

Pineal Parenchymal Tumor of Intermediate Differentiation with Gangliocytic Differentiation – A Case Report –

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A 49-year-old man presented with an extremely rare case of pineal parenchymal tumor with gangliocytic cells, manifesting as progressive gait disturbance and urinary incontinence lasting for one year. Brain MRI revealed a homogeneously enhancing mass, measuring $3.5 \times 2.7 \times 1.7$ cm, in the pineal body. The mass compressed the deep cerebral vein with superior displacement, which caused mild obstructive hydrocephalus. Histological examination revealed lobular structures consisting of isomorphic small round cells with stippled chromatin and clear cytoplasm, and less cellular areas having large pleomorphic cells and ganglioid cells. Mitotic figures and tumor necrosis were not evident. Immunohistochemically, the neoplastic cells were positive for neuronal markers (neuron-specific enolase, neurofilament, NeuN and synaptophysin), but not for glial fibrillary acidic protein or S-100. Especially, neurofilament showed diffuse interstitial immunoreactivity with accentuation in a few gangliocytic cells and Ki-67 labeling index (2.5%) was low. Therefore, this case was diagnosed as pineal parenchymal tumor of intermediate differentiation with gangliocytic differentiation.

Key Words : Pineal parenchymal tumor; Magnetic resonance imaging; Immunohistochemistry

Pineal parenchymal tumors (PPTs) comprise 14-30% of all pineal region tumors, which account for less than 1% of all intracranial neoplasia. The updated 2007 WHO Classification of Tumors of the Central Nervous System divides PPTs into three types: pineocytoma (PC, WHO grade I), pineal parenchymal tumors of intermediate differentiation (PPT-ID, WHO grade II, III), and pineoblastoma (PB, WHO grade IV). PPT-ID accounts for at least 20% of all PPTs.¹ The current WHO classification has designated these tumors as WHO grade II or III but has not provided strict criteria to distinguish between the 2 grades. Although an exact histological diagnosis is crucial for determining the optimal treatment for patients with PPTs, PPT-ID is hard to distinguish from the other two types of PPT in some cases. Moreover, very few clinical procedures for the treatment of patients with PPT-ID have been developed, and the prognosis of these patients remains unclear. Pineocytes are specialized neurons, and they are known to experience gangliocytic, glial or retinoblastic differentiation. The prognosis was reported to be relatively good when gangliocytic differentiation was observed.²

Here, we present a case of pineal parenchymal tumor of intermediate differentiation that showed gangliocytic differentiation in a 49-year-old man.

CASE REPORT

A 49-year-old man complained of morning headaches lasting for approximately 2 years. During those years, he also experienced cognitive and emotional difficulties as well as gait unsteadiness. He began to experience progressive gait disturbance and urinary incontinence one year ago. His medical history was otherwise unremarkable.

MRI revealed a $3.5 \times 2.7 \times 1.7$ cm-sized mass in the pineal region with homogenous enhancement on T2-weighted imaging (Fig. 1). Serum and cerebrospinal fluid (CSF) markers for AFP, β -hCG, and CEA were normal.

Intraoperative examination revealed an ill-defined soft tumor that was pale yellow in color. Subtotal resection was achieved. The patient died due to cerebellar edema and herniation. His-

tologically, the tumor had a lobular architecture divided by irregular and thick fibrovascular septa (Fig. 2). This tumor showed two different components: the monotonous, cellular area of small cells and a less cellular region with gangliocytic cells. Isomorphic small cells resembled oligodendroglioma or neurocytoma,

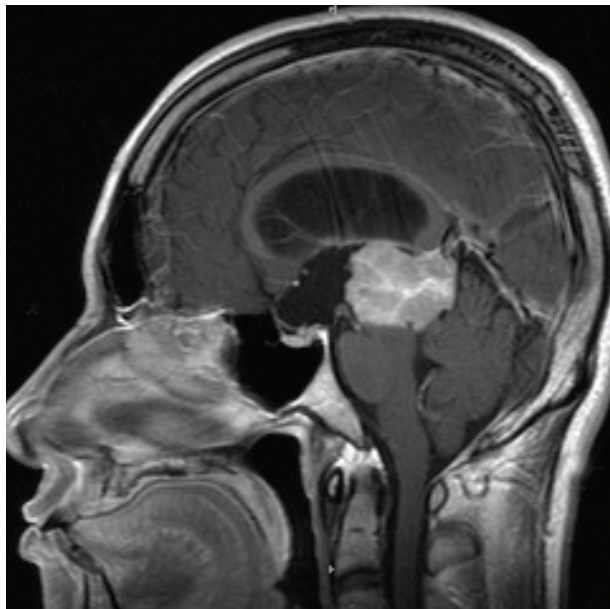


Fig. 1. Sagittal postcontrast T1-weighted image shows the pineal mass is densely enhanced. Obstructive hydrocephalus is present by the pineal mass evidenced by enlarged the 3rd and the lateral ventricle.

in which round and regular nuclei with stippled chromatin were surrounded by clear cytoplasm (Fig. 3). Dispersion and concentration of the gangliocytic cells with various degrees of differentiation, ranging from immature to mature were noted concomitantly (Fig. 4). There were also a few scattered giant cells with

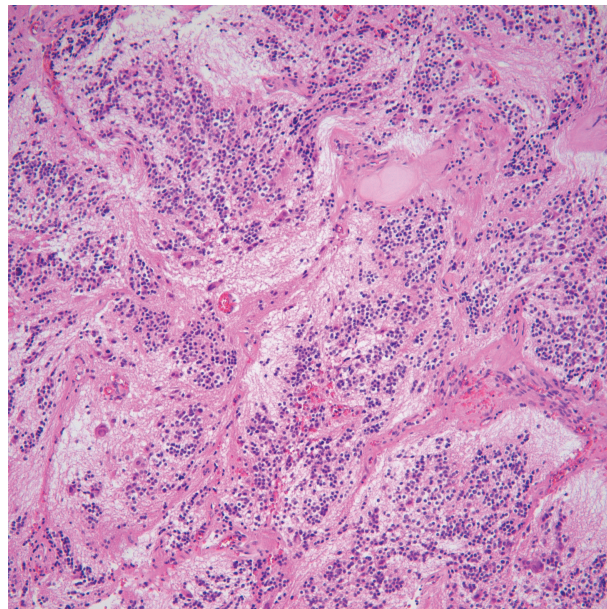


Fig. 2. The tumor is partially lobulated with fibrovascular septa in which groups of small cells and scattered large cells in the fibrillary background are observed.

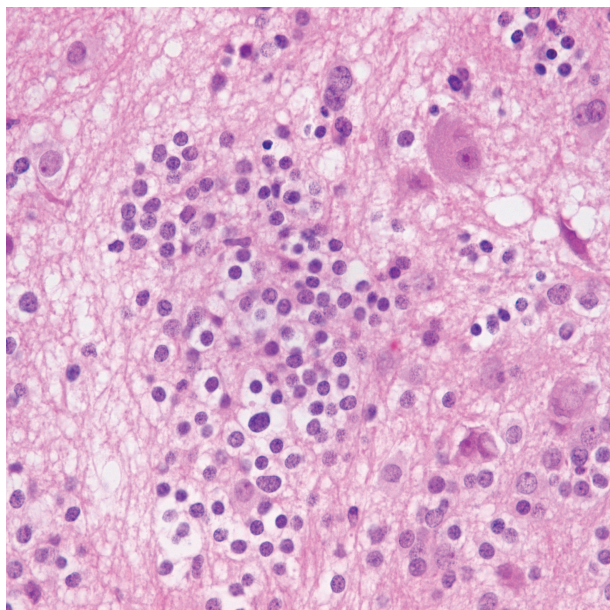


Fig. 3. Ganglion cells have eccentric nuclei, prominent nucleoli and abundant cytoplasm. Cellular group with perinuclear halos resembles an oligodendroglial component.

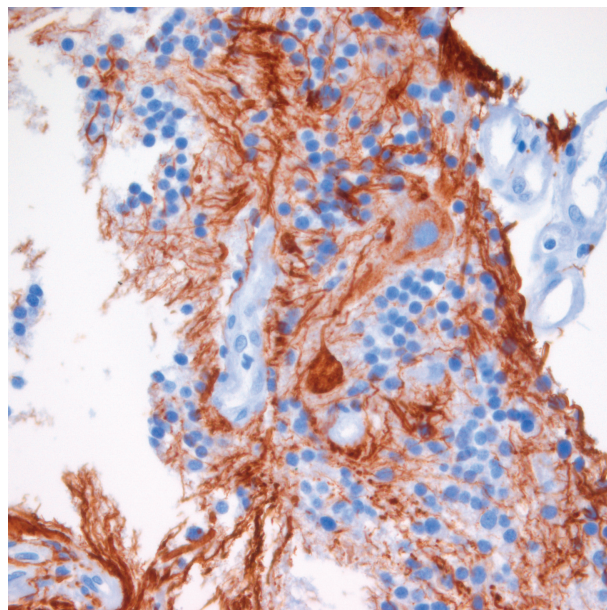


Fig. 4. Immunohistochemical staining for neurofilaments shows strong positivity in a few ganglion cells and fibrillary background.

large vesicular nuclei, either single or multiple. In addition, vascular proliferation with hyalinization was also observed in the septa. There was no mitotic activity or necrosis in any field. Intense synaptophysin (Dako Corporation, Santa Barbara, CA, USA) and neuron-specific enolase (Dako) immunolabeling were observed in the fibrillary matrix and gangliocytic cells. Immunolabeling for neurofilaments (Dako) showed diffuse interstitial immunoreactivity with accentuation in a few ganglion cells (Fig. 4). In immunohistochemical stain for NeuN (Millipore corporation, Billerica, MA, USA) there was positive nuclear staining in some small cells and gangliocytic cells. Positive immunolabeling for GFAP (GFAP; Dako) and S-100 protein (Dako) were detected in the interstitial cells.

DISCUSSION

In the differential diagnosis, glial proliferations were not observed and the neoplastic cells were negative for GFAP on immunohistochemical staining. Therefore, the possibility of a ganglioglioma was excluded. In pineocytomas, pleomorphic cells or multinucleated giant cells with large and hyperchromatic nuclei can be found. Giant or multinucleated cells are known to be made by fusion of mononuclear tumor cells in terms of nuclear morphology or immunophenotype. Pineocytoma with marked nuclear pleomorphism is often associated with gangliocytic differentiation. The subtype is designated as pleomorphic pineocytoma or the pleomorphic variant of pineocytomas with gangliocytic differentiation. However, the tumor of this case was discriminated against because a large fibrillary pineocytomatous rosette was not observed.

The histopathological diagnosis of a pineal parenchymal tumor is mandatory for determination of the therapeutic strategy. But, classification of PPT is so controversial and especially since the shapes of PPT-ID consist of various kinds. Therefore, its classification and treatment are ones of the most problematic issues. Jouvét *et al.*³ described various histopathological findings with PPT-ID tumors which included four subtypes: lobular pattern with endocrine vascularity, diffuse proliferation of mimicking oligodendroglioma, lobulated and or diffuse subtype having pineocytomatous rosette, and biphasic subtype consisting of typical pineocytoma and pineoblastoma. The updated 2007 WHO Classification of Tumors of the Nervous System also divides PPD-ID into grade II consisting of transitional, lobulated and diffuse PPT subtypes with strong immunolabeling for neurofilaments and less than 6 mitoses, and grade III consisting of lo-

bulated and diffuse PPT subtypes with either 6 or more than 6 mitoses or fewer than 6 mitoses but without immunostaining for neurofilaments.¹ Grade III also includes mixed PC/PB. According to the grading system of WHO Classification, the current case corresponded to grade II.

A multicenter retrospective study showed that the prognosis of PPT-ID was fairly good in 101 patients with malignant PPTs including 37 cases of PPT-ID.⁴ The median overall survival for patients with PPT-ID was 165 months (89, 80, 72% of 3-, 5-, and 10 year follow-up, respectively). In patients with PPT-ID, a more favorable outcome was obtained in cases with immunoreactivity to NFP and a mitotic count of less than six per 10 high-power fields.³ A 5-year follow-up showed that Grade II and III disease had 80% and 40% survival. For this tumor, because mitosis was not observed and ki-67 index was low (2.5%), it was considered to have low proliferating activity. Tsumanuma *et al.*⁵ said that MIB-1 index was very useful for distinguishing pineoblastoma (mean 15.7%) from pineocytoma (mean 3.9%). Other studies reported that MIB-1 index of most pineocytoma was less than 1%.⁶ However, the correlation between MIB-1 and tumor grade among the PPTs remains controversial due to rarity of the studies. In PPTs, the tumor behavior is more closely linked to the spectrum of differentiation than to proliferative activity.³

Most cases of PPT are not completely removed due to its location. Treatment with radiation and/or chemotherapy has been reported to be effective for the prevention of local tumor regrowth and cerebrospinal dissemination.^{7,8}

The histopathological findings in the present case were 1) lobular arrangement of cells mimicking oligodendroglioma or neurocytoma, the presence of a few giant cells and occasional large gangliocytic cells, 2) the absence of mitosis and low Ki-67 index (2.5%), and 3) the strong immunoreactivity of the neurofilament. These findings supported the diagnosis of PPT-ID, grade II with gangliocytic differentiation.

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