

Papillary glioneuronal tumour of the precentral gyrus

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Folia Neuropathol 2008; 46 (2): 158-163

Abstract

The article describes a case of a 15-year old boy after a head contusion with a five-month history of headaches and two seizure episodes. MR imaging revealed a partly solid and partly cystic cortical-subcortical tumour within the precentral gyrus with post-contrast enhancement. The patient underwent gross total resection of the lesion. Histologically the neoplasm was composed of pseudopapillary gliovascular structures surrounded by solid glioneuronal tumour areas. The expression of GFAP and nestin characterized the central parts of the tumour. Moreover the immunolabelling for synaptophysin, neurofilaments, Olig2 and NCAM was present in the peripheral part of the lesion. The neoplasm was consistent with a papillary glioneuronal tumour – one of the new entities in the last WHO CNS tumour classification.

Key words: glioneuronal tumours, brain tumour, new WHO entity.

Introduction

The WHO Classification of Tumours of the Central Nervous System 2007 incorporated eight new entities. One of them is papillary glioneuronal tumour (PGNT), which belongs to the group of mixed glioneuronal neoplasms. PGNT is a very rare, clinically benign neoplasm that corresponds to WHO grade I [9,10,15]. Histologically this glioneuronal tumour reveals gliovascular structures intermixed with solid areas [9,10,13,15]. Since the first PGNT description in 1998 by Komori et al. about 40 cases of this neoplasm have been reported in the literature [4,7,13]. The characteristic location of the tumour are the cerebral hemispheres, with a special predilection for the temporal lobes and periventricular area [3-6,16]. The

aim of our article is to show a case of PGNT with rather unusual gyral location.

Case report

A 15-year old boy was admitted to the Department of Developmental Neurology of the Medical Academy of Gdańsk in May 2002 because of secondarily generalized tonic-clonic seizures occurring twice in the last week before hospitalization. Five months before the boy had a painful left-side head contusion during a football match and after that time he suffered from recurrent headaches. Moreover, for two months he had periodic numbness of the right part of his face and neck.

On admission this right-handed boy disclosed completely normal neurological examination. The familial

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history of seizures and neurological disorders was negative. Antiepileptic drugs (carbamazepine and tiagabine) in typical therapeutic doses were introduced.

Magnetic resonance imaging revealed a cortical and subcortical mass, located superficially, involving the precentral gyrus of the left hemisphere. The tumour was partly solid and partly cystic, sharply demarcated and measured 2.5/2.3 cm in diameter. It was hypointense in T1-weighted images and was hyperintense in PD and T2 with associated subtle oedema in the surrounding white matter (Fig. 1a). In FLAIR sequence the cystic fraction of the tumour had a low signal since the solid part was hyperintense. After gadolinium contrast administration the homogeneous enhancement of the solid fraction was evident (Fig. 1b). Because of the location and contrast enhancement of the tumour, ganglioglioma was suggested.

At the beginning of June the patient underwent gross total tumour resection at the Neurosurgery Department. The boy experienced no postoperative complications and he was discharged a week later in a good status on antiepileptic drugs.

Formalin-fixed, paraffin-embedded tumour samples were sent to the Department of Pathology of the Medical University of Gdańsk and were evaluated histologically

in H&E. Immunohistochemical staining with GFAP, S100, CD56, chromogranin, synaptophysin, neurofilaments, CD34, vimentin, Ki-67, EMA, bcl-2 and p53 (all from DAKO, Glostrup, Denmark), nestin (Chemicon International) and Olig2 (IBL Co., Japan) were performed with the En Vision method (DAKO).

In H&E staining the tumour consisted of two zones: the central-pseudopapillary and outer-solid zone (Fig. 2a). Papillary neoplastic structures were composed of hyalinized vascular cores covered with small hyperchromatic oval to round cells (Fig. 2b). These intrapapillary vessels were of capillary or venule type. The solid part of the tumour was made up of compressed papillary elements intermixed with oligodendroglioma-like areas (Fig. 2c). In this zone of the tumour, ganglioid and neuronal cells were identified.

Immunohistochemically the cells covering papillae were strongly positive for GFAP, S100, NCAM and vimentin (Fig. 3a). In the solid zone of the tumour, overlapping areas of synaptophysin and GFAP-expressing cells were present. The oligodendroglioma-like fields were strongly synaptophysin-positive, reminiscent to neurocytoma fields (Fig. 3c). Scattered ganglioid cells and neurons expressed NCAM, synaptophysin and neurofilaments (Fig. 3d). There were no mitotic figures

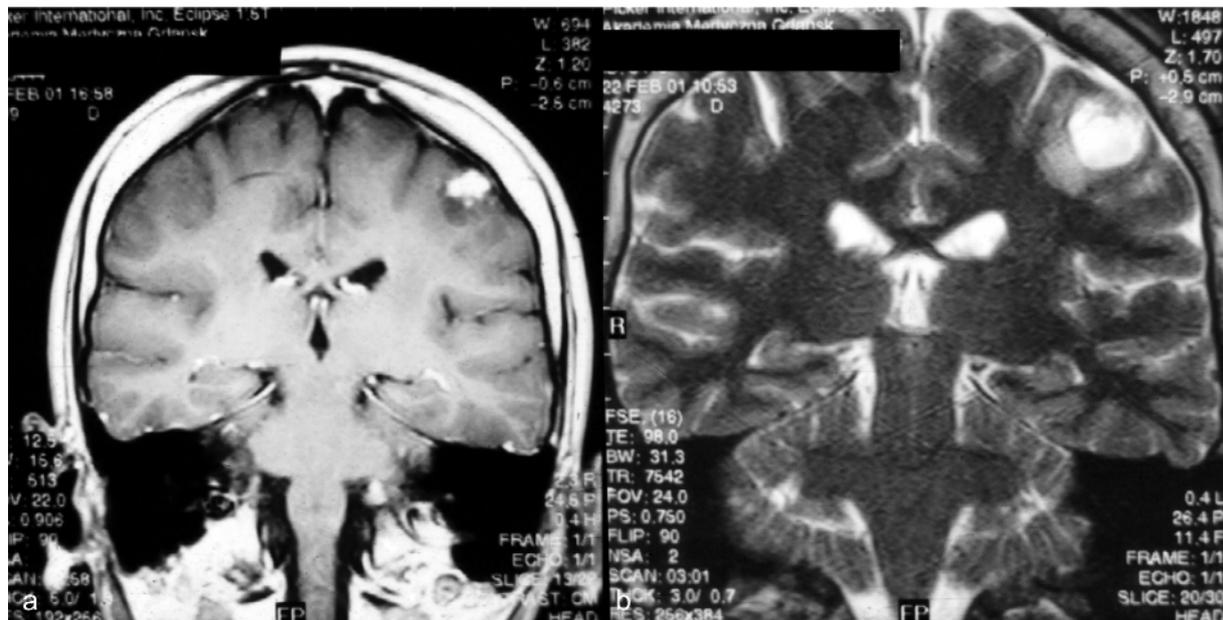


Fig. 1. (a) Coronal T2-weighted MR image shows hyperintense mass in the precentral gyrus with associated oedema. (b) The homogeneous enhancement of the solid fraction of the neoplasm in coronal T1-weighted MRI after contrast administration

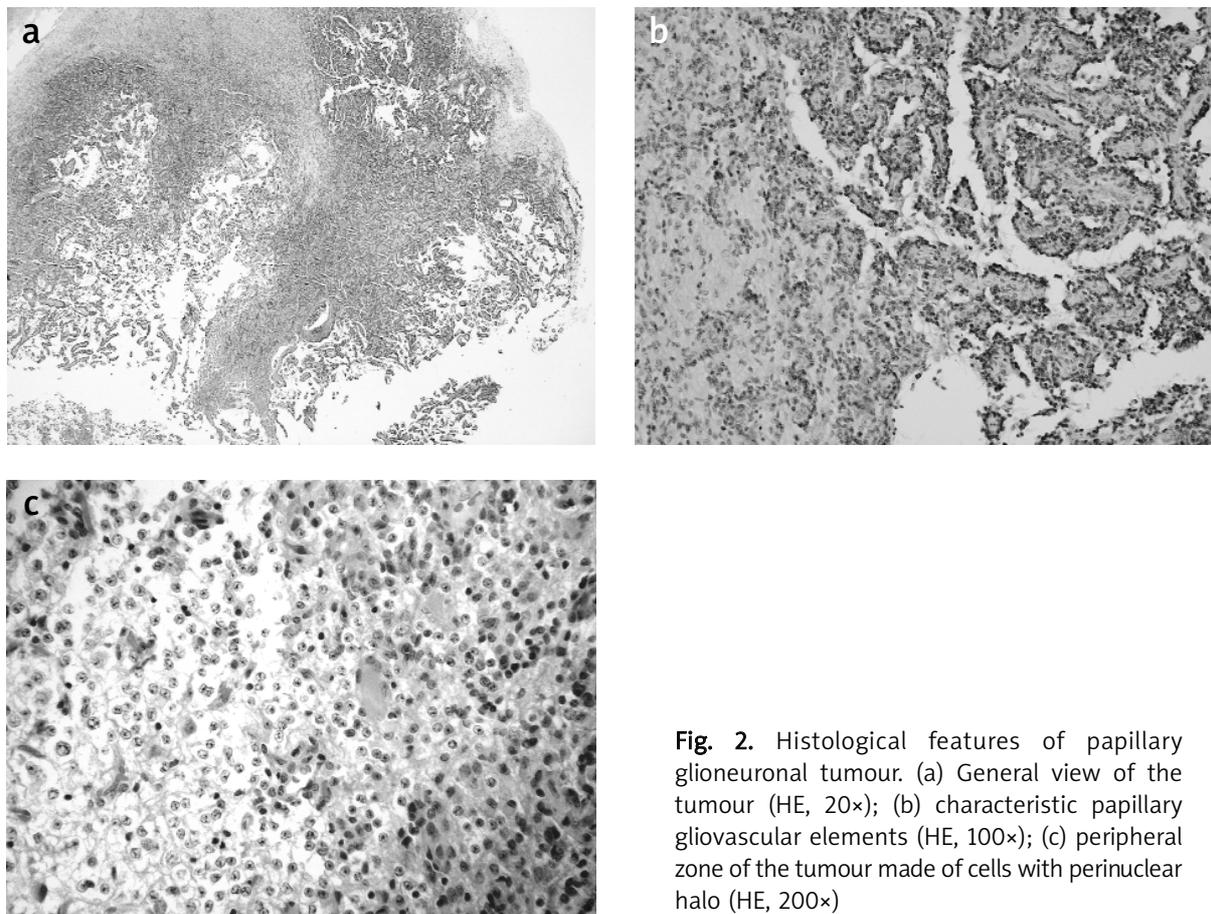


Fig. 2. Histological features of papillary glioneuronal tumour. (a) General view of the tumour (HE, 20×); (b) characteristic papillary gliovascular elements (HE, 100×); (c) peripheral zone of the tumour made of cells with perinuclear halo (HE, 200×)

in either part of the tumour. Ki-67 index was less than 1%. Olig2 and nestin immunolabelling was present within the neoplastic cells. Olig2 nuclear expression characterized some cells within the neurocytoma-like areas and the scattered cells covering the papillae (Fig. 3e). Nestin immunoreactivity was strong, found mainly within the papillary component of the tumour (Fig. 3b). Staining for CD34, EMA, bcl-2 and p53 was negative in the neoplastic cells.

The border between the tumour and the adjacent nervous tissue was sharp in the cystic parts and rather blurred in the solid parts of the neoplasm. In the rim of the resected surrounding cerebral tissue there were some pathological changes including segmental scattered cortical and white matter calcifications, cellular astrocytosis, microglial rod cell reaction and focal lymphocytic infiltrations around blood vessels. Moreover, focal perivascular glial satellitosis consisting of small oval cells and clusters of cells with a perinuclear halo was encountered (Fig. 4a, b).

Finally the diagnosis of PGNT grade I was established based on the WHO classification [9]. The boy was consulted oncologically and careful clinical observation and radiological control were advised and performed. The anticonvulsant drugs were gradually diminished and completely withdrawn in two years. Six years after the operation the patient is radiologically and clinically free of the disease and he is a university student.

Discussion

The most common causes of paediatric epilepsy are: cortical dysplasias, destructive neurometabolic diseases, posttraumatic changes and tumours [1,2,8,14]. In children frequent epileptogenic neoplasms are neuronal and mixed neuronal-glial tumours [1,2]. These neoplasms create a heterogeneous group of relatively rare entities with usually benign biology and clinically favourable prognosis [9,10,15]. Well known representatives of this group are: ganglioglioma, dysembryoplastic neuroepithelial tumour and central neurocytoma [9,10,13,15].

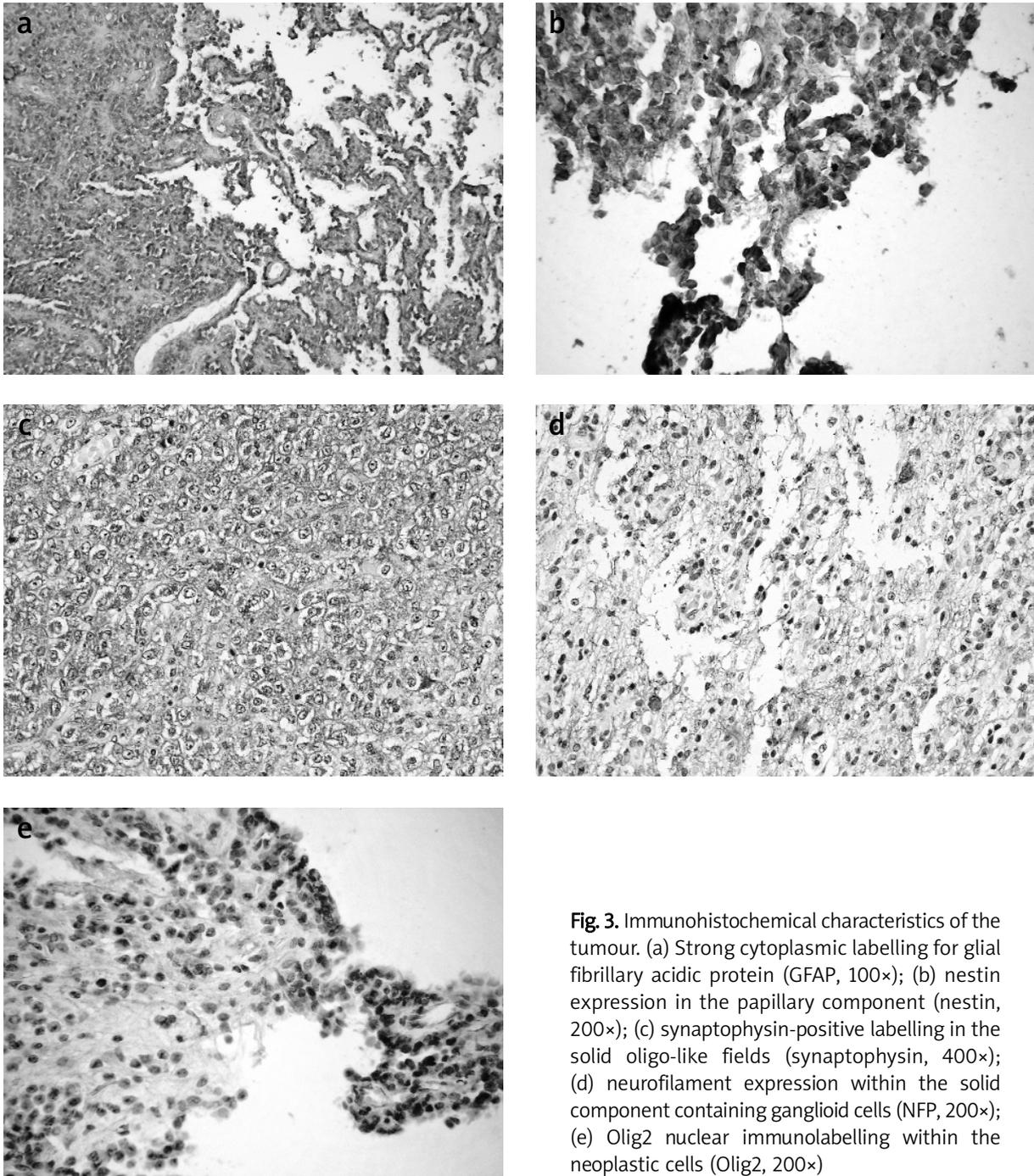


Fig. 3. Immunohistochemical characteristics of the tumour. (a) Strong cytoplasmic labelling for glial fibrillary acidic protein (GFAP, 100×); (b) nestin expression in the papillary component (nestin, 200×); (c) synaptophysin-positive labelling in the solid oligo-like fields (synaptophysin, 400×); (d) neurofilament expression within the solid component containing ganglioid cells (NFP, 200×); (e) Olig2 nuclear immunolabelling within the neoplastic cells (Olig2, 200×)

The diversity of patho-clinical characteristics of some neuro-glial lesions forced the updating of the WHO taxonomy of tumours of the central nervous system. In the newest WHO 2007 classification three new entities entered the group of mixed neuronal-glial tumours: extraventricular neurocytoma, rosette-forming glioneu-

ronal tumour of the fourth ventricle, and papillary glioneuronal tumour (PGNT), which was previously classified as a variant of ganglioglioma [9,10,15].

PGNT appears over a wide age range from 4 to 75 years, but is most prevalent in teenagers and young adults [4,5,12,13,15]. On CT and MRI images, PGNT is

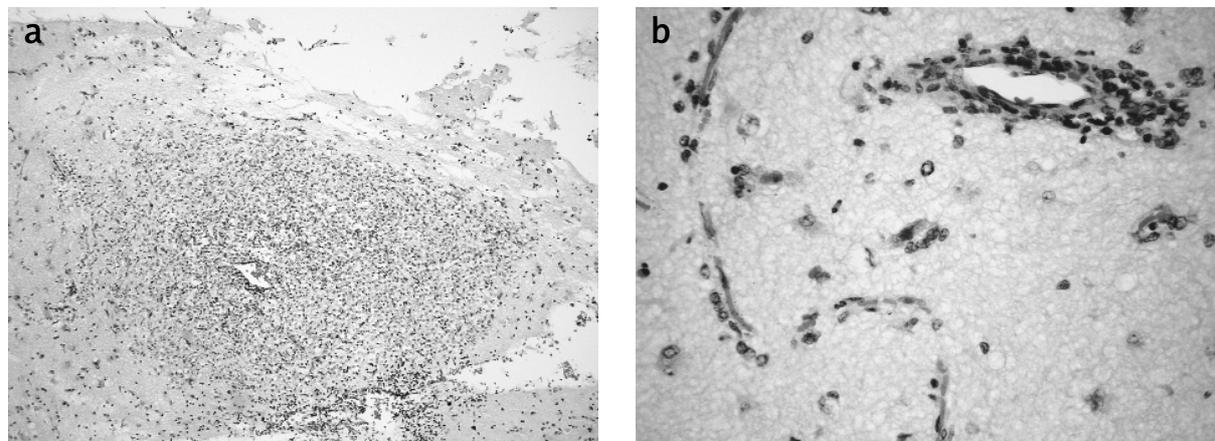


Fig. 4. (a) Focus of perivascular cortical oligodendroglia-like cells located 0.8 cm from the tumour border (HE, 100 \times). (b) Perivascular small glial cell satellitosis (HE, 400 \times)

a well demarcated, contrast-enhancing tumour with a cystic fraction, located in the temporal lobe or periventricular area [3,12,16]. In MRI solid components are iso/hypointense in T1 and hyperintense in T2-weighted images. Dimensions of reported tumours vary from 1 to 9 cm. Significant peritumoural oedema was described in masses larger than 6 cm [4,11], although in smaller lesions it is, as in our case, subtle or absent. An additional finding is the presence of calcifications in 40% of PGNT cases [7,16]. Radiological differential diagnosis of PGNT includes ganglioglioma and pilocytic astrocytoma [5,7,16].

The presented tumour had an unusual superficial location in the precentral gyrus. It was mainly a cortical mass with involvement of the adjacent subcortical white matter. This is also the first reported case of PGNT associated with previous head trauma. We can suppose that the head contusion accelerated the evolution of the tumour in our patient, because the clinical symptoms started after the accident. The clinical manifestations of the presented case in the form of headaches, seizures and paresthesias were typical for PGNT. Other clinical symptoms found in the literature include visual disturbances, focal sensory-motor deficits, vertigo and haemorrhagic stroke [4,7,9,12].

Histologically our case showed the typical pseudo-papillary gliovascular structures which are highly distinctive in conventional H&E staining. Immunohistochemical staining for glial and neuronal markers revealed both components of the tumour. Neoplastic cells surrounding blood vessels in papillary elements expressed vimentin, S-100, GFAP, Olig2 and nestin, as

in the other reported cases [4,5,9,17]. The solid zone of the tumour presented intermixed differentiation with neuronal elements of variegated morphology depending on the state of maturation. The second component of the solid zone was glial elements of the astrocytic and oligodendroglial lineage. In a few reports, as in our case, the tumours were in part immunomorphologically consistent with neurocytoma [3,4].

The presented case of PGNT had a typical, very low proliferative potential of less than 1% [5,9,15]. However, so-called atypical PGNT cases with the proliferative index up to 15% have also been reported [4,10,18]. Complete surgical resection is a satisfactory therapeutic method in PGNT, but in cases with higher proliferation adjuvant therapy was successfully introduced [4,5,9,15].

The histogenesis of PGNT is not well established. It seems that this tumour can have a developmental origin from multipotential precursor cells [6,15,17]. Expression of developmentally related proteins such as nestin, CD34, NCAM and Olig2 and signs of bidirectional differentiation indicate impaired maturation of neoplastic cells [13,15,17]. Gelpi et al. reported widespread Olig2 and PDGFR α immunoreactivity, which may suggest the possible origin of PGNT from a common progenitor cell [3]. The main population of neural progenitors is represented by the radial glia and their progeny include all cellular lineages: neurons, astrocytes, oligodendrocytes, ependymocytes and adult neural stem cells [11]. The small population of radial glia gives rise to mixed neuronal/glial cellular clones [8,11]. A limited number of neural stem cells are present during the entire life of the organism in the

“adult subventricular zone”, which may explain the most frequent location of PGNT [6,15].

The other idea concerning histogenesis of glioneuronal tumours postulates the connection between these tumours and cortical dysplasias and microdysgenesis [2,14]. Recently Arai et al. described a peculiar form of cerebral microdysgenesis characterized by white matter neurons and perineuronal and perivascular glial satellitosis [1]. These authors explained this abnormality as the histological manifestation of neuronal migration defect [1]. In our case focal perivascular glial cells were encountered in the nervous tissue surrounding the tumour. These findings according to the specific gliovascular structures in PGNT may, in our opinion, correspond to the hypothetical role of possible microdysgenesis in the development of papillary glioneuronal tumour.

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