Clinicopathological and ultrastructural study in two cases of chordoid glioma

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Chordoid glioma is a rare benign neoplasm of uncertain histogenesis occurring in the third ventricle/suprasellar region. Recently, data have emerged suggesting that chordoid glioma is a variant of ependymoma related to a specialised ependyma of the subcommissural organ or the lamina terminalis area. In this study, we report clinicopathological and ultrastructural findings in two chordoid glioma cases. In case 1, a tumour (1.5 cm in diameter) in a 62-year-old man invaded the anterior-basal part of the third ventricle in the lamina terminalis region. In case 2, a large tumour in a 51-year-old woman occupied the whole third ventricle. The tumour attached to the medio-basal hypothalamic region. Histologically, both cases revealed a distinct chordoma-like pattern and glial immunophenotype of tumour cells. Under the electron microscope the tumour cells exhibited microvilli, intercellular lumina, intermediate type junctions and focal basal lamina formations. These findings were similar to those previously reported in the chordoid glioma cases. Moreover, the intracytoplasmic cilia and subplasmalemmal pinocytic vesicles or caveoles were observed. The study supports the view of ependymal derivation of chordoid glioma. Its relation to lamina terminalis or infundibular/median eminence area presumably reflecting tumour origin from the modified ependyma of circumventricular organs of the third ventricle is discussed.

key words: chordoid glioma, third ventricle tumours, ultrastructure, ependyma, circumventricular organs

INTRODUCTION

Chordoid glioma is a rare tumour of the third ventricle, recently defined as a new clinicopathological entity. According to the last WHO classification of CNS tumours [4], chordoid glioma is included in the group of neuroepithelial tumours with uncertain histogenesis. Clinicopathological characteristics of this neoplasm was originally presented in 1998 by Brat et al. [3] based on observations of 8 patients and subsequently it was confirmed in publications of more other cases. To our knowledge, until now 29 cases of chordoid glioma have been published [3, 5–7, 10, 14–16, 18, 19, 25, 26], including the case reported by Wanschitz et al. [27], which was initially diagnosed as the GFAP-positive suprasellar meningioma. In the reported cases, the tumour occurred in adults except for one case [6], predominantly in women, involving the suprasellar/third ventricle region and exhibiting a distinct histopathological pattern of the chordoid-like low-grade neoplasm. Glial appearance of the tumour cells was demonstrated immunohistochemically and ultrastructurally [3]. Other researchers suggested that the tumour cells originated from subependymal tissue [19] or from the lamina terminalis associated tissue [14]. Recent data support the view that chordoid glioma of the third ventricle represents a variant of ependymoma related to a specialised…

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ependyma of the subcommisural organ [7] or the lamina terminalis area [15].

In this study, we report clinicopathological and ultrastructural findings in two chordoid glioma cases as a contribution to knowledge of this uncommon tumour entity. Case 1 was briefly mentioned in the publication by Taraszewska and Matyja [23] and also presented at the XIth Conference of Polish Neuropathological Association [24]. In our study, we draw attention to a specific localisation of the tumours in the antero-basal region of the III-rd ventricle and to distinct ultrastructural features with evidence of some ependymal characteristics of neoplastic cells.

REPORT OF CASES

Case 1. A 62-year-old man was admitted to the Neurosurgical Department with suspicion of the anterior communicating artery aneurysm. He had complained of headache for 6 months and polydysxia and polyuria over the last weeks before admission. Neurological and angiographic examinations were negative. Computerised tomography revealed a suprasellar, hyperdense and homogeneously contrast enhancing tumour of 1.5 cm in diameter, occupying the lamina terminalis region and compressing the optic chiasm (Fig. 1A, B). The surgery was performed via a pterional approach. Intraoperatively, an intraventricular suprachiasmatic white-greyish mass, covered by a thin capsule, was found. It appeared to be connected with the anterior left part of the III-th ventricle. The lesion was carefully separated from the ventricle walls and excised completely. After surgery, the patient had respiratory dysfunction and was unconscious for 3 days, then recovered well except for slight visual disturbances and symptoms of diabetes insipidus. At the 14-th postoperative day, the patient suffered a myocardial infarct and was transferred to cardiologic unit. Initially, he showed recovery but after 6 weeks he died suddenly because of cardiac arrest. The autopsy was not performed.

Case 2. A 51-year-old woman had complained of hypersomnia for about one year and of visual disturbances for 6 months. MRI revealed a suprasellar contrast-enhancing tumour, measuring 2.5 cm in diameter, involving the third ventricle in the optic chiasm and basal hypothalamus region (Fig. 2). The tumour was totally removed by surgical treatment through a subfrontal, translamina terminalis approach. At surgery it was found that the large tumour occupied the whole third ventricle and was attached to the ventricular floor at the region of the recessus infundibuli and tuber cinereum. The patient’s postoperative recovery was uneventful.

Control neuroimaging after 4 months revealed some residual lesion. Laboratory tests for hypothalamic endocrine function were normal.

MATERIAL AND METHODS

The tumour specimens fixed in buffered formalin were embedded in paraffin and the sections were
stained with hematoxylin and eosin (HE) Gomori’s method, mucicarmin and Alcian blue. Immunohistochemical staining was performed with (strept) avidin biotin peroxidase complex method (ABC) using the primary antibodies against glial fibrillary acidic protein (GFAP), vimentin (VIM), S-100 protein (S100), cytokeratin (CK), epithelial membrane antigen (EMA), CD34-, CD31- and factor VIII-related (FVIII) — antigens, neurofilament proteins (NF) and synaptophysin (antibodies were supplied by DAKO and Immunotech).

For ultrastructural study, small specimens of formalin-fixed tissue were postfixed in 3% glutaraldehyde and 2% osmium tetroxide in cacodylate buffer (pH 7.4) and embedded in Epon 812. Ultrathin sections were stained with hematoxylin and eosin (HE) Gomori’s methenamine silver and Alcian blue. Immunohistochemical staining was performed with (strept) avidin biotin peroxidase complex method (ABC) using the primary antibodies against glial fibrillary acidic protein (GFAP), vimentin (VIM), S-100 protein (S100), cytokeratin (CK), epithelial membrane antigen (EMA), CD34-, CD31- and factor VIII-related (FVIII) — antigens, neurofilament proteins (NF) and synaptophysin (antibodies were supplied by DAKO and Immunotech).

**RESULTS**

Histologically, both tumours were composed of eosinophilic epithelioid cells displaying chordoid-like arrangements in cords and clusters in an abundant myxoid matrix (Fig. 3) with a rich reticulin network (Fig. 4). Prominent, mostly peripherally distributed lympho-plasmacellular infiltrates and the well-demarcated tumour-brain interfaces were also seen. Mitoses were not found in case 1 and they were solitary in case 2. Necroses were absent. Immunohistochemically, the tumours exhibited strong VIM and GFAP reactivity with much intensive GFAP expression in the cells arranged in cords within peripher-ral and more chordoidal parts of tumours (Fig. 5). Moreover, strong immunoreactivity for CD34 was observed in tumour cells apart from vascular endothelia (Fig. 6). Immunostainings for CK and EMA were weakly positive in individual cells in case 2 but negative in case 1. In both cases a weak focal reaction was noted for S-100, whereas reactions for synaptophysin, NF as well as for FVIII and CD31 were negative in tumour cells.

Ultrastructural examination of both cases revealed groups of compactly arranged tumour cells, partly surrounded by basement membrane and separated by enlarged extracellular spaces with connective tissue stroma elements. The tumour cells exhibited oval or infolded nuclei and abundant cytoplasm often containing bundles of intermediate filaments and numerous mitochondria (Fig. 7). Many intercellular gaps and small lumina filled with microvilli and short cytoplasmic protrusions were observed between closely adjacent cells (Fig. 8). The cilia were absent in the intercellular lumina although they were occasionally found within the cytoplasm of tumour cells (Fig. 9). Sometimes, the cells also displayed intracytoplasmic lumina containing microvilli (Fig. 10). Intercellular junctions of the long zonula adherens type and short thigh junctions were seen between neighbouring cell membranes. Junction complexes were mostly seen between cell processes arranged around intercellular lumina (Fig. 11). There were also some adjoining cells exhibiting irregularly infolded surface with short finger-like cytoplasmic processes facing intercellular gaps without evidence of mem-brane junctions. Small caveole and subplasmalemmal pinocytic vesicles were present at cell surfaces covered by basal lamina, and at the interface of neighbouring cells (Fig. 8, 10). In addition, the plasma cells located in the extracellular space were found (Fig. 12). A small secretory-like granules were identified in cytoplasm of plasma cells and incidentally also in cytoplasm of tumour cells.

**DISCUSSION**

In the presented cases, clinicopathological and ultrastructural findings are similar to those in previously reported chordoid glioma cases [3, 7, 15, 18, 19, 26], including the suprasellar, intraventricular localisation of the tumours in the anterior-basal part of the third ventricle, a distinct chordoma-like histological pattern and glial immunophenotype of tumour cells as well as ultrastructural pattern of cells exhibiting microvilli, intercel-lular lumina, intermediate type junctions and focal bas-al lamina formation.

Suprasellar/third ventricular localisation of the well-delineated, ovoid, hyperdense mass with homogenous contrast enhancement is the constant radiological find-ings in the reported chordoid glioma cases [16]. Cystic lesions were rarely observed [3, 15, 25]. In many cases, large tumours (2.5 to 4 cm, diameter) completely filled the third ventricle and appeared to be connected with hypothalamic structures [3, 5, 16, 19, 26]. This feature often prevented complete resection of the tumour. Moreover, the site of tumour origin could not be precisely determined given the size of the lesion. In our case 1, the lesion of 1.5 cm in diameter compressed and invaded the anterior-ventral region of the third ventricle formed by the lamina terminalis. A tumour with similar size and relationship to the lamina termi-nalis has been reported by Kochi et al. [14]. Tumours occurring the suprasellar region and involving the anterior part of the 3-rd ventricle are document-ed in the many published cases [10, 15, 18, 19, 25]. Different clinical symptoms of hypothalamic dysfunc-tion such as diabetes insipidus, hypothryoidism, amenorrhea, insomnia or somnolence and visual dis-turbances were observed in cases [3, 4] similar to...
those presented in this study. On the other hand, obstructive hydrocephalus was a relatively rare complication; it is reported only in 6 chordoid glioma cases [3, 5, 10, 26]. Also, despite the large sized intraventricular tumour seen in case 2, no signs of obstructive hydrocephalus were found in the present cases. In both patients, tumours were completely removed through lamina terminalis.

Despite the low histological grade a worse postoperative outcome has been noted in some chordoid glioma cases due to the frequent inability to achieve total resection of the tumour. Moreover, a relatively large pro-
Figure 7. Closely adjacent tumour cells with cytoplasm containing intermediate filaments and numerous mitochondria, ×10 000.

Figure 8. Accumulation of microvilli in small intercellular lumen. Subplasmalemmal pinocytic vesicles (long arrows) and pericellular basal lamina (short arrows) are seen, × 22 500.

Figure 9. Long-sectioned cilium within cytoplasm and numerous microvilli on the surface of tumour cell, ×30 000.

Figure 10. Tumour cell exhibiting membrane-bound space with microvilli-like cytoplasmic projections, numerous subplasmalemmal pinocytic vesicles and pericellular basal lamina, × 36 000.
portion of the unexpected postoperative death, occurring in 6 cases including the present case 1, has been noted [3, 7, 18, 26]. Sudden death in these cases was attributed to pulmonary thromboembolism or cardiovascular disorders.

Localisation of the tumour in the suprasellar/hypothalamic/third ventricle region along with characteristic histological and immunohistochemical pattern are significant diagnostic features of chordoid glioma, which allow its distinction from other tumours, such as non-infiltrative low-grade gliomas of the third ventricle [3, 4] and, especially, the morphologically similar chordoma or chordoid meningioma [18, 23].

Based on immunohistochemical and ultrastructural studies, the glial nature of the chordoid glioma has already been recognised by Brat et al. [3] and subsequently by others [18, 19, 26]. However, precise classification and histogenesis of this tumour have not been established [4].

Immunohistochemically, chordoid glioma is characterised by consistently strong reactivity of GFAP, VIM and CD34 [3, 15, 18, 19], weak reaction for S100, inconstant EMA and CK reactivity, either focal or absent [3, 7, 18, 24, 26] as well as negative staining for neuronal markers. This immunohistochemical profile is partly reminding us of ependymomas observations, particularly as regards to GFAP, VIM, EMA and CK reactivity [28]. In ependymomas, however, GFAP reactivity is usually less prominent and CD34 has not been demonstrated yet. The significance of CD34 positivity in chordoid glioma remains unclear [18]. The CD34 is known as a marker of vascular endothelia in mature brains, whereas in development it is expressed on haematopoietic progenitor cells and transiently on stem cells during early neurogenesis. Till now, this antigen has not been found in glial neoplasms except for low-grade gangliogliomas of temporal lobe associated with focal temporal epilepsy [2, 8]. In these lesions early developmental aberrations of neoplastic neuronal and glial components have been suggested. As regards to their suggested ependymal differentiation, whether certain atypical features of chordoid glioma cells are related to developmental aberrations needs clarification in the future.

Similarities between chordoid glioma and ependymoma have been mostly stressed in electron microscopic studies [3, 7, 14, 15, 19]. In particular, ultrastructural features of cells exhibiting microvilli, intercellular lumina, long zonula adherens type junctions and focal basal lamina formation would suggest ependymal ori-

Figure 11. Long junction of the zonula adherens type between cells surrounding small intercellular lumen, × 25 000.

Figure 12. Plasma cell in neighbourhood of tumour cell. Secretory-like granules are seen in cytoplasm of both cells, × 10 000.
gin of chordoid glioma. On the other hand, lack of cilia and well-formed microrosettes, and light microscopic pattern of pseudorosettes distinguishes chordoid glioma from common ependymoma [13, 28]. Besides the previously described fine structural feature, the present study of two cases revealed the presence of cilia located within cytoplasm of tumour cells. Similar observation of intracytoplasmic cilia has been recently reported by Pasquier et al. [15], providing further evidence for ependymal characteristics of tumour cells.

The relationship between chordoid glioma cells and the specialised secretory ependyma of subcommissural organ was first suggested by Cennachi et al. [7]. These authors detected zonation of cytoplasm in apical, subapical perinuclear and intermediate regions and the presence of secretory granules in tumour cells. In our study, zonation of tumour cell cytoplasm was not a prominent feature. However, secretory granules were seen occasionally. Moreover, the cells revealed the presence of subplasmalemmal invaginating vesicles and of small cytoplasmic protrusions or blebs that previously had not been described. These findings appeared to be consistent with both secretory and absorptive activity of ependymal cells. Increased pinocytic and dense-coated vesicles have been reported in ependymal cells of the third ventricle in some experimental conditions [17]. An absorptive function and apocrine type of secretory process have also been suggested for the GFAP-reactive tanycytes persisting in the third ventricle of animals [9].

In the developing human brain, the GFAP-positive non-ciliated cells found in the ventricular zone are regarded to be transitional cells that acquire cilia and lose GFAP giving rise to the common ependymal cells during maturation [12]. However, regional and temporal differences of the ependymal cell development have been demonstrated [22]. In mature brain the ependyma of third ventricle contains different morphological and functional cell populations, including those associated with circumventricular organs (CVOs). In mammals, CVOs include subfornical organ and organum vasculosum of lamina terminalis, infundibulum, median eminence, subcommisural organ and area postrema [11]. The CVOs structures lack the blood-brain barrier and are characterised by extensive vasculature with fenestrated capillary endothelium and the large perivascular spaces. Ependymocytes covering the structures of CVOs lack ciliogenesis [20] and regionally demonstrate additional variations, such as the presence of secretory granules in the subcommisural organ region [21] or of pericellular basal lamina in the area of lamina terminalis [13].

The location of tumours in the presented cases showed some relationship with the lamina terminalis region (in case 1) and with the medio-basal hypothalamic region (in case 2). Thus the modified ependyma associated with CVOs in the lamina terminals area and median eminence was suggested as a primary site of origin of chordoid glioma in these cases. In many reported cases up to now, chordoid glioma was also found to occupy the antero-ventral rather than the dorso-caudal region of the third ventricle.

REFERENCES


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