

Pilomyxoid astrocytoma of the cervical spinal cord in a child with rapid progression into glioblastoma: case report and literature review

Dimitrios Paraskevopoulos · Ioannis Patsalas ·
Georgios Karkavelas · Nikolaos Foroglou ·
Ioannis Magras · Panagiotis Selviaridis

Received: 6 March 2010 / Accepted: 29 April 2010
© Springer-Verlag 2010

Abstract

Introduction Pilomyxoid astrocytoma (PMA) is a recently described glial tumor with similarities to pilocytic astrocytomas, yet with distinct histopathological characteristics and a more aggressive behavior. It occurs predominantly in the hypothalamic/chiasmatic region. Only four patients with spinal cord PMA have been reported in the pediatric population. The 2007 WHO Working Group recognized PMA as a new variant and recommended an assignment to WHO grade II.

Objective The purpose of this paper was to report a rare location, address the aggressive behavior and rapid progression, and based on the specific patient, to review the literature and discuss current treatment strategies.

Case presentation A 12-year-old girl presented with motor and sensory deficits of the left side as well as gait disturbance. Imaging revealed an intramedullary tumor extending from C2 to C7. The patient improved impressively after surgical resection. Histopathological findings were consistent with PMA. Three months later, the patient

presented with rapid neurological deterioration. Histopathology after the second operation was consistent with glioblastoma. The outcome was fatal 12 months after initial diagnosis, despite adjuvant therapy.

Conclusions This is the fifth pediatric spinal cord PMA in literature. Furthermore, it is the only documented patient with rapid recurrence and progression within 3 months into a glioblastoma. The question of a sampling error affecting initial pathology is raised. Based on contemporary literature data, we discuss the further treatment options, as there are no guidelines yet. Efforts towards registries should be encouraged, as the documentation of PMA might lead to more evidence based treatment strategies.

Keywords Pilomyxoid astrocytoma · Spinal cord · Pilocytic astrocytoma · Intramedullary

Introduction

Spinal cord astrocytomas are the most frequent histologic type of spinal cord tumor in children [18, 22]. The term pilomyxoid astrocytoma was introduced in 1999 by Tihan et al. [36], who also described its characteristic histopathological features. Pilomyxoid astrocytoma (PMA) occurs typically in the hypothalamic/chiasmatic region and is histologically characterized by a prominent myxoid matrix and angiocentric arrangement of monomorphous bipolar tumor cells. In contrast to the compact biphasic architecture of a pilocytic astrocytoma (PA), PMA appears as monomorphous piloid cells in a loose fibrillary and myxoid background, without Rosenthal fibers [36]. Prior to its recognition, PMA was grouped with PA, because of similar histological features, but since 2007 the WHO Classifica-

D. Paraskevopoulos · I. Patsalas · N. Foroglou · I. Magras ·
P. Selviaridis
Department of Neurosurgery, Aristotle University of Thessaloniki,
AHEPA Hospital,
St. Kyriakidi 1,
Thessaloniki, Greece

G. Karkavelas
Department of Pathology, Aristotle University of Thessaloniki,
St. Kyriakidi 1,
Thessaloniki, Greece

D. Paraskevopoulos (✉)
Nathanail 1,
54644 Thessaloniki, Greece
e-mail: dimitris.parask@gmail.com

tion has recognized it as a new histological variant. PMA affects predominantly infants and children (median age, 10 months) and appears to have a less favorable prognosis, as it tends to behave more aggressively than PA, with a decreased duration of disease-free survival and higher mortality rates. Local recurrences and cerebrospinal spread are more likely to occur in PMA than in PA. According to the 2007 WHO Classification, PMA is assigned to WHO grade II [27].

Only four patients with spinal cord PMA have been reported in the pediatric population (Table 1), at ages of 6 years old, 8 years old, and neonate [3, 22]. Two adult patients with spinal PMA have been reported so far, in a 29- and in a 45-year-old [29, 34]. The current patient is the seventh spinal cord PMA report in literature, affecting only the cervical spine in a 12-year-old girl. Furthermore, it is the only documented spinal PMA patient with rapid recurrence and progression within 3 months into a glioblastoma.

Case report

A 12-year-old female patient presented with a 2-week history of neck pain with progressive left upper and lower extremity weakness and numbness. Motor examination revealed weakness in her left arm with 3/5 strength in the hand, triceps and deltoid, and weakness in her left leg with 4/5 strength in the quadriceps, hamstring, and dorsiflexors of the left foot. Abnormal reflexes were not detected. Sensory examination revealed dysesthesias without clear dermatomic distribution and disturbed proprioception on the left side. Cranial nerves and higher mental functions were intact. Slight dysmetria on the left side and gait disturbance were observed (walking only with help possible).

Magnetic resonance imaging (MRI) revealed an intradural intramedullary lesion extending from the lower edge of C2 to the upper edge of C7, located predominantly along the posterior aspect of the thecal sac, causing anterior displacement and compression of the spinal cord. The lesion appeared hyperintense on T2-weighted MR imaging (T2WI) and hypointense on T1-weighted imaging (T1WI), with enhancement on the postgadolinium scans (Fig. 1). MRI of the brain and the rest of the neuraxis showed no further lesions.

The patient underwent laminoplasty extending from C3 to C6, in prone position with three-pin fixation of the head in a Mayfield holder. After opening the dura, arachnoid thickening, swelling of the spinal cord, and dark discoloration were observed (Fig. 2). The tumor appeared noncystic and gelatinous. Resection was performed under neurophysiological motor and sensory monitoring and had to stop when motor evoked potentials started to get affected. The

surgeon's estimation of resection was >95% of the tumor (Fig. 2b). Despite the use of an ultrasonic aspirator, it was attempted to obtain as much of the tumor as possible for pathology.

Histopathology revealed a glial tumor with monophasic pattern in a myxoid background, with angiocentric accumulation at places and hyalinized vessels (Fig. 3a, b, and c). Cells were glial fibrillary acidic protein (GFAP) and S-100 positive, and Rosenthal fibers or eosinophilic granular bodies were absent. These findings were consistent with the diagnostic criteria for PMA [9, 10, 22, 23, 27, 36]. The staining with the MIB-1 antibody revealed a labeling index of up to 20% at places, which in combination with necrotic regions detected, might indicate a more aggressive behavior. This highly elevated Ki-67 was worrisome that a more aggressive neoplasm was missed, and the whole specimen sent was therefore reexamined, and a second external opinion for confirmation of diagnosis was obtained.

Postoperatively, neurological examination revealed a progressively improving motor strength on the left side, reaching 4/5 in the left deltoid and triceps and 5/5 in the left hand within the first five postoperative days. The left leg recovered full strength. Slight dysesthesias and numbness remained. Physiotherapeutic rehabilitation before discharge resulted in walking independently. Postoperative MRI after 45 days revealed a slight spot of residual enhancement on postgadolinium scans (Fig. 4b), but the patient was asymptomatic at that time apart from slight intermittent dysesthesias of the left arm. After consulting with a radiation oncologist and a pediatric oncologist and discussing further treatment options with the family, close clinical follow-up and serial neuroimaging with MRI of the whole neuraxis in 3-month intervals postoperatively were decided.

Twelve weeks after the operation, the patient presented with rapid neurological deterioration. While being fully mobilized and able to visit school, within 48 h, severe gait disturbance and progressive tetraparesis (left upper extremity 2/5, all other extremities 3/5) appeared. Walking and standing without help were no longer possible. Magnetic resonance imaging confirmed the suspicion of recurrence, revealing an intradural intramedullary lesion at C2 to C7 levels, compressing the spinal cord. The lesion appeared hyperintense on T2-weighted MR imaging (T2WI) and hypointense on T1-weighted MR imaging (T1WI), with enhancement on the postgadolinium scans (Fig. 4c). In comparison to the first preoperative MRI, the enhancing part of the lesion was more extensive (Fig. 4a and c). MR imaging of the brain and the rest of the neuraxis showed no further lesions.

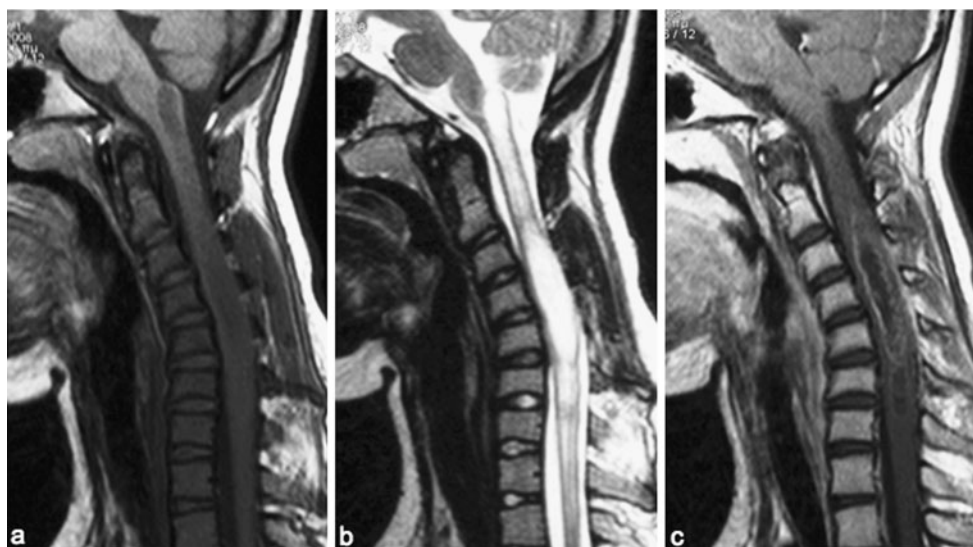
The patient underwent urgent re-operation. This time, laminectomy of C2–C7 was performed, in order to decompress the spinal cord. After opening the dura, the

Table 1 Literature review by author of the seven spinal cord cases of pilomyxoid astrocytoma (PMA) reported. Location, treatment choice, and outcome are presented, where available. Including the present case, only five pediatric cases have been reported

Author (year)	Age (gender)	Location	Treatment	Outcome
1 Komotar et al. (2005) [18]	6 years old (m)	Intradural T9–T11 with diffuse abnormal signal up to C2–C3	T2 laminectomy—partial resection 4× decompressive laminectomies and cyst/tumor removal Posterior allograft fusion External beam radiation—chemotherapy	At 5-year follow-up: absent lower extremities sensation, normal strength in upper extremities, stable scoliosis Residual enhancement in MRI throughout the spine
2 Komotar et al. (2005) [18]	8 years old (m)	Intradural T9–T12 with syrinx below and above	Thoracic laminectomy, GTR, laminoplasty	At 9-months follow-up: neurologically stable, recurrent back and left leg pain
3 Komotar et al. (2005) [18]	Newborn (m)	Abnormal signal from 4 th ventricle into cervical spine. Hydrocephalus, IVH (grade 2), T2 hyperintensity of the entire spinal cord, enhancement at level of medulla	Monitored with MRI at 3-month intervals Selker reservoir T1–T3 laminectomy and biopsy	New enhancement on spine MRI Stable after 3.5 years VP-shunt with multiple revisions Tumor untreated—Supportive care Modest tumor increase on MRI
4 Mendiratta-Lala et al. (2007) [25]	29 years old (f)	Intradural extradural, midcervical to lumbosacral	Laminectomy C5–T1, partial resection External beam radiation from T1 to L3	—
5 Sajadi et al. (2008) [29]	45 years old (f)	Intradural, foramen magnum to C5	C1–C2 laminectomy, tumor biopsy Radiation	Fatal one month after admission
6 Arulrajah et al. (2008) [3]	Child (f)	Cervical cord with diffuse leptomeningeal metastasis involving brain and spinal cord	—	Peritoneal carcinomatosis 2 years after VP-shunt
7 Present case	12 years old (f)	Intradural C2–C7	Laminectomy C3–C7, GTR, laminoplasty C3–C7 Laminectomy C2–C7, partial resection Radiation—chemotherapy	Recurrence after 3 months Fatal 12 months after initial diagnosis

m male, *f* female, *GTR* gross total resection, *IVH* intraventricular hemorrhage, *VP-shunt* ventriculoperitoneal shunt

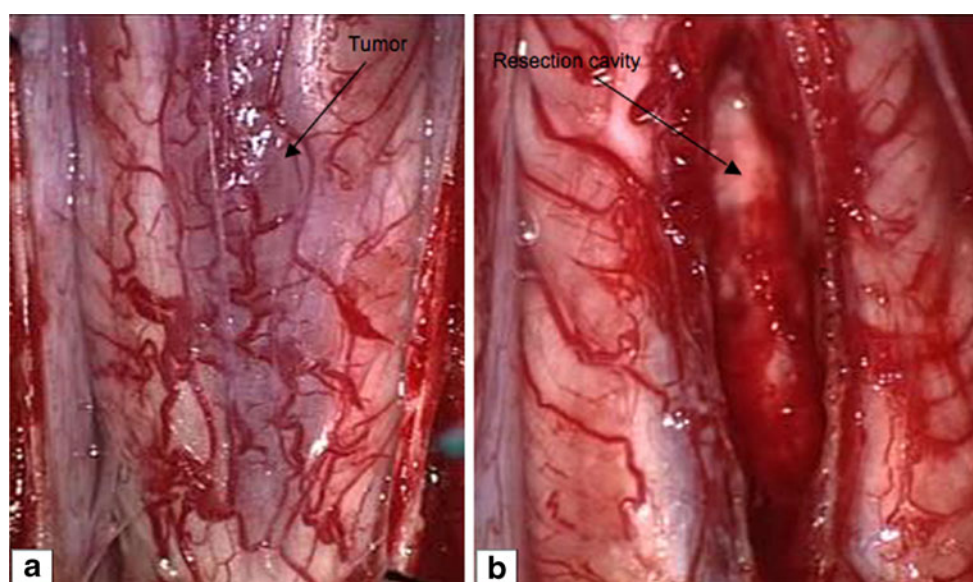
Fig. 1 Preoperative MRI of the cervical spine showing the intramedullary lesion: **a** Low signal in T1 weighted sagittal, **b** High signal in T2 weighted sagittal, **c** Enhancing tumor margin in T1 weighted plus gadolinium sagittal



tumor had similar macroscopic characteristics as before. True borders with normal tissue were not identified, as the resection effort was not as aggressive as in the first operation. Neurophysiological monitoring was not available due to the emergency of the operation. Subtotal removal of the tumor was attempted, with the goals to decompress, reduce tumor load in the sense of cytoreduction and gain new material for histology and further treatment planning. Once again, the ultrasonic aspirator was used, although it was attempted to obtain as much tumor specimens as possible for pathology.

Postoperatively, the patient improved neurologically, achieving antigravitational movement in the left upper extremity (3/5) and almost normal muscle strength in all other extremities (4/5). Walking became possible again under physiotherapy within the first postoperative week.

Fig. 2 Intra-operative photos of the cervical spinal cord at level C2 to C6 (cranial direction towards the bottom of the picture, as intra-operatively in prone patient position): **a** After opening the dura, the tumor is recognized with dark discoloration, **b** resection cavity



The patient was discharged on the ninth postoperative day, after an early postoperative MRI. Histopathology was consistent with a glioblastoma this time (Fig. 3d), showing necrosis and a Ki-67 up to 45%, and very few sites with myxoid features were detected. Hence, adjuvant radiotherapy was arranged, followed by chemotherapy (Vincristine, Etoposide, Carboplatin) treatment. The patient completed 10 cycles of chemotherapy without any major adverse effects. Patient outcome was fatal 12 months after the initial diagnosis.

Discussion

PMA represents a recently described histopathological entity, having been recognized since 2007 as a new variant in the WHO classification [27]. Its close relation-

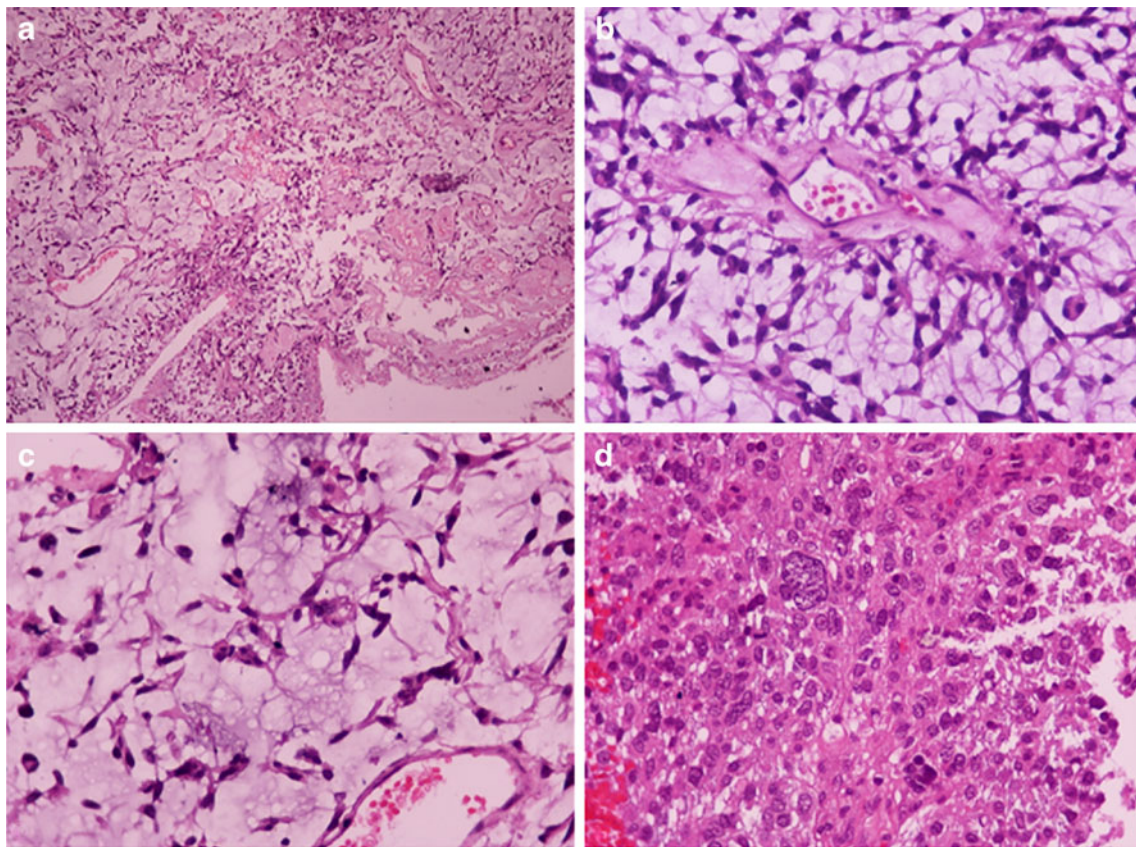


Fig. 3 Histopathology, hematoxylin and eosin (H.E.) stain: **a** Specimen from the first operation: pilomyxoid astrocytoma. Monomorphous, bipolar cells in a myxoid matrix, **b** Specimen from the first operation: PMA with angiocentric accumulation, **c** specimen from the

first operation: PMA (H.E. $\times 400$), **d** specimen from the second operation: Glioblastoma; cellular, astrocytic tumor with pleomorphic nuclei and giant-cell forms. H.E. $\times 400$

Fig. 4 Serial MRI imaging of the cervical spine in T1 weighted plus gadolinium sagittal: **a** preoperative MRI at initial presentation, **b** postoperative MRI (45 days after the first operation), showing the resection and a slight spot of residual tumor, **c** after clinical deterioration showing recurrence (85 days after the first operation) with extensive enhancement, as opposed to the initial presentation and the previous MRI



ship to PA is underscored by a report of two patients with neurofibromatosis type 1 [27, 33]. However, it is differentiated from PA through specific histologic features. Pilomyxoid astrocytoma shows a monomorphous population of tumor cells in a homogeneously myxoid background with angiocentric accumulation [27]. The absence of Rosenthal fibers and eosinophilic granular bodies is characteristic [22]. Necrosis within the tumor occurs in PMA as opposed to PA and PMA is more likely to invade other structures [15, 36]. PMA recurs sooner and more frequently than PA, and CSF dissemination is more common [15, 20–23, 36]. In general, PMA has a more aggressive biological behavior, with a significantly shorter progression free and overall survival than PA [23], as well as possible cerebrospinal spread [1]. After a comparison of PMA and PA as well as a genome copy number analysis, Jeon et al. [19] suggested that pilomyxoid astrocytoma might be a histopathologically and genetically related, aggressive variant of pilocytic astrocytoma with partially different genetic alterations.

Neuroimaging characteristics of this neoplasm are already described in literature [2, 23, 25, 30]. The lesion is usually isointense on T1-weighted MRI and hyperintense on T2-weighted MRI, with variable, but usually solid enhancement on postgadolinium scans [2, 23, 29]. However, since no radiological criteria that reliably differentiate PMA from PA have been identified yet, the diagnosis of PMA is made from the histopathological findings [20, 23, 26, 29]. Serial neuroimaging in PMA is reported to show early progression of predominantly solid and later progression of predominantly cystic component [20].

Location of PMA is usually in the hypothalamic/chiasmatic region. Nevertheless, there are reports in various other locations [8, 26]. Only four patients with spinal cord PMA have been reported in literature in the pediatric population (Table 1) [3, 22]. In adults, two patients with spinal PMA have been reported so far [29, 34]. There are also reports of juvenile PMA with spinal metastases, probably due to CSF dissemination [13, 37].

The mean age of diagnosis of PMA is 18 months, although it can present in early childhood [22, 36]. However, recognition of the PMA pattern in older children and adults expands the currently accepted epidemiology for this lesion [8, 24, 29, 34]. Furthermore, there seem to exist even patients with familial PMA [34].

Currently, the management of PMA, as with pediatric low-grade astrocytomas, remains controversial; explicitly for PMA, there is no standard of care so far [23]. Surgery is often the primary treatment strategy, aiming at gross total resection, provided it can be performed without excessive morbidity [4, 11, 16, 17, 32]. Usually, the lesions are not amenable to total resection because of high

morbidity of surgery, but gross total resection remains the most reliable predictor of favorable outcome [16, 17, 32, 40]. In order to achieve this, neurophysiological monitoring is of immense value. Management strategies also involve surgical debulking, and patients usually require adjuvant chemotherapy or radiotherapy, given the higher chance of local recurrence and CSF dissemination [9, 36]. Adjuvant therapy is frequently indicated for tumor recurrence, partially resected tumors causing neurological impairment and partially resected tumors with growth on follow-up imaging [23]. Enting et al. [14] reported of radiotherapy plus concomitant and adjuvant temozolomide for leptomeningeal pilomyxoid astrocytoma. There are reports claiming maturation of PMA after adjuvant therapy to a more benign tumor with biphasic pattern and Rosenthal fibers [15]. In a series of five patients, Tsugu et al. [37] reported of their positive impression of the value of chemotherapy mainly with the combination of cisplatin/carboplatin and etoposide; even if initial chemotherapy is ineffective, they recommend continued cisplatin/carboplatin-based chemotherapy with new drug combinations. Cytogenetic analyses studies report of a possible rearrangement of the Breakpoint cluster region (BCR) gene that could act in a similar way to chronic myeloid leukemia with formation of a chimeric tyrosine kinase protein, suggesting a possible use of inhibitors of tyrosine kinase proteins as an alternative treatment approach in patients with refractory or disseminated PMA [28].

The present case report is of interest for the following reasons. First of all, it is an uncommon entity, recently described and officially recognized in the WHO classification, in need of systematic documentation, so that patients from different institutions can be accumulated and analyzed, in order to develop diagnostic criteria and treatment strategies. Hence, the already existing efforts for registries ought to be encouraged [12, 35]. Secondly, we only came across six patients with PMA within the spinal cord in English literature so far, this being the seventh (Table 1). Four of the reports of spinal cord PMA were in the pediatric age group but in children less than 8 years of age; two patients were adults, 29 and 45 years of age; the reported patient is a 12-year-old girl, indicating the variety of ages at diagnosis. Furthermore, this is a patient without major extent or dissemination at diagnosis, which was amenable to resection (>95%) and with clear improvement of the neurological status of the patient postoperatively. Last but not least, this is the only spinal PMA with rapid recurrence and progression within 3 months into a glioblastoma, which is documented with neuroimaging, intra-operative, and corresponding histopathological findings.

Malignant transformation (MT) of low-grade gliomas in children is unusual and is linked to a poor prognosis

[38]. The pathophysiology of transformation for PMA in particular remains unclear. The inconsistency due to the accumulation of a heterogenous group with distinct histopathological features and biological behavior under the term low-grade might lie underneath [6, 7, 31]. Dedifferentiation is a biologic phenomenon observed in low-grade gliomas independent of the treatment received [39]. Radiotherapy may control symptoms and delay time to tumor recurrence but does not seem to have any effect on MT [7, 38, 39]. Unlike adults, little is known about the mechanisms of tumorigenesis of high-grade gliomas in children [5]. While adults with WHO grade II infiltrative astrocytoma frequently experience MT (more than 90%), the long-term risk of MT of these neoplasms in children is rare [6, 38]. In a clinical and molecular analyses, Broniscer et al. [6] estimated the risk of MT in low-grade gliomas in children as less than 10%. In this study, the median latency for the development of MT was 5.1 years, the median survival after MT was 0.6 years, the histologic diagnoses after transformation were commonly glioblastomas, and the molecular abnormalities occurring during MT of low-grade gliomas in children were similar to those observed in primary and secondary glioblastomas in adults [6]. Since the features of low-grade gliomas appear to be closely related with the molecular and cellular biologic characteristics [7], large series of children with MT of low-grade gliomas (and PMA in specific) involving clinical, molecular, and outcome analyses are warranted to elucidate the pathophysiological mechanisms [6].

A recent literature report of a female child with cervical cord PMA with leptomeningeal metastasis involving the brain and spinal cord and peritoneal carcinomatosis through a ventriculoperitoneal shunt confirms the aggressive behavior of this neoplasm [3]. However, in our patient, the extremely short interval of recurrence and conversion raises the question of a possible sampling error of a higher-grade glioma at the initial surgery. In spite of the PMA histopathological characteristics, the high value of Ki-67 from the first operation is worrisome and may be indicative of a higher-grade tumor from the start. We attempted to send as much material as possible during both operations for pathology. Nevertheless, the use of an ultrasonic aspirator and suction cannot guarantee examination of the entire tumor. An external review and confirmation of the pathology were therefore sought. The possibility of a sampling error is always one that should be kept in mind in classifying a tumor as low-grade glioma, especially when the specimen comes from biopsies or partial resection. The cumulative incidence of malignant transformation may be overestimated by the inadequate representation of areas with more malignant characteristics at the time of diagnosis of low-grade gliomas [6].

The combination of these facts raises the question of the preferred further treatment options. Whether adjuvant therapy in the form of chemotherapy or radiation is indicated and at which timing remains open for discussion in the neurosurgical community [7]. Radiation may delay time to tumor recurrence, but it neither increases nor decreases the likelihood of malignant transformation [39]. Given the age of the patient, her clinical and radiological findings at the time and respecting family wishes, we initially chose the strategy of close follow-up with regular clinical examinations and serial MRI of the whole neuraxis at 3-month intervals or immediately at neurological deterioration, keeping the option of adjuvant therapy open for a possible recurrence or dissemination. Obviously, the aggressive biological behavior of this tumor proved this choice to be inadequate retrospectively. Adjuvant therapy should have been considered after the first operation, since the tumor (mainly due to its location) was not amenable to a true gross total resection judging from the postoperative MRI. Furthermore, one could suggest that PMAs with worrisome histopathological or clinical findings, such as elevated Ki-67 or rapid deterioration, should be considered for adjuvant therapy at an early stage of diagnosis.

The importance of an interdisciplinary tumor board for individualized decision-making on adjuvant radiotherapy and/or chemotherapy is emphasized by this case. Interactive consultation with radiation oncology, pediatric oncology and pathology, especially when a high proliferation index (Ki-67) is documented, is essential in particular for uncommon tumors like PMA, which do not have any standard ordinary treatment protocol. After all, low-grade gliomas are a heterogenous group of neoplasms, whose natural history depends primarily on pathologic type and patient age, and there is still ongoing research and debate on treatment strategies and their timing [7].

In conclusion, this case report confirms that pilomyxoid astrocytomas are not necessarily limited to the hypothalamic/chiasmatic region and moreover accentuates the aggressive biological behavior of these neoplasms. Furthermore, the assignment to WHO grade II might not always reflect the less favorable prognosis of some PMAs and a lower threshold for early adjuvant therapy might be indicated, especially when histopathology is suspicious, or a sampling error cannot be excluded. Registering these patients and their outcome might provide a more profound insight into the entity and lead to more evidence-based treatment regimens.

Acknowledgements The authors wish to thank Prof. J. C. Tonn (Department of Neurosurgery, LMU, Munich, Germany) and his department for providing an external second opinion on the histopathological diagnosis.

Conflict of interest The authors declare that they have no conflict of interest.

References

- Amatya VJ, Akazawa R, Sumimoto Y, Takeshima Y, Inai K (2009) Clinicopathological and immunohistochemical features of three pilomyxoid astrocytomas: comparative study with 11 pilocytic astrocytomas. *Pathol Int* 59:80–85
- Arslanoglu A, Cirak B, Horska A, Okoh J, Tihan T, Aronson L, Avellino AM, Burger PC, Yousem DM (2003) MR imaging characteristics of pilomyxoid astrocytomas. *AJNR Am J Neuro-radiol* 24:1906–1908
- Arulrajah S, Huisman TA (2008) Pilomyxoid astrocytoma of the spinal cord with cerebrospinal fluid and peritoneal metastasis. *Neuropediatrics* 39:243–245
- Bauman G, Lote K, Larson D, Stalpers L, Leighton C, Fisher B, Wara W, MacDonald D, Stitt L, Cairncross JG (1999) Pretreatment factors predict overall survival for patients with low-grade glioma: a recursive partitioning analysis. *Int J Radiat Oncol Biol Phys* 45:923–929
- Broniscer A, Gajjar A (2004) Supratentorial high-grade astrocytoma and diffuse brainstem glioma: two challenges for the pediatric oncologist. *Oncologist* 9:197–206
- Broniscer A, Baker SJ, West AN, Fraser MM, Proko E, Kocak M, Dalton J, Zambetti GP, Ellison DW, Kun LE, Gajjar A, Gilbertson RJ, Fuller CE (2007) Clinical and molecular characteristics of malignant transformation of low-grade glioma in children. *J Clin Oncol* 25:682–689
- Brown PD (2006) Low-grade gliomas: the debate continues. *Curr Oncol Rep* 8:71–77
- Buccoliero AM, Gheri CF, Maio V, Moncini D, Castiglione F, Garbini F, Sanzo M, Taddei A, Genitori L, Taddei GL (2008) Occipital pilomyxoid astrocytoma in a 14-year-old girl—case report. *Clin Neuropathol* 27:373–377
- Burger PC, Cohen KJ, Rosenblum MK, Tihan T (2000) Pathology of diencephalic astrocytomas. *Pediatr Neurosurg* 32:214–219
- Ceppa EP, Bouffet E, Griebel R, Robinson C, Tihan T (2007) The pilomyxoid astrocytoma and its relationship to pilocytic astrocytoma: report of a case and a critical review of the entity. *J Neurooncol* 81:191–196
- Cirak B, Horska A, Barker PB, Burger PC, Carson BS, Avellino AM (2005) Proton magnetic resonance spectroscopic imaging in pediatric pilomyxoid astrocytoma. *Childs Nerv Syst* 21:404–409
- Cohen K, Burger P, C. E (2010) Pilomyxoid Astrocytoma Registry. The Johns Hopkins University. <http://www.hopkinskimmelcancercenter.org/index.cfm/cid/1759>. Accessed 19 March 2010
- Darwish B, Koleda C, Lau H, Balakrishnan V, Wickremesekera A (2004) Juvenile pilocytic astrocytoma ‘pilomyxoid variant’ with spinal metastases. *J Clin Neurosci* 11:640–642
- Enting RH, van der Graaf WT, Kros JM, Heesters M, Metzmaekers J, den Dunnen W (2006) Radiotherapy plus concomitant and adjuvant temozolomide for leptomeningeal pilomyxoid astrocytoma: a case study. *J Neurooncol* 80:107–108
- Fernandez C, Figarella-Branger D, Girard N, Bouvier-Labit C, Gouvernet J, Paz Paredes A, Lena G (2003) Pilocytic astrocytomas in children: prognostic factors—a retrospective study of 80 cases. *Neurosurgery* 53:544–553, discussion 554–545
- Finlay JL, Wisoff JH (1999) The impact of extent of resection in the management of malignant gliomas of childhood. *Childs Nerv Syst* 15:786–788
- Gajjar A, Sanford RA, Heideman R, Jenkins JJ, Walter A, Li Y, Langston JW, Muhlbauer M, Boyett JM, Kun LE (1997) Low-grade astrocytoma: a decade of experience at St. Jude Children’s Research Hospital. *J Clin Oncol* 15:2792–2799
- Houten JK, Cooper PR (2000) Spinal cord astrocytomas: presentation, management and outcome. *J Neurooncol* 47:219–224
- Jeon YK, Cheon JE, Kim SK, Wang KC, Cho BK, Park SH (2008) Clinicopathological features and global genomic copy number alterations of pilomyxoid astrocytoma in the hypothalamus/optic pathway: comparative analysis with pilocytic astrocytoma using array-based comparative genomic hybridization. *Mod Pathol* 21:1345–1356
- Komakula ST, Fenton LZ, Kleinschmidt-DeMasters BK, Foreman NK (2007) Pilomyxoid astrocytoma: neuroimaging with clinicopathologic correlates in 4 cases followed over time. *J Pediatr Hematol Oncol* 29:465–470
- Komotar RJ, Burger PC, Carson BS, Brem H, Olivi A, Goldthwaite PT, Tihan T (2004) Pilocytic and pilomyxoid hypothalamic/chiasmatic astrocytomas. *Neurosurgery* 54:72–79, discussion 79–80
- Komotar RJ, Carson BS, Rao C, Chaffee S, Goldthwaite PT, Tihan T (2005) Pilomyxoid astrocytoma of the spinal cord: report of three cases. *Neurosurgery* 56:191
- Komotar RJ, Mocco J, Jones JE, Zacharia BE, Tihan T, Feldstein NA, Anderson RC (2005) Pilomyxoid astrocytoma: diagnosis, prognosis, and management. *Neurosurg Focus* 18:E7
- Komotar RJ, Mocco J, Zacharia BE, Wilson DA, Kim PY, Canoll PD, Goodman RR (2006) Astrocytoma with pilomyxoid features presenting in an adult. *Neuropathology* 26:89–93
- Komotar RJ, Zacharia BE, Sughrue ME, Mocco J, Carson BS, Tihan T, Otten ML, Burger PC, Garvin JH, Khandji AG, Anderson RC (2008) Magnetic resonance imaging characteristics of pilomyxoid astrocytoma. *Neurol Res* 30:945–951
- Linscott LL, Osborn AG, Blaser S, Castillo M, Hewlett RH, Wieselthaler N, Chin SS, Krakenes J, Hedlund GL, Sutton CL (2008) Pilomyxoid astrocytoma: expanding the imaging spectrum. *AJNR Am J Neuroradiol* 29:1861–1866
- Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, Scheithauer BW, Kleihues P (2007) The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol* 114:97–109
- Melendez B, Fiano C, Ruano Y, Hernandez-Moneo JL, Mollejo M, Martinez P (2006) BCR gene disruption in a pilomyxoid astrocytoma. *Neuropathology* 26:442–446
- Mendiratta-Lala M, Kader Ellika S, Gutierrez JA, Patel SC, Jain R (2007) Spinal cord pilomyxoid astrocytoma: an unusual tumor. *J Neuroimaging* 17:371–374
- Morales H, Kwock L, Castillo M (2007) Magnetic resonance imaging and spectroscopy of pilomyxoid astrocytomas: case reports and comparison with pilocytic astrocytomas. *J Comput Assist Tomogr* 31:682–687
- Perry A (2003) Pathology of low-grade gliomas: an update of emerging concepts. *Neuro Oncol* 5:168–178
- Reddy AT, Packer RJ (1998) Pediatric central nervous system tumors. *Curr Opin Oncol* 10:186–193
- Rodriguez FJ, Perry A, Gutmann DH, O’Neill BP, Leonard J, Bryant S, Giannini C (2008) Gliomas in neurofibromatosis type 1: a clinicopathologic study of 100 patients. *J Neuropathol Exp Neurol* 67:240–249

34. Sajadi A, Janzer RC, Lu TL, Duff JM (2008) Pilomyxoid astrocytoma of the spinal cord in an adult. *Acta Neurochir (Wien)* 150:729–731
35. SIOP (2004) Multicenter Study for Children and Adolescents with Low Grade Gloma. International Society of Paediatric Oncology. <http://siop-igg.cineca.org/>. Accessed 19 March 2010
36. Tihan T, Fisher PG, Kepner JL, Godfraind C, McComb RD, Goldthwaite PT, Burger PC (1999) Pediatric astrocytomas with monomorphous pilomyxoid features and a less favorable outcome. *J Neuropathol Exp Neurol* 58:1061–1068
37. Tsugu H, Oshiro S, Yanai F, Komatsu F, Abe H, Fukushima T, Nomura Y, Matsumoto S, Nabeshima K, Takano K, Utsunomiya H (2009) Management of pilomyxoid astrocytomas: our experience. *Anticancer Res* 29:919–926
38. Unal E, Koksall Y, Cimen O, Paksoy Y, Tavli L (2008) Malignant glioblastomatous transformation of a low-grade glioma in a child. *Childs Nerv Syst* 24:1385–1389
39. van den Bent MJ, Afra D, de Witte O, Ben Hassel M, Schraub S, Hoang-Xuan K, Malmstrom PO, Collette L, Pierart M, Mirimanoff R, Karim AB (2005) Long-term efficacy of early versus delayed radiotherapy for low-grade astrocytoma and oligodendroglioma in adults: the EORTC 22845 randomised trial. *Lancet* 366:985–990
40. Wisoff JH, Boyett JM, Berger MS, Brant C, Li H, Yates AJ, McGuire-Cullen P, Turski PA, Sutton LN, Allen JC, Packer RJ, Finlay JL (1998) Current neurosurgical management and the impact of the extent of resection in the treatment of malignant gliomas of childhood: a report of the Children's Cancer Group trial no. CCG-945. *J Neurosurg* 89:52–59