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Case study

A case of oligodendroglioma with prominent neuronal differentiation

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Summary We report a case of oligodendroglioma showing marked neuronal differentiation, which arose in the right frontal lobe of a 46-year-old woman. The resected tumor was composed of a mixture of oligodendroglioma, gangliocytoma, and neurocytoma areas with predominance of gangliocytoma-like areas. The oligodendroglioma areas showed immunoreactivity for Olig2 and mutant isocitrate dehydrogenase 1 protein, whereas the gangliocytoma and neurocytoma areas were positive for synaptophysin and NeuN. Ki-67 labeling index was approximately 5% to 10% in the oligodendroglioma areas. Molecular cytogenetic analyses demonstrated chromosomal losses of 1p and 19q and a mutation of *isocitrate dehydrogenase 1* (G395A, R132H) in both the oligodendroglioma and gangliocytoma areas. These data suggest that this tumor is an oligodendroglioma associated with prominent neuronal differentiation. There seems to be a close relationship between oligodendroglial progenitor cells and neuronal cells.

1. Introduction

The 2007 *World Health Organization Classification of Tumors of the Central Nervous System* contains a large number of neuronal and mixed neuronal-glial tumors, most of which are relatively rare and clinically indolent tumors [1]. In addition to these classic neuronal tumors, aberrant neuronal differentiation has recently been recognized in some conventional glial tumors as well. For example, infiltrating astrocytic tumors, grade II or III, infrequently have small well-defined, round areas filled with synaptophysin-positive neuropil, and they are designated as "glioneuronal tumor with neuropil-like islands" [2,3]. Neuropil-like islands have also been reported in ependymomas [4].

As for oligodendroglial tumors, Perry et al [5,6] have coined 2 new tumor types of oligodendroglial tumors showing focal neuronal differentiation: "oligodendrogliomas with neurocytic differentiation" and "oligodendroglial neoplasms with ganglioglioma-like maturation." The former is characterized by Homer Wright or perivascular pseudorosettes of neurocytic cells, which are intermingled with oligodendroglioma areas [5]. The latter, representing a mixed or combined tumor of oligodendroglioma and ganglioglioma components, was described in 2010 [6]. In contrast to the

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classic glioneuronal tumors, these glial tumors expressing focal and aberrant neuronal differentiation usually follow the clinical courses corresponding to those of grade-matched glial tumors devoid of such differentiation [6].

In this report, we present a frontal lobe oligodendroglial tumor, which shows notable neuronal features and mimics "oligodendroglial tumors with ganglioglioma-like maturation" reported by Perry et al [6]. In our case, a neuronal component, gangliocytoma and neurocytoma areas, is wider than an oligodendroglial component. Furthermore, molecular and cytogenetic studies revealed 1p and 19q deletions and an *isocitrate dehydrogenase 1* (*IDH1*) mutation in both oligodendroglioma and gangliocytoma areas.

2. Case report

2.1. Case history

A 46-year-old woman was found to have a tonic seizure, which lasted 5 minutes, during sleep by her husband and was transferred to an emergency department of a hospital. At arrival, her consciousness was alert, and no neurologic abnormalities were detected by a physical examination. Imaging analyses, however, disclosed a sizable mass in the right frontal lobe. Computed tomography demonstrated a convoluted, 3.5 × 3 cm sized, calcified mass, associated with surrounding edema and the compression of the lateral ventricle. In magnetic resonance imaging studies, the tumor exhibited a low-intensity signal in T1-weighted images and heterogeneous, high and low, intensity signals in T2-weighted images. No enhancement was seen after the administration of gadolinium. Under the clinical diagnosis of oligodendroglioma, the tumor was subtotally resected through a right front-temporal craniotomy. The soft tumor was located in the superficial portion of the right frontal lobe and was highly vascular. A small, calcified mass was noticed in the postoperative images; however, no additional chemoradiotherapy was performed, and no enlargement of residual lesion was detected for 16 months after the operation.

2.2. Pathologic findings

The resected specimen was 4 × 4 × 3 cm in size and showed a gray-whitish, gritty cut surface with calcification.

Microscopically, round to ovoid tumor cells diffusely proliferated from the white matter to the gray matter and were associated with large numbers of small to large particles of calcification. Based on the cytological characteristics of the tumor cells, the tumor was subdivided into 3 distinctive areas, namely, oligodendroglioma, gangliocytoma, and neurocytoma areas (Fig. 1). The oligodendroglioma area was characterized by diffuse proliferation of uniform round cells with clear cytoplasm, associated with perineuronal satellitosis and chicken-wire vessels (Fig. 1A and B). These features corresponded to typical microscopic findings of oligodendroglioma. Although some cellular areas were present, mitotic figures were rare, and no necrosis or microvascular proliferation was identified. On the other hand, ovoid tumor cells in the gangliocytoma area mimicked moderate- to large-sized ganglion cells (Fig. 1C). They had relatively wide, amphophilic cytoplasm containing Nissl-like granules and ovoid nuclei with a prominent nucleolus. Binucleated neuronal cells were occasionally observed (Fig. 1D). Their diffuse and monotonous distribution could exclude the possibility that they represented preexisting neurons in the cortex. The neurocytoma area was localized superficially in the cortex and was composed of small, round neurocytic cells and neuropil-like, fibrillary matrices (Fig. 1E). Their nuclei were uniform in size and shape and devoid of a perinuclear halo (Fig. 1F). The 3, oligodendroglioma, gangliocytoma, and neurocytoma, areas were irregularly blended with each other, and their borders were relatively ill defined. The gangliocytoma areas were the most predominant, followed by oligodendroglioma and then neurocytoma areas. Astrocytic cells were not a principal component in any of the areas.

The oligodendroglioma, gangliocytoma, and neurocytoma areas exhibited distinctive immunohistochemical profiles, which corresponded to their microscopic features. In the oligodendroglioma area, oligodendroglia-like, round tumor cells were diffusely positive for Olig2 (Fig. 2A), and mutant IDH1 protein (Fig. 2C) and GFAP-positive gliofibrillary oligodendroglial cells were frequently observed (Fig. 2B). On the other hand, the expression of neuronal markers, such as synaptophysin, NeuN, neuron specific enolase (NSE), and chromogranin A, was lacking. Ki-67 labeling index ranged from 5% to 10% in the oligodendroglioma areas (Fig. 2D). In contrast, ganglioid and neurocytic tumor cells and matrices of gangliocytoma and neurocytoma areas were diffusely immunoreactive for synaptophysin (Fig. 2F), and NSE and neurofilament-positive processes were numerous in these neuronal areas. In addition, a few neuronal cells were positive for chromogranin A in the gangliocytoma area. NeuN was positive in many ganglioid cells in the gangliocytoma area (Fig. 2E), whereas it was negative in the neurocytoma area. GFAP- and Olig2-positive cells were rare in these areas. The expression of mutant IDH1 protein in ganglioid and neurocytic cells was ambiguous (Fig. 2G), whereas some positive stellate cells, probably astrocytic in nature, were intermingled. Neuronal cells lacked labeling of Ki-67 in their nuclei (Fig. 2H). CD34-immunoreactive tumor cells and the overexpression of p53 could not be detected in any areas.

2.3. Molecular and cytogenetic findings

The loss of 1p and 19q was evaluated in the oligodendroglioma and gangliocytoma areas by the dual-color fluorescence in situ hybridization (FISH) method, as they