austria
[f] Center for Biomarker Research in Medicine, Graz, Austria
[g] German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany

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ABSTRACT

We describe an adult female patient diagnosed with spinal melanotic ependymoma. She underwent surgery with the aim of gross total resection, but only subtotal resection was possible. Therefore, the patient was re-evaluated 6 weeks following surgery. Radiotherapy was considered as further treatment. The diagnosis, clinical course, etiology and pathology are discussed on the basis of the current literature.

1. Introduction

Ependymomas originate from neoplastic ependymal cells. Radial glial cells are suggested as the histogenetic source of these tumors. Microscopically perivascular pseudorosettes and ependymal rosettes are considered as key features of ependymomas. Immunohistochemistry typically reveals cells positive for S-100 protein and vimentin. The majority of ependymomas show immunoreactivity for epithelial membrane antigene (EMA), glial fibrillary acidic protein (GFAP), as well as a low Ki-67 labeling index [7].

Classic ependymomas affecting the spinal cord are most frequently located in the cervical and cervicothoracic spine [7]. The clinical symptoms depend on tumor localization, the clinical outcome on the extent of surgical resection, adjuvant radiation therapy, and molecular group [7].

Melanotic ependymomas (ME) represent a rare entity of ependymomas, and the literature concerning MEs is scarce [1,2,6,7,8,11]. So far, clinicians and researchers have failed to clearly point out putative pathological and clinical differences between ME and non-melanotic epedymomas (NME). Due to the great variety of prognostic factors in ependymal tumors, it is of utmost importance to collect and compare such rare cases. We report a patient with spinal ME and discuss our case on the basis of the existing literature. The overall follow up time was 30 months.

2. Case report

2.1. History and clinical findings

A 75-year-old female patient presented with a four-month history of back pain that was fairly controlled by analgesics. One week before admission, she developed a gait disturbance followed by ischuria. Neurological examination revealed motor weakness. According to the medical research council, the muscular strength of hip flexion was 3+/5 (left) and 4/5 (right); knee extension: 3/5 (left) and 4/5 (right); foot lift: 3/5 (left), 5/5 (right 5); as well hypoesthesia on the left side corresponding to the level of Th 8/9 and a spinal ataxia with hyperreflexia of the lower extremities (Table1).

2.2. Radiological findings

Magnetic Resonance Imaging (MRI) exhibited an intra-/extramedullary mass lesion (4,2 × 2,3 × 1,9 cm) at the level of Th 7-9. The lesion showed a homogeneous contrast enhancement with small areas of micro bleedings or calcification (Fig. 1).

2.3. Intraoperative findings

The spinal canal was opened by unilateral osteoplastic laminectomy (Th7/Th8). A bluish-livid mass was found underneath the dura mater

Abbreviations: ME, Melanotic ependymoma; NME, Non-melanotic ependymoma; EMA, Epithelial membrane antigene; GFAP, Glial fibrillary acidic protein; HMB-45, Human melanoma black-45; MRI, Magnetic resonance imaging; PET- CT, Positron emission tomography- Computed tomography

* Corresponding author at: Department of Pathology, Medical Faculty, Otto-von-Guericke University Magdeburg, Leipzigerstraße 44, Haus 28, D-39120, Germany.
E-mail address: johannes.haybaeck@med.ovgu.de (J. Haybaeck).

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Table 1
Clinical characteristics of our patient with the diagnosis of a spinal melanotic ependymoma.

Age	Gender	Location	Onset (time before admission)	Pathological grade	Therapy	Outcome discharge	Outcome follow-up	Follow-up time
75y	F	Th7-9	Back pain (4 month), gait disturbances (1 week), ischuria (1 week)	WHO II	subtotal resection, adjuvant radiotherapy	Lower extremity paresthesia, paraparesis	mild paraparesis, hyperreflexia, moderate ataxia, Nurick-scale: 3	30 month

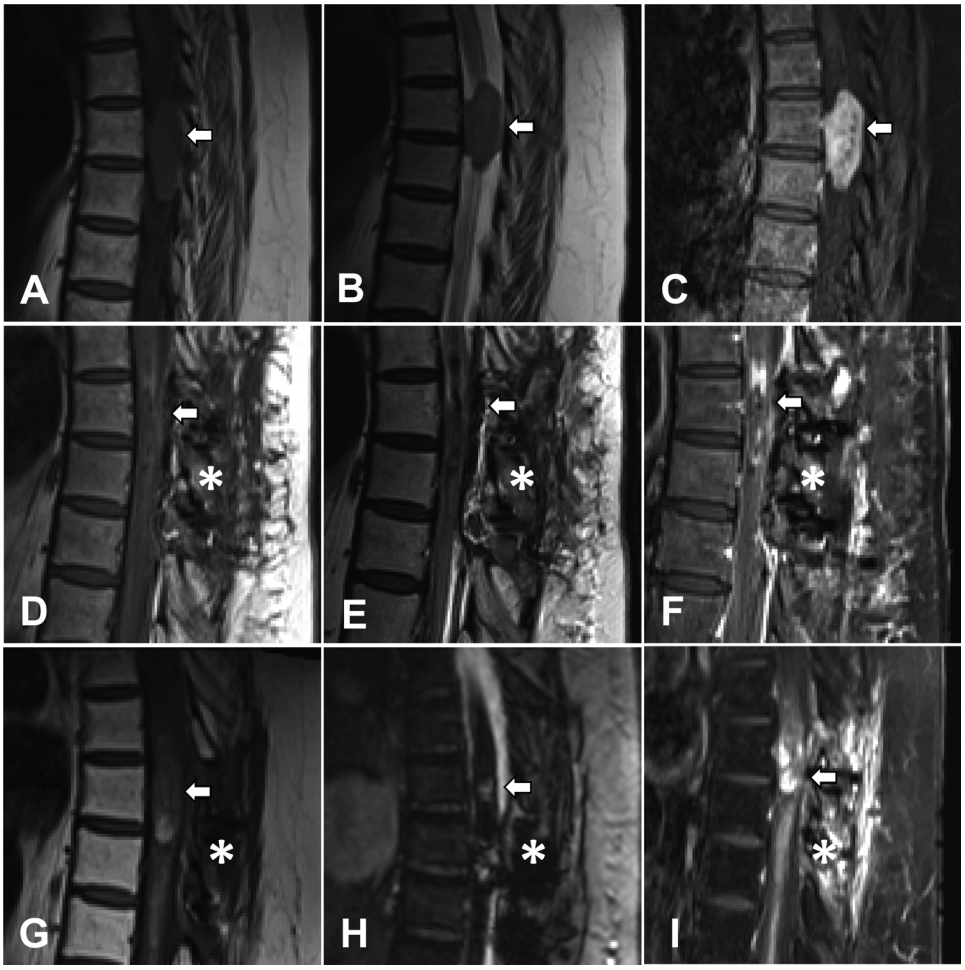

Fig. 1. MRI of a spinal melanotic ependymoma in a 75 year old female patient, T1-weighted (A, D, G), T2-weighted (B, E, H), contrast enhanced (C, F, I). (A–C) Preoperative MRI showing an intra-/extramedullary mass lesion (white arrow), level Th 7–9; (D–F) postoperative MRI showing tumor remains (white arrow) and postoperatively changed tissue (asterisk); (G–H) MRI after a 30-month follow up showing tumor remnants with partial cystic transformation (white arrow) and postoperatively changed tissue (asterisk).

and arachnoid membrane. After identifying the tumor borders, a biopsy and instantaneous frozen section identified an ependymoma. Cranial and caudal poles of the tumor were mobilized and resected along a well-defined cleavage plane. The tumor showed signs of previous microbleedings. Tendencies of bleeding still remained even after decompression. At the anterior border of the tumor, the cleavage plane vanished against the edematous myelon; hence, this area had to be considered as matrix. An intrinsic growing part was removed as much as possible using an ultrasound microaspirator. The result was considered a subtotal resection.

2.4. Histopathological report

Instantaneous section showed a highly cellular neoplasm consisting of glial tumor cells with round to oval nuclei and a small, bright-basophilic cytoplasm. The nuclear chromatin was speckled. True rosettes with centers free of cells and perivascular pseudorosettes became apparent. No signs of CNS-infiltration, elevated mitotic activity or necrosis were present. As a sign of earlier bleeding, siderin-rich macrophages were found. Immunohistochemistry revealed strong positivity for S100, HMB-45 and Melan A, focal positivity for EMA and singular GFAP-positive cells. Ki-67 staining showed a proliferation-rate of about 2%. A melanotic ependymoma WHO-II was diagnosed (Fig. 2).

2.5. Postoperative treatment and follow-up

A postoperative MRI scan of the spine confirmed a subtotal resection of the tumor. The subtotal resection and the final diagnosis led to the decision to carry out an adjuvant conventional radiation therapy of 23 fractions of 2 Gy (total 46 Gy).

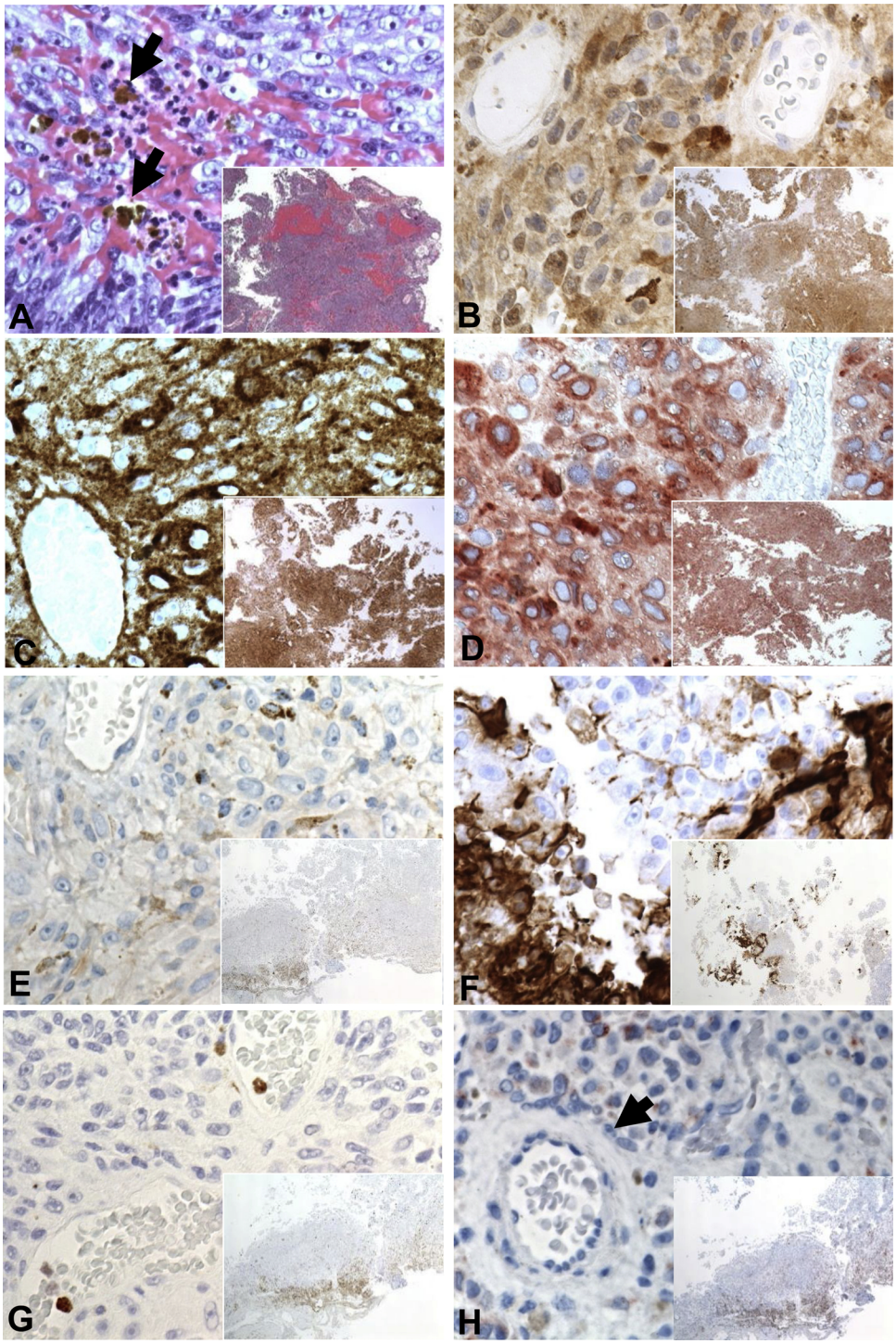

Fig. 2. Histology and immunohistochemical staining.
(A) Hematoxylin-eosin, melanin deposits (black arrow heads), (B) S-100, (C) HMB-45, (D) Melan A, (E) EMA, (F) GFAP, (G) Ki-67, (H) Tyrosinase, pseudorosette (black arrow heads). Immunohistochemistry was mostly performed on an OMNIS autostainer from DAKO with a Flex Detection System, using AEC as Chromogen for S100, HMB45, Melan A and DAB for Ki67 and GFAP. These antibodies were used ready to use from the DAKO Flex System, especially for Omnis and pretreated with envision Flex TRS low pH for Ki 67 and TRS high pH for the others. Tyrosinase (Novocastra, 1:50) was performed on a Dako autostainer classic using a HIER pH9,0 in microwave for 40 min at low wattage, cooling down for 20 min at RT and Dako K5007 for detection with AEC as chromogen. EMA (Ventana confirm, ready to use) was performed on a Ventana autostainer using Ultra View DAB for detection and CC1 as Epitope Retrieval.

A nine-month clinical follow-up showed a spastic paraparesis: left leg 5-/5, right leg 5/5 with distinct hyperreflexia, slight hypoesthesia left leg, moderate ataxic gait, and normal sphincter functions. This corresponded to a Nurick-scale of 3 [9], including secondary diagnosis of restless-leg- syndrome and a global neuropathy. In summary, the patient improved markedly by the combined therapy, however a residual neurological deficit persisted. Thirty months after diagnosis, the patient was brought to the hospital after a downfall. MRI and PET-CT performed 30 months after surgery revealed bleeding originating from the tumor but no significant tumor progression (Fig. 1).

3. Discussion

Melanogenesis in the developed human brain usually affects the leptomeningeal melanocytes and a few neurons located at the roof of the fourth ventricle [6]. The melanin production in ependymal tumors is explained by their origin from the primitive neuroepithelium. This property is usually lost during the normal maturation process [6,8]. A case of pigmented ependymoma showed intracytoplasmic lipofuscin and neuromelanin. Positivity for HMB-45 indicated a melanin component [2]. In another case of intracranial ME, HMB-45 was not expressed by tumor cells [6]. The case presented here shows the histopathological characteristics of an ependymoma with accumulations of melanin,

strong staining for S-100, HMB-45 and Melan A. There was focal positivity only for EMA and Tyrosinase (Fig. 2). To the best of our knowledge there are no reports about ependymomas positive for markers of melanogenesis without expressing melanin pigment.

In gadolinium-enhanced MRI scans, ependymomas appear as well circumscribed lesions with different levels of contrast enhancement. Intramural hemorrhage and calcification can be observed occasionally. Infiltration of adjacent structures and edemas are rare [7]. As there is a probability that melanin binds paramagnetic metals, high signal intensity on T1W images can be expected [4]. Interestingly, superficial pial melanosis together with characteristic MRI alterations was observed in a case of ME [1]. Moreover, an analysis of 6 cases of ME revealed melanin-related MRI alterations in association with melanin content and distribution [11]. However, in our case, heterogeneous MRI signal alterations, together with intraoperative and histopathological findings, most likely resulted from bleedings (Fig. 1). In contrast to other cases, our case did not display macroscopic dark pigmentation intraoperatively [1,11].

The analysis of 6 patients with a course of cranial or spinal ME reported a behavioral similarity to normal ependymomas despite their melanin component. The functional outcome is considered favorable in all patients. The authors recommend gross total resection. The benefits of radiotherapy are under debate, although this therapy may be considered useful for cases with histologically anaplastic features [11].

In spinal NME some major prognostic factors, such as the extent of resection, radiation dose or multifocality, are also still under discussion [5]. Factors like tumor localization and histological subtype were considered to be less significant [3]. On the other hand, according to a recent study investigating NMEs of other spinal localizations, thoracic NME appeared to be the most aggressive type. Also, the rate of gross total resection varied in different spinal localizations of NME [10].

In general, invasion of CNS parenchyma is very rare among ependymomas. Typically, the tumor and the adjacent CNS parenchyma show a well-demarcated interface [7]. Gross total resection is considered as therapy of choice in ependymomas and also seems to be adequate for the treatment of ME [3,5,3]. Nonetheless, gross total resection might be difficult to achieve as seen in our and some other cases [1,2]. Since the characteristics and behavior of ependymomas in general show certain variations, MEs might present features different from NMEs. For example, as in other tumors [7], it might be of interest for future research whether ME and NME are similar on the molecular level.

This case report describes a case of spinal ME that has undergone subtotal resection and postoperative radiotherapy. This combined therapy led to an improvement of our patients' symptoms; however, some neurological deficits persisted. To the best of our knowledge, only a few cases of ME have been reported so far, especially MEs affecting the spinal region. Therefore, it is of utmost importance to collect data of this rare tumor entity. Since the diagnosis "Melanotic ependymoma" does not exist according to the WHO 2016 classification of CNS tumors [7], we propose that "Spinal ependymoma with melanotic differentiation" might be a more appropriate term for this tumor entity.

Declarations of interest

None.

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