Diffuse spinal leptomeningeal spread of a pilocytic astrocytoma in a 3-year-old child

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Abstract

Pilocytic astrocytomas correspond to low-grade gliomas and therefore metastasize exceedingly rare. However, pilocytic astrocytomas are able to and leptomeningeal dissemination may be seen. What are the treatment options of these cases? We present a case report of a 3-year-old child with a pilocytic astrocytoma of the optic chiasm with leptomeningeal dissemination of the spinal meninges. Partial resection of the cerebral tumor has been performed. Since the leptomeningeal dissemination was seen all over the spinal meninges, the child did not undergo further surgical treatment. A wait and watch strategy were followed. Chemotherapy was initiated, if a 25% tumor growth was seen. Leptomeningeal dissemination of a pilocytic astrocytoma is seen so infrequently that no standard therapy is established. Since these metastases may occur even up to 2 decades after primary tumor resection, long-term follow-up is indicated. In case of spinal metastases, surgical treatment should be performed if feasible. Otherwise observation should be possessed and/or chemotherapy should be initiated.

Introduction

Leptomeningeal spread of primary tumors of the central nervous system (CNS) through cerebrospinal fluid (CSF) is uncommon. It may appear in tumors like medulloblastomas [World Health Organization (WHO) grade IV], ependymomas and high-grade gliomas, but exceedingly rare in low-grade gliomas.[1] Up to now, only nine cases of pilocytic astrocytoma with dissemination in the spinal meninges have been published. Interestingly, only three of these nine cases have been described in children;[2-4] the other six cases concerned adult patients.[1,5-9] This may be due to the fact that intradural extramedullary spinal dissemination occurred even 10-20 years after the primary surgery of the cerebral tumor. Although the first report of spinal seeding of pilocytic astrocytomas was published in 1976,[10] no standard treatment modality is established until today, due to its rarity. Here, we report the case of a 3-year-old boy with a pilocytic astrocytoma of the optic chiasm with contact to the third ventricle, hypothalamic invasion and leptomeningeal dissemination in the spinal meninges.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Patient consent

The patient's guardian (the father) has consented to the submission of the case report for submission to the journal.

Case Report

A 3-year-old child presented to our department after he had undergone a surgery 5 months ago in another country to obtain a biopsy from the tumor around the optic nerve. Because of bleeding complications, the colleagues performed only a biopsy and a further tumor removal was aborted. Histological examination of this biopsy (realized in the country where the operation was performed) revealed a pilocytic astrocytoma. Now, six months after the first operation, the patient was admitted to our hospital. After the first surgery and before the diagnosis was made, the child developed cry attacks, affective changes, loss of satiety, continuous thirsty, hyperactivity and sleep disturbance. We renewed the cranial magnetic resonance imaging (MRI) and performed additionally an MRI of the spine (Figure 1). The tumor did not show any further growth in the 5 months period, nevertheless the tumor was still large and a surgical reduction of the tumor was indicated. In the MRI of the spine we saw multinodular tumors (intradural/ extramedullary), which indicated a leptomeningeal spread. Since the tumor was invading the hypothalamus, we only removed the large intracranial tumor partially in order to prevent hormonal insufficiencies. We did not remove any of the spinal lesions because of the wide spread of the tumor.

On neuropathological examination the scanty tumor fragments showed loosely textured multipolar cells with round to oval, cytologically bland nuclei and microcysts. Cellularity was low to moderate. Focally, a basophilic mucoid matrix was seen. The tumor lacked Rosenthal fibers, eosinophilic granular bodies and hyaline droplets. No satisfying angiocentric cell arrangement was observed. The scanty fragments showed no mitoses and no necrosis. Only few slightly pathologic blood vessels were seen. The tumor cells showed a strong positivity for the glial fibrillary acidic protein (GFAP). MIB-1 labeling was typically low, showing proliferating activity in up to 2% of tumor cells.

Because of the location of the tumor in the hypothalamic/chiasmic region, the focal basophilic myxoid matrix und lack of Rosenthal fibers, eosinophilic granular bodies and hyaline droplets, the possibility of a pilomyxoid astrocytoma (WHO grade II) was considered. However, since we did not observe a markedly mucoid matrix and a predominantly angiocenctric cell arrangement, which is typical for this entity, the tumor was classified as pilocytic astrocytoma (WHO grade I).

Liquor obtained from lumbar puncture revealed some tumor cell aggregates that varied in size and showing tumor cells with round to oval cytologically bland nuclei and rarely definable cytoplasms, leading to the diagnosis of meningeosis gliomatosa. In accordance with the radiological finding, the cytomorphology of the tumor cells was consistent with that of the glial tumor described above.

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Discussion

Pilocytic astrocytomas are low-grade gliomas corresponding to WHO grade I with an excellent prognosis, particularly if complete resection can be achieved. The present case reveals a cerebral low-grade astrocytoma growing from the optic chiasm towards the hypothalamus and the third ventricle with leptomeningeal spreading all over the spine through the CSF. Up to now, only two cases concerning pilocytic astrocytomas of the optic chiasm metastasizing into the spine have been published in the literature[3,9] although the WHO classification of tumors of the CNS described the hypothalamic as the usual primary site of neuraxial seeding within this tumor entity. Other pilocytic astrocytomas with spinal dissemination occurred in adult patients almost two decades after the primary surgical treatment emphasizing a long-term follow-up in patients with diagnosed pilocytic astrocytoma.[6] Nevertheless, the prognosis of this tumor remains excellent after resection of a solitary spinal metastasis since the proliferative activity is low.[6] Interestingly, despite metastasizing, these tumors do not seem to show any signs of secondary malignisation.[1,3] Indeed, very few examples of pilocytic astrocytoma undergoing malignant changes have been reported.[11] Since most of them had previously undergone radiation therapy, it should be taken into account that radiation may promote malignant transformation.

One reported case even reveals a patient with a cervical low-grade astrocytoma with a cerebral metastasis, indicating the possibility of such history and also emphasizing that - to prevent further metastases - metastases should be rejected if possible.[2]

In the present case we performed a partial resection of the cerebral tumor, since invasion into the hypothalamus did not allow complete resection. The CSF showed tumor cells in neuropathological examination. Radiologically, an intradural contrast enhancement through a long distance was seen, building a thin film of tumor cells, which did not deliver a specific target for surgical resection. Under these circumstances we did not perform tumor resection around the nerve roots S1 and S2 where the tumor seemed to be solid. In addition to our case, two of three pediatric cases with spinal dissemination occurred after optic chiasm astrocytomas,[3,7,9] revealing that contact to the ventricular system seems to increase the possibility of spinal cord dissemination. Because of the rarity of dissemination within this benign tumor entity, a standardization of treatment misses. Shapiro *et al.*[10] advocate an aggressive surgical treatment, while Fellgiebel *et al.* admit that treatment of these cases is always difficult because of the lack of a stan-

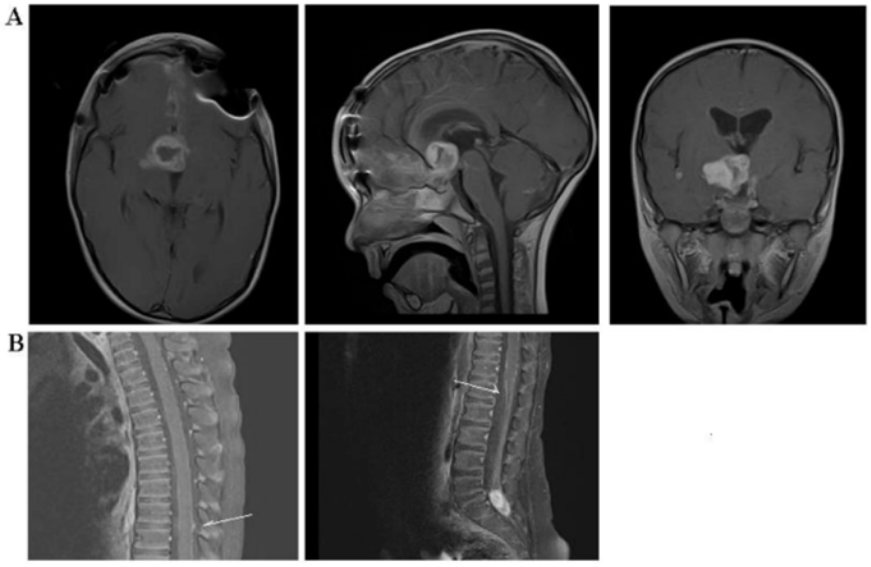

Figure 1. Pilocytic astrocytom of the opticchiasm disseminated leptomeningeally into the spine. A) Cranial magnetic resonance image shows the pilocytic astrocytoma growing from the optic chiasm and invading the hypothalamus and the third ventricle; B) Leptomeningeal contrast enhanced areas in the spine with a node around the nerve roots S1 and S2.

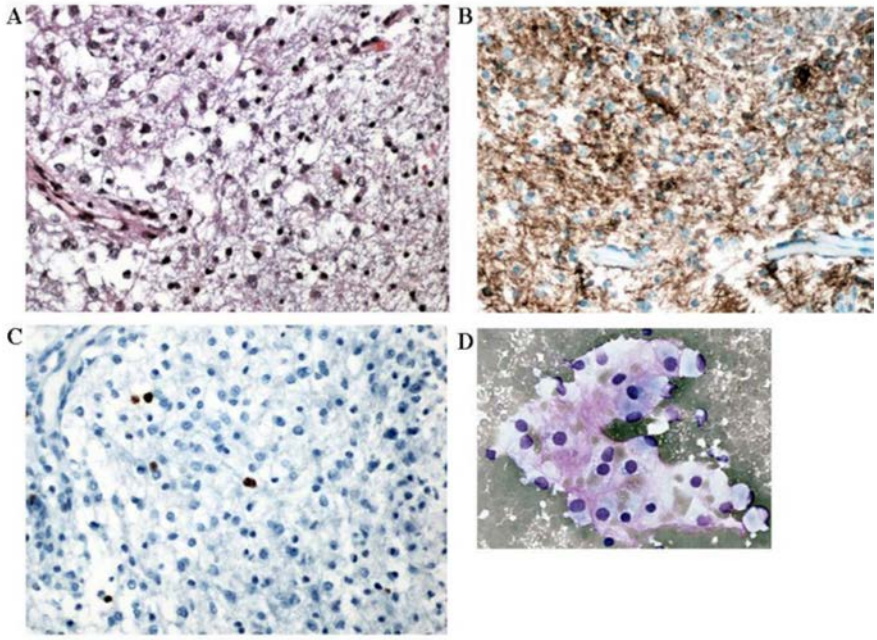

Figure 2. Histological presentation of the pilocytic astrocytoma. A) Loosely textured multipolar cells with round to oval, cytologically bland nuclei in a microcystic matrix without Rosenthal fibers and eosinophilic granular bodies. Mitotic figures and necrosis are absent (hematoxylin&eosin staining, 20-fold magnification); B) The tumor cells show a strongly positive reaction for glial fibrillary acidic protein (20-fold magnification); C) Ki67 staining reveals few proliferating tumor cells (20-fold magnification); D) Liquor obtained from lumbar puncture with few tumor fragments, varying in size and cell count. Cell morphology is consistent with a glial tumor in terms of meningeosis gliomatosa (May-Grünwald-Giemsa, 20-fold magnification).

dard therapy scheme.[8]

Chemotherapy does not seem to be the optimum therapeutic approach since at least vincristine and carboplatin did not exhibit good treatment results in one patient.[5] Again, because of the very few reports it is impossible to conclude if a therapeutic approach with chemotherapy could be efficient or not. Since in our case the meninges were infested by tumor over a long distance, complete surgical resection was not possible. Therefore, we decided, after many consultations in the pediatric oncology department in our hospital as well as in other expert pediatric oncology centers to choose a chemotherapeutic approach and the tumor growth should be observed in the 3-month-follow-up. As the child moved with his Family to another city, the child was admitted there to another hospital for the further treatment, where the colleagues decided to follow the wait and watch strategy and no chemotherapy was initiated. A 3-month follow-up MRI did not show any further growth of the tumor, the patient had no complaints and therefore chemotherapy is not needed.

Conclusions

Leptomeningeal dissemination of pilocytic astrocytomas into the spine is rare. Even two decades after resection of the primary tumor metastases of the spine could be observed. Fortunately, there is usually no secondary malignisation. Long-term follow-up is important for early detection of multifocal spreading of pilocytic astrocytomas and MRI of the spine should be performed always when the primary pilocytic astrocytoma is in proximity to the ventricular system. Treatment options in cases of spinal dissemination are the surgical tumor resection in cases of solid lesions as a first line therapy, we recommended that further follow-up and observation of tumor growth and/or chemotherapy, if the tumor is disseminated over a great area of leptomeninges.

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