

Papillary ependymoma with unique superficial cortical location: immunohistochemical and ultrastructural studies. A case report

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Folia Neuropathol 2009; 47 (4): 354-361

Abstract

Ependymomas are relatively rare neoplasms of the central nervous system that typically develop along cerebral ventricles and central canal of spinal cord. Occasionally, the tumours of ependymal origin arise supratentorially in brain parenchyma as ectopic cortical mass without any connection to the ventricular system. Ependymomas are heterogeneous group of tumours including cellular, papillary, clear cell and tanacytic histology. The papillary ependymoma is an unusual variant of ependymoma characterized by distinct morphology resembling other papillary tumours and corresponding to WHO grade II malignancy.

We present an unique case of ependymoma with distinctive papillary morphology at ectopic superficial cortical localization. The tumour occurred in eleven-years-old girl as a large, well-circumscribed mass in the left parietal lobe without continuity with the ventricular system. The patient presented with severe headache, vomiting and sudden-onset right hemiparesis. Histopathologically, the tumour revealed distinct papillary pattern with numerous pseudorosettes. Immunohistochemically, the neoplastic cells of both papillary structures and pseudorosettes were positive for glial fibrillary acidic protein and vimentin, whereas they were only slightly immunoreactive for epithelial membrane antigen and negative for cytokeratins. Ultrastructural findings revealed the presence of cilia usually located in the neoplastic cell bodies and intermediate glial-like filaments. The final diagnosis of papillary ependymoma at ectopic superficial localization was based on both, immunophenotypic profile and ultrastructural features that confirmed ependymal nature of neoplastic cells.

Key words: ependymoma, papillary variant, papillary tumours, extraventricular ependymoma, pediatric brain tumours.

Introduction

Ependymomas are glial neoplasms derived from ependymal cells lining the cerebral ventricular system and the central canal of spinal cord [2,9,15].

These neoplasms occur at any age but mainly affect children or young adults and account for 5 to 10% of all paediatric brain tumours. Ependymomas in children are located mostly infratentorially in the fourth ventricle [7], whereas spinal localization is more typi-

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cal for adults. Classic ependymomas usually grow as a well-circumscribed mass related to the ventricular system. CT scan reveals a hyperdense mass located within ventricular system, or sometimes in periventricular regions.

Ependymomas arising within the brain parenchyma has been reported only sporadically and considered as supratentorial ectopic ependymal tumours [5,11,13,16,18,25,27,28].

Concerning the morphology of ependymomas, it should be mentioned that this group of tumours exhibits marked variability including cellular, papillary, clear-cell or tanacytic histological pattern. The papillary variant of ependymoma is very rare and resembles other tumours with distinct papillary morphology.

We present an unusual case of papillary ependymoma that occurred as a large, well-circumscribed, cortical mass in right frontal lobe in eleven-year old girl with a history of severe headache, vomiting and sudden-onset right hemiparesis.

Case report

An eleven-years-old girl with a few weeks history of severe headache was admitted to a Department of Neurosurgery, The Children's Memorial Health Institu-

te due to a sudden-onset right-sided hemiparesis. A computed tomography (CT) scan of the brain revealed a well-demarcated, large, partially cystic tumour of left cerebral hemisphere with significant contrast enhancement and slight mass-effect. The tumour was located in the parietal lobe near the surface of the brain and did not reveal any relationship to the ventricular system. Magnetic resonance imaging (MRI) scan confirmed a large left-hemispheric tumour not adherent to the falx (Fig. 1A-B). Funduscopy showed bilateral papilloedema. The child was operated on September 12th 2003. The left parietal craniotomy with total tumour resection was performed. Postoperative course was uneventful and the child was discharged home on 14th postoperative day in a good general condition, neurologically intact. Pathological examination established the diagnosis of papillary variant of ependymoma. Postoperative radiotherapy was performed. No local tumour recurrence and distant metastasis have been shown after 6 years of post-surgical follow up.

Material and Methods

The biopsy specimen was fixed in 10% formalin, embedded in paraffin and routinely stained with hematoxylin and eosin (H&E). Immunohistochemical

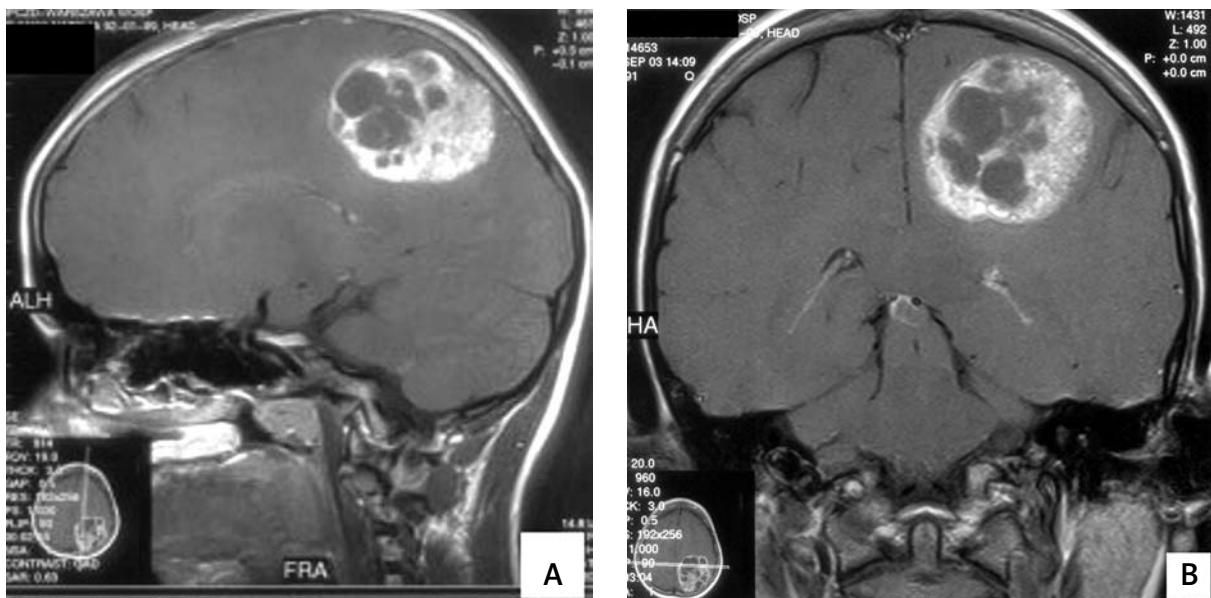


Fig. 1A-B. Magnetic resonance imaging (MRI) scans of the brain. Well-demarcated, large, partially cystic tumour of left cerebral hemisphere. Superficial tumour localization without connection to the ventricle system.

staining was performed on paraffin-embedded specimens according to the labelled avidin-biotin complex method (ABC) with DAB as chromogen using antibodies against glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA), vimentin, S-100 protein and cytokeratins cocktail AE1/AE3 (all antibodies from Dako). MIB-1 labelling index was established.

For electron microscopy, the small blocks of formalin-fixed tissue was postfixed in 2.5% cold glutaraldehyde for 1 hour, washed in cacodylate buffer, postfixed in 1% osmium tetroxide, dehydrated in graded alcohols and embedded in Epon 812. Ultrathin sections were counterstained with uranyl acetate and lead citrate and examined in a JEOL 1200EX electron microscope.

Results

Histopathological findings

The routine microscopic study revealed a highly cystic tumour with numerous cysts of various size and shape (Fig. 2A-B). Solid parts of tumour exhibited prominent papillary pattern (Fig. 2C). The majority of papillary structures were created by multiple layers of neoplastic cells arranged radially around fibrovascular cores (Fig. 2D). The cores often contained fibrillar processes of neoplastic cells and vascular elements. Occasionally, the formation of epithelial-like smooth surfaces could be noticed. The compact parts of tumour exhibited numerous typical perivascular pseudorosettes (Fig. 2E-F). True ependymal rosettes were detected only sporadically. The tumour contained foci of necrosis (Fig. 3A) and scattered mitotic figures (Fig. 3B).

Immunohistochemically, the neoplastic cells of both papillary structures and pseudorosette formations were strongly positive for glial fibrillary acid protein (GFAP) (Fig. 4A-B) and vimentin (Fig. 4C), whereas they were only slightly immunoreactive for epithelial membrane antigen (EMA) (Fig. 4D) and negative for cytokeratins (CK). Ki-67 labelling index was about 5%.

Ultrastructural findings

The cytoplasm of tumour cells often contained a large amount of intermediate, glial-like filaments that were arranged in interweaving bundles or for-

med compact whorls of filaments (Fig. 5). Some cells revealed the presence of cilia usually located in the cell bodies (Fig. 6). The cellular processes along surfaces of papillary structures usually were filled with bundles of filaments. The apical cell surface was lined by basal lamina material (Fig. 7).

Discussion

The clinico-pathological characteristics of presented tumour, including its superficial localization in left parietal lobe parenchyma without continuity with ventricular system and microscopical papillary growth pattern, resulted in difficulties in differential diagnosis. The critical diagnosis of papillary ependymoma at ectopic superficial localization was finally established. Both, immunohistochemical staining and ultrastructural studies were required to confirm the ependymal nature of neoplastic cells.

Supratentorial ependymomas occur typically in the brain ventricles and only occasionally develop within the brain parenchyma with no attachment to ventricular system [5, 19]. So far only few cases of ectopic ependymomas located in subcortical white matter have been reported [5,11,13,18,25,27,28]. These tumours can arise from heterotopic ependymal remnants [23,24]. Recently, the stem radial glia cells has been also suggested as a candidate cells of origin of ependymoma cancer stem cells [22].

The fourth edition of WHO classification of tumours of central nervous system identifies three subtypes of ependymal tumours of different grade of malignancy: subependymoma and myxopapillary ependymoma (grade I), ependymoma and its variants – cellular, papillary or clear cell (grade II) and anaplastic ependymoma (grade III) [15]. Considering the tumour malignancy, the proliferation of vessels play an important role [6]. The most common type is classic ependymoma that exhibits typical perivascular pseudorosettes and less commonly true ependymal rosettes created by columnar cells oriented radially around central lumen. Histopathological heterogeneity of ependymomas is also reflected by the presence of various cellular elements including clear cells, tanacytic cells or occasionally giant cells [26]. Ependymomas may also contain structures resembling central canal or ventricular lining [15]. The molecular alterations in ependymomas are not well defined but they may be considered as one of prognostic factors important in tumour biology [3,12]

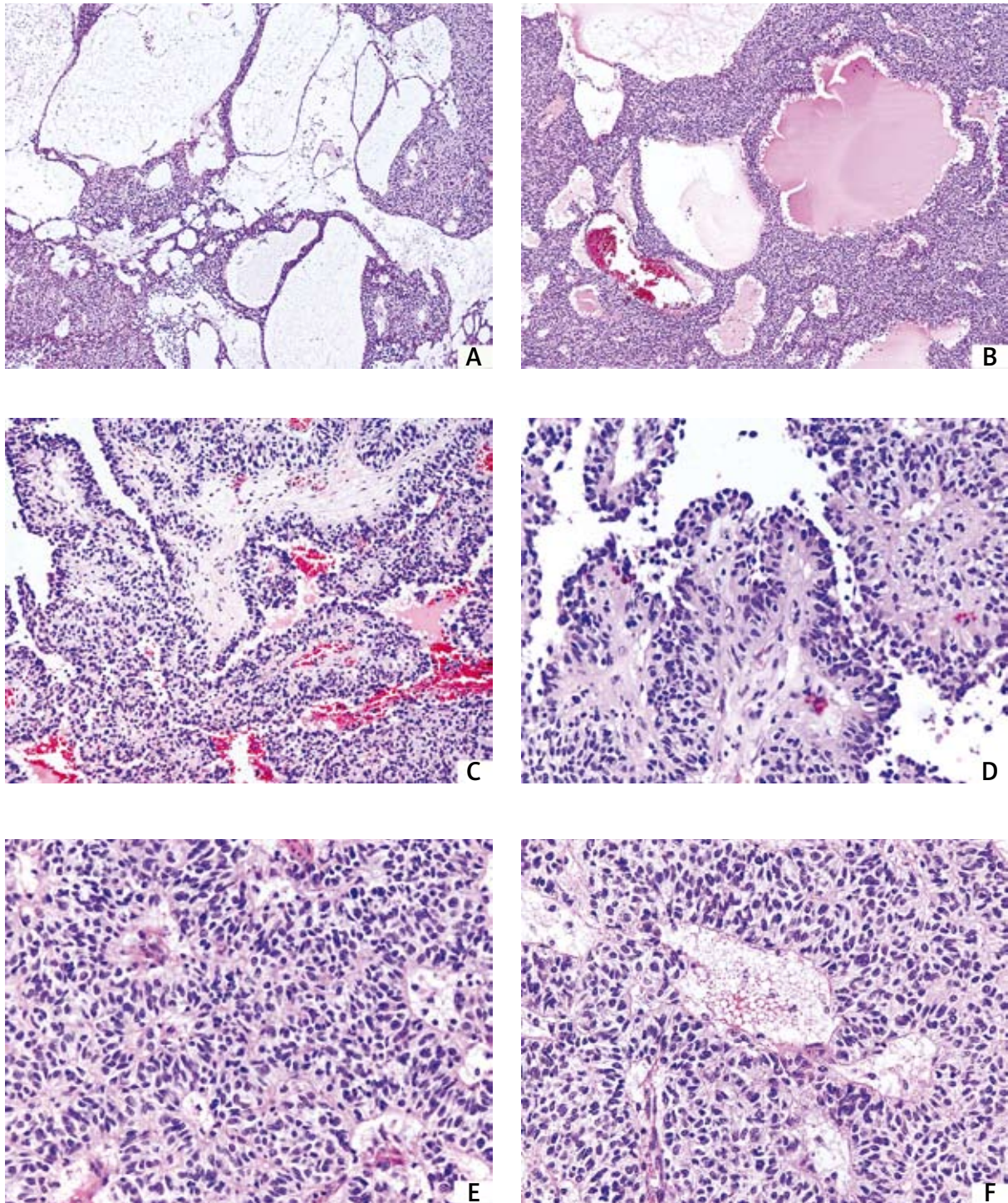


Fig. 2A-F. Histopathological features of papillary ependymoma. A. Cystic structure of tumour, H&E. B. Numerous cysts of various size within tumour mass, H&E. C. Solid part of tumour with distinctive papillary pattern, H&E. D. Papillary structures created by multiple layers of neoplastic cells arranged radially around fibrovascular cores, H&E. E. Compact part of tumour with numerous pseudorosettes, H&E. F. Pseudorosettes around small vessels, H&E. Original magnification: A, B $\times 40$; C $\times 100$; D, E, F $\times 200$.

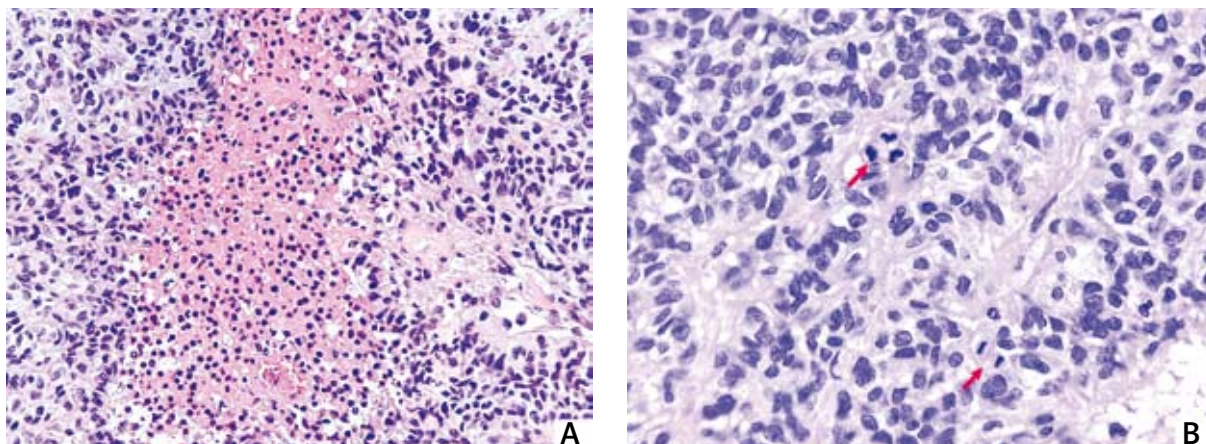


Fig. 3A-B. Histopathological features of papillary ependymoma. A. Focus of necrosis, H&E. B. Scattered mitotic figures, H&E. Original magn.: A \times 200; B \times 400.

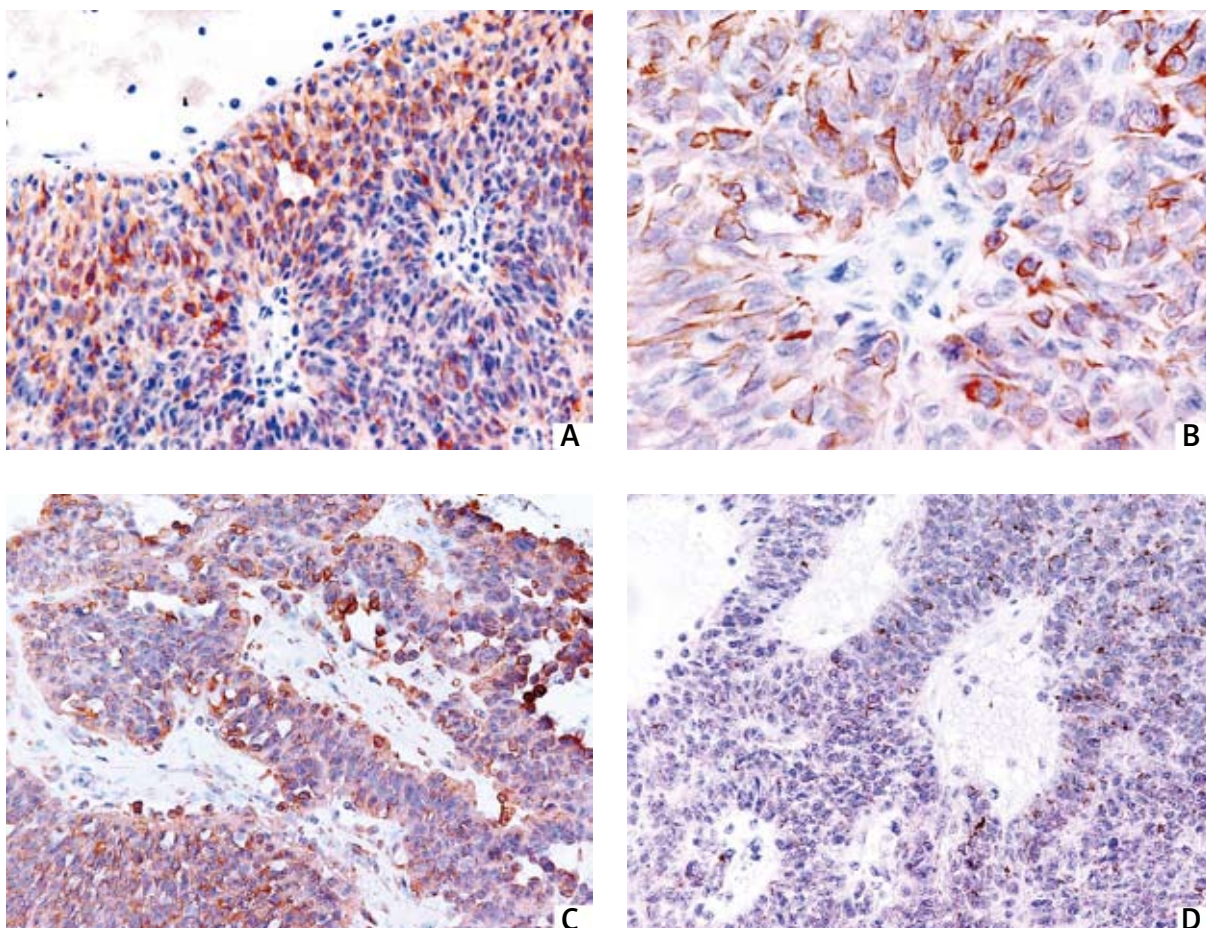


Fig. 4A-D. Immunohistochemical staining. A. Papillary structures with strong positivity for glial fibrillary acidic protein (GFAP). B. Pseudorosettes with immunoreactivity for GFAP. C. Strong immunoreactivity for vimentin. D. Slight immunostaining for epithelial membrane antigen (EMA). Original magn.: A, C, D \times 200; B \times 400.

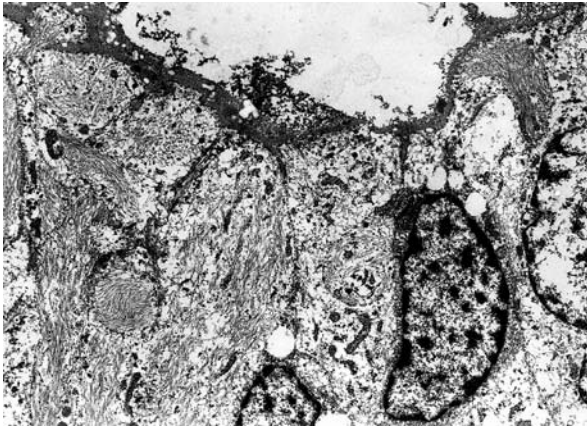


Fig. 5. Tumour cells and cellular processes along papillary surfaces filled with numerous intermediate, glial-like filaments; original magnification: $\times 5000$.

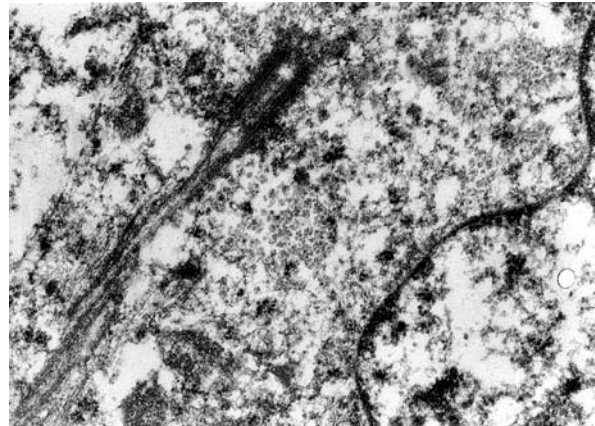


Fig. 6. Presence of cilia in the cell bodies; original magnification: $\times 12\,000$.

The papillary ependymoma represents a very rare variant of ependymomas [4]. It should be distinguished from other papillary paediatric brain tumours that range from WHO grade I (choroid plexus papilloma) to grade III lesions (papillary meningiomas) and require different treatment. Other papillary tumours including papillary glioneuronal tumour ought to be also considered [10].

The characteristic morphology of papillary ependymoma consists of papillary structures covered by single or multiple epithelial tumour cells with smooth surfaces. The papillary structures of ependymomas usually display strong immunoreactivity for GFAP. Ultrastructural features including cilia, blepharoblasts, microvilli at the luminal surface and microrosettes formation are very characteristic of ependymal tumours. The cell processes usually contain intermediate filaments. The electron microscopic findings support the ependymal nature of neoplastic cells that is very important for critical diagnosis [8, 14]. So far only a few cases of papillary ependymomas have been described and they were located mostly within ventricular system [20]. Only one case of anaplastic ependymoma with papillary features was reported at parenchymal localization [11].

We present the first case of typical papillary variant of ependymoma WHO grade II at superficial localization in the parietal left lobe without any relation to the ventricular system. Both CT and MRI scans revealed a well-demarcated, extraventricular mass exhibiting multicystic structure. Strong GFAP reactivity of cells creating papillary structures and ul-

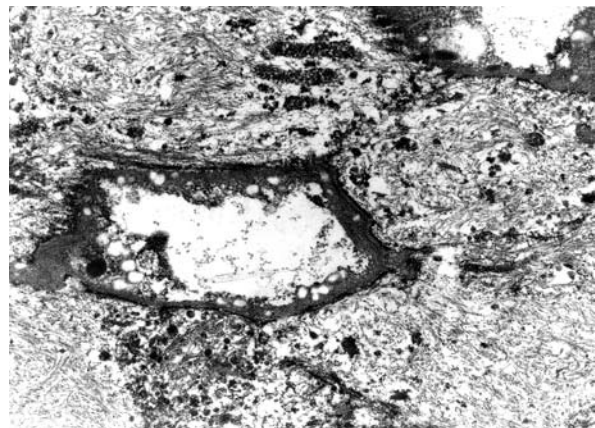


Fig. 7. Cellular processes filled with numerous compact whorls of filaments. The apical cell surface was lined by basal lamina material; original magnification: $\times 4000$.

trastructural features such as cilia and intermediate glial-like filaments of neoplastic cells were warrant for the diagnosis of papillary ependymoma.

In children, the differential diagnosis of brain papillary lesions includes choroid plexus papilloma or carcinoma, papillary meningioma, and very rare metastatic carcinoma [17,20]. Choroid plexus papilloma or carcinoma, and metastatic carcinoma exhibited strong immunoreactivity of cytokeratins, whereas GFAP-positivity is slight or non-existent. Nevertheless, many choroid plexus papillomas contained numerous GFAP-positive cells [1]. In general, the papillomas with ependymal differentiation reve-

al strong immunoreactivity of low-molecular-weight keratin, whereas ependymomas with papillary features show predominantly glial immunophenotype. Additionally, the superficial location in the brain is not typical for choroid plexus papilloma and choroid plexus carcinoma. Metastatic carcinomas with papillary structures are much more typical for adults however metastasis of papillary thyroid carcinoma must be considered also in children. Other intracranial tumour with papillary structures and superficial location such as papillary meningioma ought to be considered in differential diagnosis. The papillary meningioma preferentially affects children and is characterized by locally aggressive behavior and late distant metastases. The WHO classification of CNS tumours defines papillary meningioma as grade III of malignancy [2,21]. Microscopically, this distinctive meningeal tumour exhibits pseudopapillary structures created by ependymoma-like cells arranged around blood vessels. The tumour cells show reactivity for epithelial membrane antigen (EMA) and to a less degree for cytokeratins, whereas they are negative for GFAP. The correct diagnosis is very important as both, treatment and clinical outcome of papillary variant of ependymoma as opposed to meningioma is different. The total resection accompanied by postoperative irradiation is recommended for papillary ependymoma, whereas papillary meningioma requires more aggressive approach. The presented child with papillary ependymoma is well after 6 years' follow up with no evidence of tumour recurrence.

This case illustrates the importance of accurate histopathologic diagnosis in CNS tumours of papillary appearance. So far it is the first description of papillary ependymoma WHO grade II in superficial hemispheric localization.

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