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## 21.1 Overview

- Papillary glioneuronal tumor (PGNT) is a benign (WHO grade I), relatively circumscribed, biphasic cerebral neoplasm occurring predominantly in the temporal lobe; it most commonly affects young adults.
- No population-based epidemiologic data are available to date.
- PGNT was initially described as “pseudopapillary ganglioglioma” or “pseudopapillary neurocytoma with glial differentiation.”
  - Established as a distinct clinicopathologic entity in 1998 by Komori et al.
  - Regarded as a variant of ganglioglioma in the 2000 World Health Organization (WHO) classification of central nervous system tumors.
  - Added as a new entity in the 2007 WHO classification.
- The most common clinical manifestations include headache and seizures.
- Patients may also present with nausea, vertigo, visual and gait disturbances, focal sensorimotor deficits, syncope, memory loss, and mood changes.

## 21.3 Neuroimaging

- The tumor presents as well-defined, circumscribed lesion centered in subcortical or periventricular cerebral white matter. Small lesions lack peritumoral edema. Mass effect and mild peritumoral edema are present with large lesions.
  - PGNT occurs in all lobes, with the temporal lobe being the most commonly involved.
  - Rare intraventricular examples have been reported.
  - *MRI*: The tumors are typically heterogeneous on T2-weighted imaging, although small lesions may be homogeneous, and marked hyperintensity may be present in cystlike regions (Figs. 21.1 and 21.2).
  - PGNTs are usually hypointense on T1-weighted imaging (Fig. 21.3) unless intratumoral hemorrhage is present.
  - These tumors may show postcontrast enhancement (Fig. 21.4), with the enhancing component isointense or hyperintense to cortex on T1-weighted imaging.
  - Enhancement may be peripheral, solid, or peripheral with mural nodule.
  - Diffusion weighted imaging (DWI) usually shows no restriction of diffusion (Fig. 21.5).
  - *CT scans*: Calcification and intratumoral hemorrhage are uncommon.

## 21.2 Clinical Features

- PGNT occurs over a wide age range (4–75 years), with a mean age at presentation of 27 years. It is more prevalent in the second and third decades of life.
- No gender predilection has been reported.

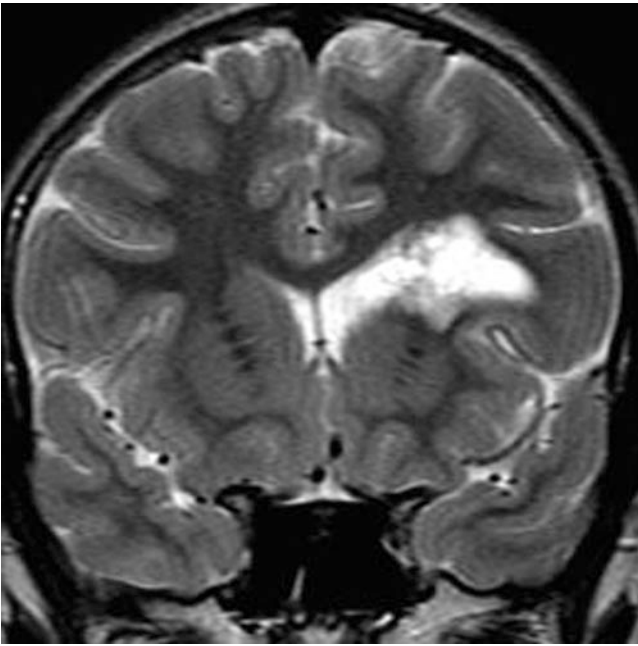
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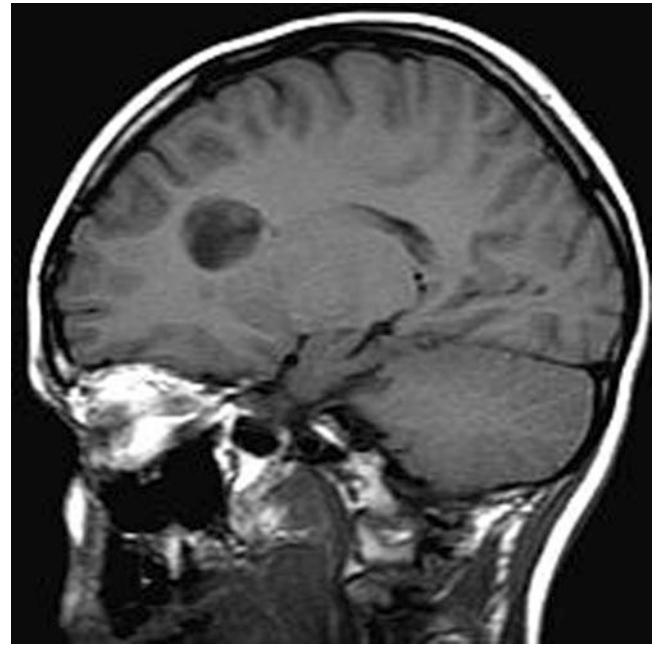
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## 21.4 Pathology

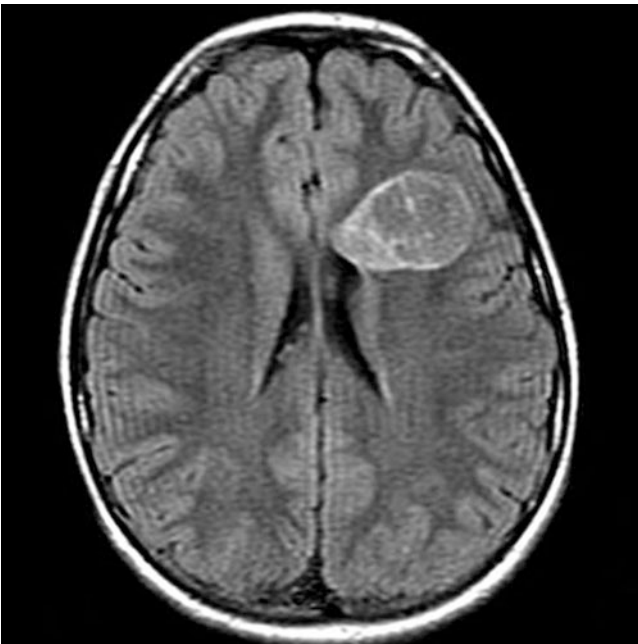
- *Smear preparations*
  - Smear preparations reveal a mixture of cells (Figs. 21.6, 21.7, and 21.8), including ganglion cells with large, eccentric nuclei; prominent nucleoli; delicate nuclear



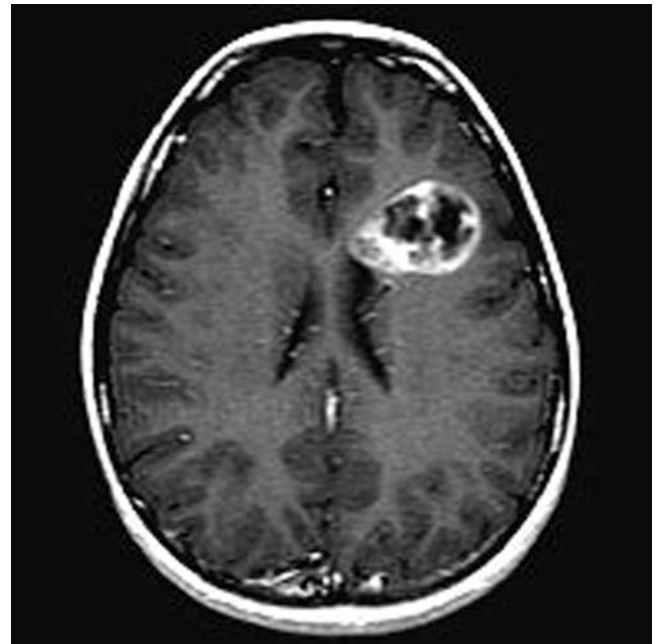
**Fig. 21.1** Papillary glioneuronal tumor (PGNT). Coronal T2-weighted MRI shows a heterogeneous tumor in the left periventricular white matter, with a markedly hyperintense central cystlike component and a less intense peripheral nodular component



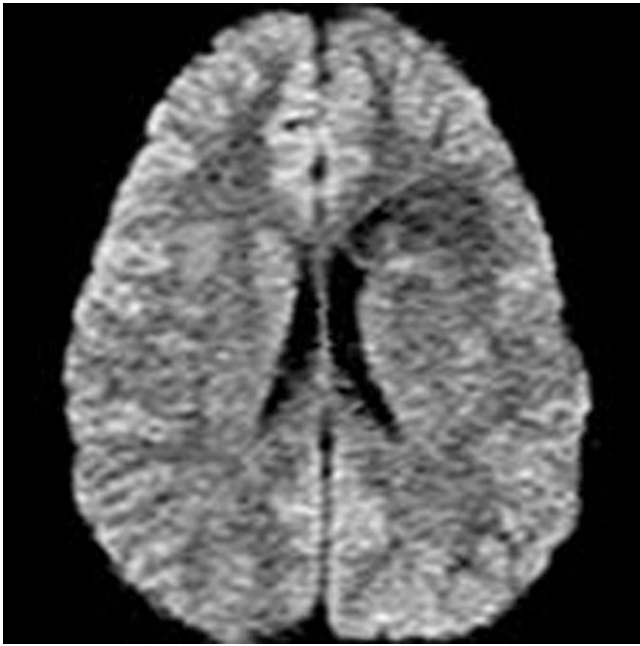
**Fig. 21.3** Sagittal T1-weighted MRI shows a well-circumscribed tumor with marked hypointensity in the central, cystlike component



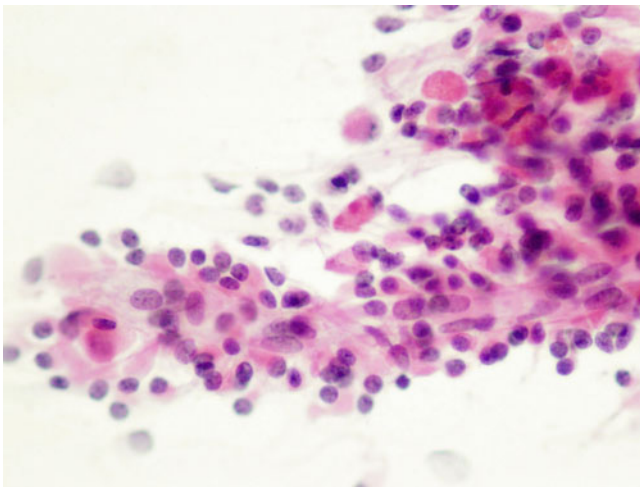
**Fig. 21.2** Axial fluid-attenuated inversion recovery (FLAIR) MRI showing attenuation of signal in the central, cystlike component. Note the lack of peritumoral edema



**Fig. 21.4** Axial T1-weighted postcontrast images showing a PGNT with irregular peripheral nodular enhancement. The central, cystlike component does not enhance



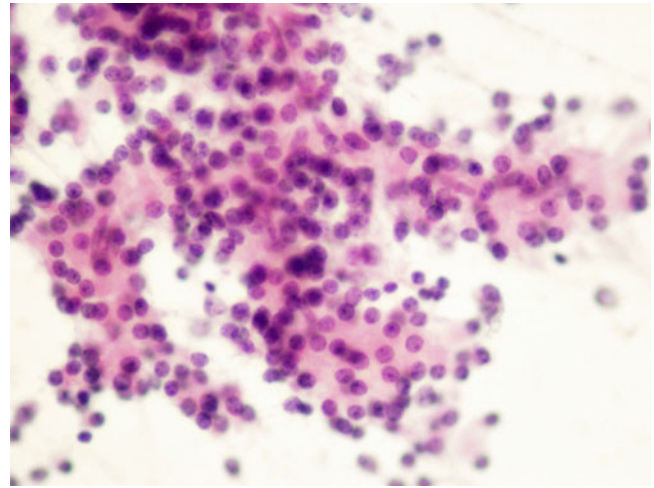
**Fig. 21.5** Axial diffusion weighted imaging (DWI) shows no diffusion restriction within the tumor



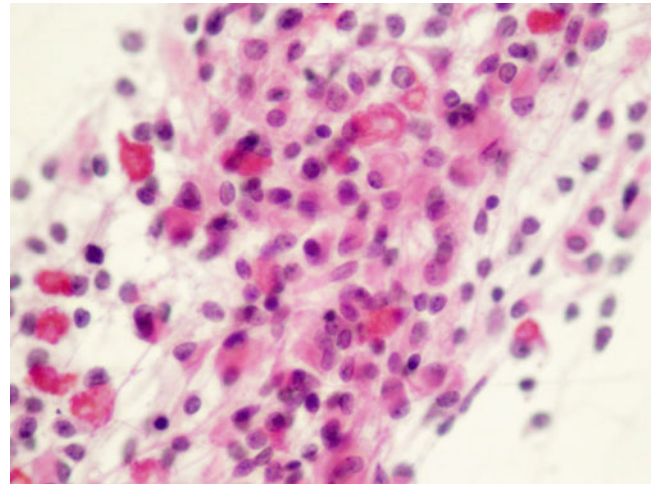
**Fig. 21.6** Intraoperative cytologic preparation showing a mixed cell population with some of the cells having eosinophilic cytoplasm and eccentric nuclei

membranes; and Nissl substance in the cytoplasm. Intermediate cells with less prominent nucleoli and relatively scant cytoplasm also are seen. Cells with dense nuclei, scant cytoplasm, and occasional processes represent perivascular astrocytes.

- *Histology*
  - Two distinct histologic components are identified: glial and neuronal.
    - The glial component consists of pseudopapillary structures with hyalinized blood vessels surrounded



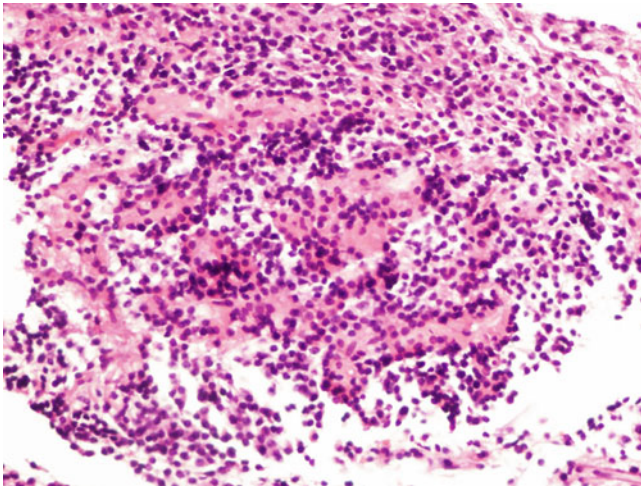
**Fig. 21.7** Intraoperative cytologic preparation showing pseudopapillary architecture



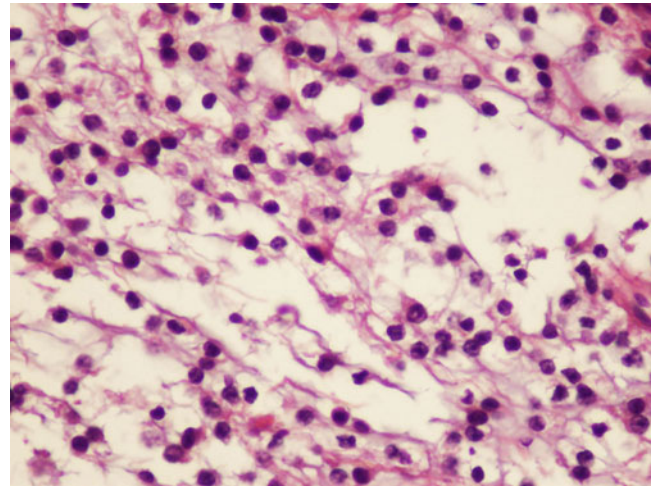
**Fig. 21.8** Intraoperative cytologic preparation showing fibrillary background

by a single or pseudostratified layer of cuboidal glial cells (Figs. 21.9 and 21.10). These cells have rounded nuclei, moderately dense chromatin, and scant eosinophilic cytoplasm and do not elaborate perivascular cytoplasmic processes. Mitotic activity and cellular atypia are absent in this component.

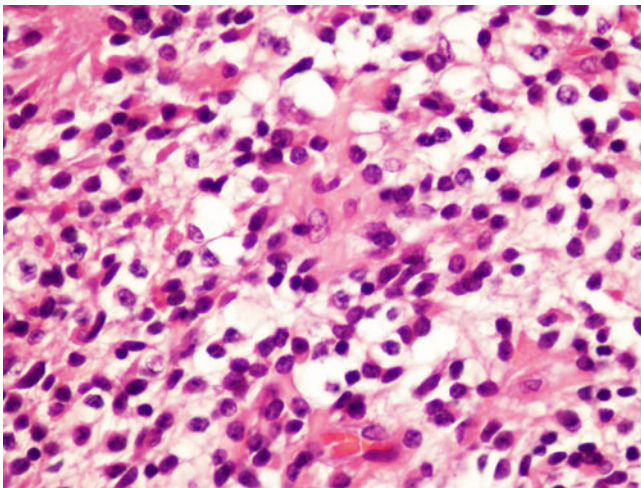
- The neuronal component consists of interpapillary sheets or focal collections of neurocytes, ganglion cells, and intermediate “ganglioid cells” in a fibrillary, neuropil-like matrix.
  - Neurocytic cells have dark, round, uniform nuclei; scant cytoplasm; and sometimes an oligo-like halo (Fig. 21.11). The ganglion cells feature large, vesicular nuclei; prominent nucleoli; and abundant cytoplasm with well-developed Nissl substance.



**Fig. 21.9** Characteristic pseudopapillary pattern in PGNT



**Fig. 21.11** Intervening cells with clear cytoplasm may be seen



**Fig. 21.10** Higher magnification showing the core of pseudopapillary structures and the mixed glioneuronal population of cells

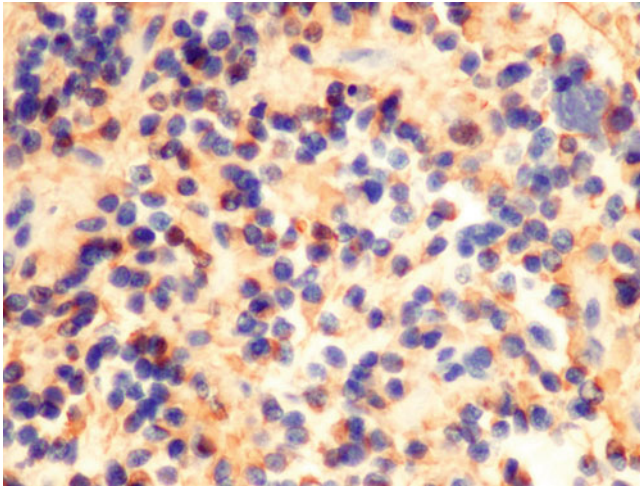
- The intermediate-sized “ganglioid cells” feature less-abundant cytoplasm and smaller nucleoli.
- Occasional pleomorphic and binucleated ganglion cells are identified.
  - Minigemistocytes with eccentrically placed nuclei and eosinophilic hyaline cytoplasm may be found in the interpapillary regions or nestled among neuronal cell types (see Figs. 21.6 and 21.10).
  - A narrow zone of tumor infiltration or a discrete pushing border may be seen with the adjacent neural parenchyma. In this region, prominent gliosis, Rosenthal fibers, eosinophilic granular bodies, hemosiderin deposition, foamy cell infiltration, and dystrophic calcifications may be identified.
  - Mitotic activity is usually inconspicuous.
  - Necrosis and microvascular proliferation, when present, are exceptional.

## 21.5 Immunohistochemistry

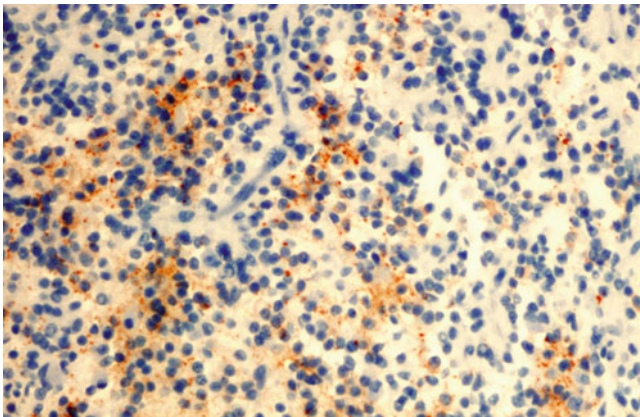
- The small, cuboidal glial cells surrounding the hyalinized vascular pseudopapillae are positive for glial fibrillary acidic protein (GFAP) (Fig. 21.12) and S-100.
- Neuronal cells of all sizes are immunopositive for synaptophysin (Fig. 21.13), neuron-specific enolase (NSE), and class III  $\beta$ -tubulin (MAP2) (Fig. 21.14).
- Most of the neuronal cells are also positive for NeuN; immunopositivity for neurofilament protein (NFP) is confined to ganglion cells and intermediate “ganglioid cells.”
- Chromogranin A expression has not been observed.
- Minigemistocytes show intense GFAP immunoreactivity.
- Tanaka et al. described a subpopulation of cells that fail to label with GFAP and neuronal markers but express the Olig2 transcription factor. These cells are mainly found in the interpapillary areas surrounding GFAP-positive perivascular elements. They also found that minigemistocytes are in close association with these Olig2-positive cells and may be derived from them.
- MIB-1 labeling indices are low, in the range of 1–2%.

## 21.6 Electron Microscopy

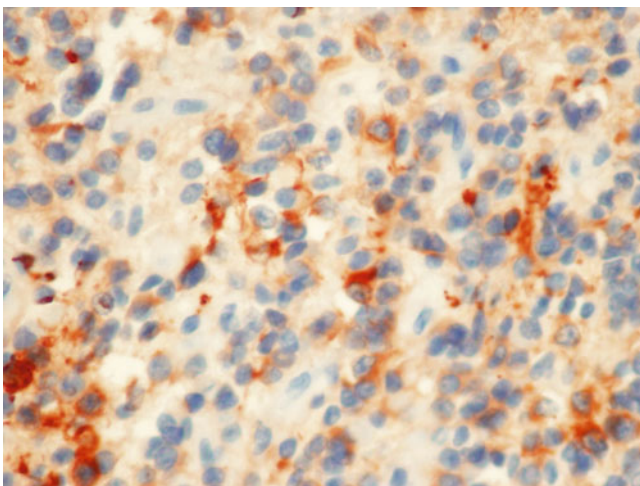
- The perivascular glial cells show cytoplasmic bundles of intermediate filaments and form juxtavascular basal lamina.
- The neuronal cells exhibit cytoplasmic extensions filled with aligned microtubules, dense-core granules, clear vesicles, and synaptic contacts of varying organization.
- A third cell component of poorly differentiated cells has been described at the ultrastructural level. These cells contain mitochondria, ribosomes, occasional dense bodies,



**Fig. 21.12** A large subpopulation of tumor cells are positive for glial fibrillary acidic protein (GFAP)



**Fig. 21.13** Synaptophysin positivity is granular but patchy



**Fig. 21.14** Diffuse positivity for microtubule-associated protein 2 (MAP2) is observed in this tumor

intermediate filaments, and microtubules, but no definitive dense-core granules. They are thought to represent glioneuronal progenitor cells.

- Hybrid glioneuronal cells have not been described.

## 21.7 Molecular Pathology

- PGNT has been reported in patients with cleft lip and orbital schwannoma, but association with familial syndromes has not been established.
- Several cases have been studied for 1p status by fluorescence in situ hybridization (FISH) and have been found to be intact.
- Faria et al. reported a case of PGNT with gains and alterations involving chromosome 7p22. Using comparative genomic hybridization, they also observed high-level amplification at 7p14~q12.
- *SLC44A1-PRKCA* fusion has been detected in several cases of PGNT, thus suggesting a potential biomarker for this tumor.
- Mutations in *IDH1* or *IDH2* are not detected in PGNT.

## 21.8 Differential Diagnosis

- The pseudopapillae with surrounding astrocytic cells may resemble the perivascular pseudorosettes of ependymoma, but cellular processes radiating to the vessel wall are not seen in PGNT. In addition, PGNT does not show ultrastructural evidence of ependymal differentiation.
- The presence of neurocytic, ganglionic, and glial components may raise the possibility of ganglioglioma as a differential diagnosis, but the presence of pseudopapillary glio-vascular structures and the broad spectrum of neuronal differentiation in PGNT help distinguish between the two entities.
- PGNT should be distinguished from dysembryoplastic neuroepithelial tumor (DNET), which also presents at a young age with seizures. Histologically, DNET is characterized by the specific glioneuronal element, microcysts with floating neurons, and cortical dysplasia in the adjacent cortex. None of these features are seen in PGNT.

## 21.9 Prognosis

- In general, PGNT shows a favorable clinical outcome.
- Gross total resection without adjuvant therapy results in recurrence-free, long-term survival in the majority of cases.
- One case of atypical papillary glioneuronal tumor has been reported as showing mitotic activity and an MIB-1

labeling index of 15%. The patient remained symptom-free without tumor recurrence 5 years after radical resection and radiotherapy.

- Very rare examples of tumor recurrence or progression have also been reported.

## Suggested Reading

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