Pleomorphic xanthoastrocytoma in the spinal cord

Case report

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The authors present the clinical, radiological, and pathological features of a patient with a recurrent pleomorphic xanthoastrocytoma located in the spinal cord. This is the first report of a pleomorphic xanthoastrocytoma at this location; until now, only cerebral supratentorial pleomorphic xanthoastrocytomas have been described. The treatment of this case is discussed.

Key Words • pleomorphic xanthoastrocytoma • spinal cord tumor • glial fibrillary acidic protein • leptomeninges • tumor recurrence

Since 1979, when Kepes, et al.,12 first described 12 cases of a distinctive clinicopathological neoplastic entity, to which the term "pleomorphic xanthoastrocytoma" (PXA) was given, many similar cases have been reported.1,7-11,13-16,21-23 The description included predominantly cellular pleomorphism, giant cells displaying bizarre unique or multiple nuclei, and abundant lipid droplets in the tumor cell cytoplasm alternating with fusiform cells arranged in a storiform pattern. Mitoses are only occasionally found, or are even absent. No necrosis is seen. The astrocytic origin of the tumor is proven by its positive immunoperoxidase staining for glial fibrillary acidic protein (GFAP);2-4,7,9-16,18,21-23 nevertheless, some authors argue that the tumor is of mesenchymal origin.18 Subpial astrocytes are implicated as the origin of the tumor, particularly based on electron microscopic and immunohistochemical evidence of the astrocytic formation of basal lamina.7,9,12,16

The tumor usually presents in young patients 7 to 25 years of age; however, PXA has been reported in two older patients, aged 46 and 62 years.1,18 A relatively good prognosis with long-term survival is reported, regardless of whether a primary total or subtotal tumor removal or adjuvant radiotherapy has been performed.23 Nevertheless, a potentially aggressive biological tumor behavior has been described, depending on the histological dedifferentiation.1,2,15 We report the case of a 66-year-old man in whom spinal cord presentation of a PXA with local recurrence after 8 months, without histological dedifferentiation, is described for the first time.

Case Report

This 66-year-old man underwent neurological assessment in January, 1992. He described a 2-year history of progressively ascending sensory disturbance in both legs including both paresthesias and numbness. The left side seemed to be more affected than the right, and involved the genital and sacral areas; however, during the 2 months before presentation, numbness had spread over the right lower back and into the right axillary area. There was no paresis or bladder dysfunction, but a progressive gait disturbance was noted. Furthermore, he had experienced increasing problems with sexual function over a period of 2 or 3 years. The patient had never been seriously ill before nor had he undergone previous surgery. He did not use any medications or drugs.

First Admission. Neurological examination revealed hypesthesia from the T-12 dermatome ascending over the right lower back to the axilla. Slight disturbances in proprioception were found in both legs, and there was no paresis. Reflexes were symmetrical in both arms and legs; a Babinski sign was elicited in the right foot and a physiological plantar reflex in the left foot.
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from left-sided stimulation. Magnetic cortical stimulation showed only a delayed response in the right anterior tibial nerve.

Magnetic resonance (MR) imaging (T1- and T2-weighted sagittal projection and T1-weighted transverse images) revealed a diffusely infiltrating, partly cystic hypointense lesion in the spinal cord at T2-4, with thin hypointense components ascending into the cervical region. Administration of gadolinium-diethylene-triamine penta-acetic acid (DTPA) enhancement led to intensive enhancement of only the thoracic part of the lesion (Fig. 1). No enhancement in the cervical region was seen; so the abnormalities found there were interpreted as edema or as a possible early sign of a syrinx.

First Operation. A T2-4 laminectomy was performed and the dura mater appeared normal. The leptomeninges were firmly attached to the spinal cord over the exposed area. The spinal cord was distorted dorsally with a tumor overlying it, and there was leptomeningeal ingrowth of soft bluish-red tumor tissue at two points roughly 1 cm apart. The transition between tumor tissue and spinal cord tissue was rather difficult to establish superficially. Within the spinal cord itself, however, a good demarcation zone was found between the partly cystic tumor tissue and the surrounding nervous tissue. Macroscopically, complete tumor removal seemed to be established. No tumor extension was found rostral to the T-2 level.

First Postoperative Course. The patient made a good postoperative recovery. Initially, he walked with the aid of a cane because of a slight worsening of the preoperative disturbances in proprioception of both legs. There was no paresis and he had normal bladder function. Postoperative radiotherapy was not considered to be necessary. During the 8-month follow-up period, the patient complained of an inconvenient "bandage sensation" around both knee regions which developed gradually, spreading upward to the umbilical level.

Second Admission. Neurological examination revealed a progressive spastic paresis in both legs, much worse on the right than the left. There was increased loss of sensation in both legs and bladder dysfunction. Magnetic resonance investigations showed a diffusely infiltrating gadolinium-DTPA-enhancing process in the spinal cord almost identical to and at the same location as that seen preoperatively. However, the spinal cord rostral and caudal to the T2-4 region was more diffusely swollen than before. Again no contrast enhancement was seen in these regions.

Second Operation. At repeat surgery, it was only possible to perform a debulking of the local recurrent tumor. The tumor tissue was again bluish-red, but this time it was infiltrating the leptomeninges more diffusely as well as the surrounding spinal cord tissue at the first operation site. Parts of the tumor consisted of noduli with a firmer consistency resembling meningioma tissue for which CO₂ laser debulking was needed. Because of the short interval to tumor recurrence, a more aggressive biological behavior was expected and therefore radiotherapy was started.


Normal anal, cremaster, and upper and lower abdominal reflexes were found. A slight ataxic gait disturbance was seen.

All blood tests including Treponema pallidum hemagglutination assay were normal. Cerebrospinal fluid investigations showed normal glucose concentration and a raised albumin level of 1.42 gm/liter. Somatosensory evoked potential investigations showed an intact cortical response with stimulation of the median nerve on both sides. On stimulation of both tibial nerves, a reduced cortical response was elicited only

FIG. 1. Upper Left and Lower: Magnetic resonance (MR) T1-weighted images showing a partly cystic, diffusely infiltrating hypointense lesion in the thoracic spinal cord, with thin hypointense components ascending into the cervical region. Upper Right: After administration of gadolinium-diethylene-triamine penta-acetic acid, MR imaging shows intense enhancement of the thoracically located lesion only.
Second Postoperative Course. After the second operation the spastic paraparesis did not resolve completely. The patient is now able to walk short distances with the aid of two crutches.

Pathological Examination. Light microscopic findings showed a moderate cellular tumor composed of intertwined bundles of fusiform cells in a storiform pattern blending with foci of pleomorphic giant and multinucleated cells. Some of the large cells showed vacuolization and xanthomatous changes. Sporadic intracytoplasmic eosinophilic droplets were found. Necrosis, vascular proliferation, and mitoses were absent (Fig. 2). A reticulin stain showed granular deposits between tumor cells and continuous fibers around the blood vessels (Fig. 3). Infiltrating lymphocytic cells in the absence of necrosis were seen.

Immunohistochemical studies were performed on sections of routinely processed formalin-fixed and paraffin-embedded tissue using either a peroxidase-antiperoxidase or an avidin-biotin complex technique and incubation with the primary antibody for 45 minutes at room temperature. The giant and multinucleated tumor cells showed intracytoplasmic positivity for GFAP (diluted 1:1000), whereas the processes of the fusiform cells reacted strongly (Fig. 4). Positivity for vimentin (diluted 1:1000), alpha-1-antichymotrypsin (diluted 1:2500), and alpha-1-antitrypsin (diluted 1:10,000) was also seen. With a polyclonal antibody to collagen type IV (diluted 1:500), previously characterized by Havenith, et al., a granular and linear pericellular pattern was seen (Fig. 5 left), some of the tumor cells being totally surrounded by collagen type IV deposits (Fig. 5 right).

Electron microscopy showed the same pattern of basal membrane deposition as found with the collagen type IV immunohistochemical stain. The granular...
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Fig. 5. Photomicrographs showing linear and granular pericellular staining for collagen type IV (left, × 200), and multinucleated giant cell tumor, surrounded by basal membrane granular deposits (right, × 250). Collagen type IV immunohistochemistry.

depositions correlated with focal reduplication of the basal membrane. The tumor cells contained a moderate amount of rough endoplasmic reticulum, intermediate filaments, and mitochondria. A well-differentiated Golgi complex was often present. Near the inner side of the plasma membrane, densities suggestive of hemidesmosomes were present (Fig. 6). Except for a larger amount of collagen tissue, the pathological anatomical findings of the recurrent tumor were fully consistent with the findings described above.

Fig. 6. Electron micrograph showing basement membrane deposition alongside tumor cells, with densities on the inner side of the plasma membrane (arrows). Intermediate filaments in the tumor cells are indicated (asterisk). × 3200.
Discussion

The operative findings included a superficially located tumor which was partly infiltrating the leptomeninges locally. There was a very clear demarcation zone between the tumor tissue (which was partly cystic) and the inner part of the spinal cord, which seemed to suggest that total tumor removal was possible.

No necrosis, mitosis, or vascular proliferation was found histologically, whereas reticulin stains showed a continuous fiber system around the tumor cells and blood vessels. A variable number of lymphocytes not related to necrosis were also found. Immunohistochemically, both the giant and multinucleated cells as well as the fusiform cells were GFAP-positive. Some tumor cells were completely surrounded by collagen type IV deposits. Electron microscopy showed tumor cells partly covered with basal membranes and some even with focal reduplication of the basal membrane, suggesting tumor origin from subpial astrocytes.

Although most reported PXA's have a subpial localization in accordance with their presumed subpial astrocytic origin, few cases have been described without obvious meningeal contact. Kros, et al., described the tumor in their Case 4 as located in the thalamus and diagnosed by stereotactic biopsy. In our opinion, astrocytes at the velum interpositum could be the source of a PXA at this site. This is also true for the tumor in their Case 5, which was remarkable for its gangliomatous component. In Case 2 of Heyerdahl Strom and Skullerud, the tumor was located at the optic foramen, but it is doubtful from the description whether this lesion was continuous with the optic nerve; if it was, theirs is the first description of an optic PXA, which concurs with the idea of a subpial astrocytic origin. In our opinion, these cases do not contradict but in fact support the concept of a subpial origin. Due to its postulated origin, PXA could also be expected to be found at other sites.

The rather typical operative, immunohistochemical, and electron microscopic findings described here characterize this spinal cord tumor as a PXA. As originally reported by Kepes, et al., PXA is an unusual supratentorial astrocytoma found in young patients. Therefore, differential diagnoses such as glioblastoma, ependymoma, giant-cell sarcoma, meningioma, fibrous xanthoma, or fibrous histiocytoma can in our opinion be ruled out. The existence of PXA in older patients has been described before; however, this is the first report of a PXA found in the spinal cord.

Reviewing the literature, we found several treatment modalities for the supratentorially localized PXA, but the role of radiotherapy in the management of such tumors remains unclear. In about one-half of the reported cases, the patients received postoperative radiotherapy in different doses; adjuvant cytostatic treatment was given in only two cases. The other reported patients underwent surgery alone, including for local tumor recurrence. No significant difference with regard to the reported survival period could be established for patients in the two treatment groups, and Whittle, et al., even reported a slightly longer mean survival period for the nonirradiated patient group. Rather short survival times have been reported, even with postoperative radiotherapy. However, histological classification of these tumors as a PXA may not have been completely accurate. On the other hand, obvious malignant changes of PXA have been described, even after long recurrence-free intervals.

In considering the clinical course of this case, starting with the atypical complaints of disturbances of sensation for more than 2 years prior to the operation, and given the rather superficial localization as well as the apparently gross total tumor removal from the spinal cord tissue, there seemed to be no decisive reason for adjuvant radiotherapy after the first operation. Furthermore, reports of the rather unpredictable biological behavior of the PXA's were based on supratentorial tumors. It is possible that the biological behavior of a PXA located in the spinal cord might not be predictable at all. However, the rather short interval (8 months) to recurrence of this tumor without evident histological signs of malignancy or malignant changes seems to suggest a more aggressive biological behavior of PXA's in the spinal cord. Considering that the second operation involved only debulking of the tumor, adjuvant radiotherapy was thought to be advisable.

Conclusions

The spinal cord tumor presented in this report is a PXA, based on the operative, histological, immunohistochemical, and electron microscopic findings. Gross total tumor removal appeared at first to have been achieved; however, a local recurrence within 8 months emphasized the unpredictability of the biological behavior of PXA's in general. Whether the more biologically aggressive behavior of a PXA located in the spinal cord can be attributed to its site remains to be substantiated by future reports.

References


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