Ten years observation and treatment of multifocal pilocytic astrocytoma

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Abstract

Pilocytic astrocytoma (PA) usually occurs in younger patients. It is a benign, generally well-delineated, WHO grade I tumour with favorable prognosis, which makes it different from diffuse astrocytomas, classified as higher grades of malignancy.

A case study of PA was presented in a young female patient, observed and treated at the Neurosurgical Department for the period of 10 years, during which time she had frequent surgical procedures due to recurrence and dissemination of the tumour. The initial symptom of the disease was epileptic seizure at the age of 16. Neuroradiological study revealed cerebral tumour in the right temporal lobe, then the first temporal lobe surgery followed by re-operation and radiotherapy was performed. The patient developed hydrocephalus, treated with the ventriculo-peritoneal shunt.

After 5 years local recurrence of the tumour appeared in the right temporal region. The patient was operated and the tumour was totally removed. Initially, the histopathological diagnosis of ganglioglioma was suggested for primary tumour, finally the diagnosis of pilocytic astrocytoma for both recurrent and primary tumour was established.

During the next years of observation increasing neurological symptoms in lower limbs developed. Subsequently, the patient reported pain syndrome in lumbosacral and perineal area. Consecutive MRI studies revealed a spinal canal tumours localized at the thoracic level and next at sacral level. The spinal tumour was surgically treated in both locations; the last operation was done 10 years after surgery of the primary temporal lobe tumour. Histopathological examinations of the excised foci from spinal canal revealed neoplasm consistent with WHO grade I pilocytic astrocytoma.

The presented case indicates that despite the spread of the neoplastic process, a histopathologically benign tumour (WHO I grade) allows for long-term survival and observation period. Unfortunately, multifocal tumour involving midline structures causes major neurological symptoms and deficits. In the presented case we dealt now with the ascending spread process and the occurrence of the new foci in both subtemporal and parameningeal spaces inside the cranial cavity. It is a rare clinical manifestation of a disease ever described in the literature.

Key words: pilocytic astrocytoma, temporal lobe tumour, multifocality, subarachnoid spread, hydrocephalus.

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Introduction

Pilocytic astrocytoma (PA) usually occurs in younger patients, the most frequently in children. It is a benign, well-defined astrocytic tumour, which makes it different from diffuse astrocytomas, classified as other WHO grades II-III. The tumour is usually located at the anatomic midline (optic chiasm, optic tract, thalamus, brain stem, cerebellum) [6,26]. If a tumour occurs in an older or adult patient, it is often located in cerebral hemispheres [26].

Histologically, the tumour typically reveals a biphasic tissue pattern consisting of varying proportions of loose microcystic regions containing protoplasmic astrocytic cells and of highly fibrillated areas with elongated piloid cells and GFAP-immunopositivity. Other histological properties are Rosenthal fibres, eosinophilic granular bodies, calcospherites as well as the presence of hyalinized and glomeruloid vessels and frequent involvement of leptomeninges [6,26].

Historically, pilocytic astrocytoma used to be called cerebellar astrocytoma or juvenile pilocytic astrocytoma (JPA) [23,31]. Some cases of the tumour were reported in patients with neurofibromatosis syndrome type 1 (NF 1) [26].

PA are relatively well-circumscribed tumours, growing either exophytic or along the course of nerve fibers, depending of the site of origin. Peculiar, really few, cases encompass the clinical course with the formation of metastatic tumours, which do not demonstrate malignancy in histopathological examination after performed resection, and are classified as WHO grade I [7,8,19,23,26,27]. A benign pilocytic astrocytoma may spread within the ventricular system and inside the spinal canal via fluid spaces [4,12,21], it is also possible for the tumour to grow via ascending pathways. Early detection of tumour expansion, although it is histopathologically benign, is very important due to the subsequent management strategy.

The authors present a very rare case of a patient, in whom PA, initially confined to cerebral hemisphere (number of consecutive tumour foci), spread within the spinal canal leptomeninges and was treated surgically.

Case report

The patient (A.L., female, aged 26) has been observed and clinically controlled for the period of 10 years. The beginning of the disease was in 1998 with an epileptic seizure and intracranial hypertension. During several months preceding the hospitalization, the patient reported learning difficulties and lack of appetite. At admission to the Neurosurgical Department she presented papillary stasis. The brain CT scan revealed the right temporal lobe tumour. The patient underwent surgery of a partial right temporal lobotomy and tumour resection. Due to concomitant cerebral oedema, bone flap was removed during the surgery, the patient was decompressed. Postoperatively, there was paresis of the left upper limb accompanied by central facial nerve paresis; neurological disorders were resolved to a major degree within a month. After 6 months, the patient developed symptoms of papillary stasis. In a CT scan, amorphous calcifications in the right temporal lobe and, in the same area, contrast-enhanced pathological foci concomitant with the oedema, were revealed. Because of these findings, suggesting subtotal tumour resection, the re-operation was performed. During postoperative period a mild left hemiparesis and rare epileptic seizures were observed. Histopathological examination of the tissue resected during the first surgery showed no obvious tumour pattern while after the re-operation a possibility of ganglioglioma was suggested, based on scanty fragments of tumour tissue containing foci of ganglion cells and oligodendroglia-like cells. Foci of pilocytic fibrous gliosis with microcalcification were also observed. Adjusted diagnosis of pilocytic astrocytoma was established in 2003 after re-examination of the specimens due to the tumour recurrence. According to the oncological consultation the patient was given radiotherapy. At the follow up, 6 months postoperatively, in 1999, the control CT scan revealed a significant widening of the ventricular system whereas no contrast-enhanced areas were found. Laboratory tests showed high levels of protein in CSF, several times greater than the normal limits. The patient was initially treated with lumbar drainage, followed by ventriculostrial and later ventriculoperitoneal shunt implantation. Due to the shunt occlusion it was replaced with Orbis Sigma valve. After the next 3 months a recurrence of clinical manifestation of intracranial hypertension symptoms was observed. The CT scan revealed active hydrocephalus but no recurrent tumour within the postoperative compartment. Shunt replacement surgery was performed. In 2001 the patient was hospitalized for the third time, and the fourth hospitalization was in 2002, due to shunt occlusion and the distal tip of a drain was re-implanted into the peritoneal cavity.
In the same year the patient was hospitalized due to acute appendicitis, after a month she was admitted to hospital with the symptoms of the increased intracranial pressure (ICP) and meningitis. The shunt system was removed, and the external drainage system was used. After the targeted antibiotic therapy, the sterile CSF was attained, and the medium pressure Pudenz valve was implanted.

At the beginning of 2003, tumour recurrence within the temporal lobe compartment was revealed, with concomitant focus in the left cerebellopontine angle. The patient was admitted to the Department of Neurosurgery and underwent the surgery of resection of the recurrent tumour and cranioplasty. The cranioplasty (filling of the cranial defect) using artificial material was performed due to cosmetic reasons (upon the patient’s request) and due to the increased epileptic seizures in order to prevent secondary head trauma. Neurologically a mild left hemiparesis was present.

In the specimen examination, collected at the resection of a recurrent tumour, there was an obvious tumour pattern, consistent with pilocytic astrocytoma. Histological study (Fig. 1) demonstrated a biphasic compact and loose pattern with predominance of microcystic areas, frequently with significant perivascular arrangement of tumour cells and numerous eosinophilic granular bodies. Less prominent compact areas exhibited Rosenthal fibers and dispersed microcalcifications. Mitoses were absent. Immunohistochemistry revealed strong reaction for GFAP in fiber-rich, compact areas and weaker GFAP reactivity in loose and microcystic areas. The reactions for NF, synaptophysin and MBP were negative. Proliferative index for MIB-1 was low, under 2%.

The next hospitalization, after one year, in 2004, was caused by the exacerbation in lower limb spastic paresis, more severe in the left lower limb. In a neurological examination, left brachiofacial syndrome, disturbances of visual field and bilateral se-

![Fig. 1A-D. A. Characteristic compact and loose tumour pattern. HE, original magn. ×200. B. Perivascular glial cell arrangements accompanied by the presence of eosinophilic granular bodies. HE, original magn. ×200. C. Microcalcifications in compact part of tumour. HE, original magn. ×200. D. GFAP immunoreactivity in compact fibrillar area. Original magn. ×200.](image-url)
vere spastic paresis with the bilateral Babinski sign were shown. The MRI imaging revealed widening of the central canal, from C3 to Th8 in a form of a large cavity and compression of the spinal cord below, at the level of Th8-Th9, by a solid-cystic tumour. No contrast-enhanced area was shown at the tumour level. The patient underwent a surgery of laminectomy Th8-Th9 and subtotal tumour resection. Gross total tumour resection was not possible due to lack of the sharp border line towards the frontal part of the spinal cord. During the surgery, syringostomy was performed, followed by the implantation of a distal tip of the drain into the subarachnoid. Postoperatively, a significant spasticity reduction was noted, the patient was non weight bearing. The patient was aided in daily functioning with a wheelchair. Histopathological examination, made on the scarce tumour specimens, shown predominantly loose-textured tissue (Fig. 2), composed of GFAP-positive tumour cells, with significant predilection for angiocentric arrangements, numerous hyalinized blood vessels and eosinophilic granular bodies.

In an MR imaging of the lumbosacral segment performed in 2004, a contrast-enhanced heterogeneous mass sized 2 × 3 × 3 cm was shown, at the level of S2-S3 (Fig. 3).

At the next hospitalizations in 2005 and 2007 clinical presentation was stable. Brain and spinal canal MR imaging showed no tumour progression. The patient persistently refused surgical treatment and spinal canal tumour resection. At the end of 2007 the patient complained severe pain in sacral vertebral segments. In neurological examination severe lower limb spastic deficit was seen. In January 2008, laminectomy at the level of S2-S3 was performed and gross total resection of tumour, which had been observed until then, was achieved. The tumour was well-demarcated, yet closely attached to the nerve roots. Histopathology of the

Fig. 2A-C. Tumour specimens from thoracic level of the spinal canal. A. Loose structure with abundant blood vessels. HE, original magn. ×200. B. GFAP-positive tumour cells between blood vessels. Original magn. ×200. C. Angiocentric arrangement of tumour cells. HE, original magn. ×200.
sacral tumour specimens (Fig. 4) exhibited compact and loose-textured pilocytic astrocytoma structures, with Rosenthal fibers, eosinophilic granular bodies and strong GFAP-immunoreactivity of tumour cells. The postoperative material contained also abundant mesenchymal tissue with fibrous cicatrices, numerous vessels and organized or recent haemorrhagic foci.

After 15 months the patient was hospitalized again in order to perform follow-up imaging. In a MRI examination, contrast-enhanced multifocal lesions were manifested in cerebropontine angles, in the right paraventricular area and additionally in dural region at the cerebral base (Fig. 5). A control MRI scan of the thoracic segment showed a widening of intraspinal fluid spaces as well as “garland-shaped paraspinal masses”, suggesting vascular malformation, however, as the patient was explored at that level this suggestion was not verified with spinal angiography. No tumour was revealed in MRI exam of the sacrolumbar and thoracic segments of the spinal canal (Fig. 6). The patient’s neurological state of severe spastic lower limb paresis and disturbances of visual field did not change.

Discussion

The presented clinical case illustrates the process of multifocal metastatic tumour spread, rarely concerning PA, classified as WHO grade I glioma [6,26]. In the literature there are several reported cases of the PA dissemination to the spinal column, mostly of the tumors localized primary in the chiasmo-hypothalamic region and cerebellum [3,7,8,14-16,19,27], rarely of the PA originated in cerebral hemisphere [12]; one of the recent paper from 2006 presents the spread process of a tumour located initially in the spinal cord to intracranial subtentorial and subsequently also supratentorial spaces [1].

A very rare course of tumour spread concerns only those reported cases of PA, in which the metastatic foci do not change their histopathological character [1,11,15,21-23,31]. There were also relatively rare cases of spread of low-grade astrocytoma, but usually the spread foci have a different histopathological character qualified as WHO grades II or III astrocytomas [6,10,30]. In the case of a local recurrence confined to the spinal cord, presence of multifocal spread within intracranial space and change of the histopathological character the patients often were given an adjuvant chemotherapy or radiotherapy [3,7,12,14,15,27].

The report concern the patient 16 years of age, hospitalized at short intervals due to local tumour relapse. In the follow-up observation period of several years, in control MRI scans of the brain and spinal cord multifocality of lesions was manifested. The intracranial focus was treated with radiotherapy, as there was no possibility to perform total tumour resection due to infiltration into the optic tract. Ra-
Radiotherapy has no any influence to the histopathological character of the tumour.

In the presented case we can conclude that all the surgically treated foci were consistent with WHO grade I pilocytic astrocytoma; no malignancy was shown. The first collected meagre tumour specimens in 1998, suggesting ganglioglioma, were re-assessed after the recurrent tumour resection, when the histopathological pattern consistent with PA was manifested. However, in cases with inadequate biopsy samples the differentiation between PA and pilocytic-like glial component, occurring in glioneuronal tumours [9,26,32] and in other lesions [20,28], can be difficult. In our case the final evaluation of the histopathological material, performed in 2003, allowed to recognize the same histopathological character of PA for both primary and recurrent tumour. After 10-year observation with no local recurrence, the management strategy can be debated over, whether with the tumour characterized by 90% of positive prognosis and slow growth, the decision made by the oncologists was right (as histologically low-grade pilocytic astrocytoma was revealed it led to the decision of refuse of chemotherapy).

It is very debatable and unclear why the benign glioma (WHO grade I), which grows well-circumscribed, without infiltration into neighbouring structures, acquires the tendency to spread. The cases of multifocal tumour expansion are explained by tumor location close to CSF spaces thus creating the possibility for the tumour cells to migrate [4,15,21-23]. Hydrocephalus [11], seeding of tumor after placement of a ventriculoperitoneal shunt [13,25] or surgically induced dissemination [31,33] may be another possible mechanism of metastasis. The factors are quoted related to the slow CSF flow in some regions of the cranio-spinal system, which may promote specific locations of the diffuse tumour foci. Gravity

Fig. 4A-D. Histopathological examination of the spinal canal tumour in the sacral segment. A. Compact fibrillar structure of pilocytic astrocytoma with Rosenthal fibers and vascular fibrosis. HE, original magn. ×200. B. GFAP positive fibrillar pattern of tumour. Original magn ×200. C. Loose structure of the tumour with a lot of eosinophilic granular bodies. HE, original magn. ×200. D. GFAP positive tumour cells. Original mag. ×200.
Fig. 5. Control MRI of the brain during the last hospitalization. Multifocal growth is visible.

Fig. 6A-B. Control spinal MR images during the last hospitalization. A. Status post tumour resection and cyst drainage in thoracic segment of spinal canal. B. Sacrolumbar segment of the spinal canal, status post tumour resection within the sacral bone.
factor is considered. It also seems that if the tumour is initially located in the spinal cord, it tends to spread towards the intracranial space rather than distally towards cauda equina [1,11,12,15,22].

In the presented case we deal also with the ascending dissemination process of tumour initially involving temporal lobe, thoracic segment of the spinal cord, and cauda equina. In the last MRI images two symmetrical foci were shown within the cerebropontine angles, which are observed but have not been verified histopathologically yet. The manner and nature of the disseminated disease may be related to the nature of the tumour rather than to physical factors, such as fluid flow, partial tumour resection and CSF space opening during the surgery. It is more evident, as the foci of spread occur in the presented case within 4-5 years following the successful craniotomy. Correspondingly, most reports detected PA dissemination after a long postoperative period [6,19,26,27] or parallel at diagnosis of primary tumour [8,12,19].

In the literature may be found the reports of low-grade glioma, defined by Tihan et al. [29] as monomorphic pilomyxoid astrocytoma (PMA), which have a particular tendency to spread. It resembles the classic pilocytic astrocytoma in structure, so it could be its subtype [2,5,9,18,20,29]. Komotar et al. [17] indicated that some of the cases defined histologically as classical PA might be reclassified as PMA because of a predominant myxoid pattern and absence or rarity of other signs of PA.

In our case the multifocal tumours were characterized as PA, although there was evidence of loose angiocentric growth pattern, characteristic for PMA [2]. However, histological signs of PA such as biphasic growth pattern, granular bodies, protoplasmic cells, calcifications and Rosenthal fibers, were evident in primary and recurrent tumour in temporal lobe as well as in disseminated tumours in spinal leptomeninges.

The view currently predominant in the literature is that the histopathological examination techniques used in contemporary practice do not allow for the evaluation of potential spread of a low grade glioma [11]. The possible etiologic factor contributing to the formation of the tumour subtype with the tendency to spread is an excessive expression of epidermal growth factor receptor (EGFR) [24].

Rarely reported disseminated tumour or multifocal growth of pilocytic astrocytoma constitutes a peculiar clinical case. Only a few such cases have been already described.

Conclusions

1. The presented case of the patient with PA indicates that despite the spread of the neoplastic process, and initial subtotal, followed by a gross total resection, a histopathologically benign tumour (WHO I grade) allows for a long-term survival and observation period.

2. Multifocal tumour involving midline structures causes, unfortunately, major neurological defects.

3. In the presented case we deal with the ascending spread process and the occurrence of the new foci in both subentorial and parameningeal spaces in the intracranial cavity. It is a rare clinical manifestation of a disease ever described in the literature.

References


