Central Neurocytoma with Lipofuscin Granules

—Case Report—

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Abstract

A 30-year-old male presented with a large calcified intraventricular mass. The tumor was completely resected *via* the transventricular route. Light microscopy showed the tumor was composed of small round cells with perinuclear halo, typical of oligodendroglioma. Electron microscopy revealed marked neuronal differentiation, including neurosecretory granules, well-formed numerous synapses, and lipofuscin granules. The tumor was diagnosed as well-differentiated central neurocytoma.

Key words: central neurocytoma, neurosecretory granule, synapse, lipofuscin granule, ultrastructure

Introduction

Primary neurogenic tumors of the central nervous system predominantly occur in childhood, and are extremely rare in adults.^{2,15} Central neurocytoma is a well-differentiated neuronal tumor with predominant neuronal ultrastructural features, and histological features resembling oligodendroglioma.

We describe a case of central neurocytoma which had well-formed numerous synapses and lipofuscin granules, and discuss the electron microscopic findings as this is the most differentiated neurocytoma to be reported.

Case Report

A 30-year-old male was admitted to the Saitama Cancer Center in February 1980 with an 8-month history of diplopia. Neurological examination revealed bilateral choked discs, unsteady gait, and increased muscle stretch reflexes in the left extremities. No motor or mental disorder was observed. Computed tomography (CT) revealed a calcified mass filling the anterior horn of the right lateral ventricle, with dense postcontrast enhancement (Fig. 1). Right carotid angiography showed a large tumor stain fed through the right anterior choroidal artery (Fig. 2).

The tumor was totally extirpated *via* the right fron-

tal transcortical-transventricular approach. The tumor was soft, easy to bleed, and quite well defined, but adhered to the septum pellucidum.

His postoperative course was uneventful. Local irradiation (56.5 Gy) was given to the tumor attachment. He was discharged ambulatory. He was alive without tumor recurrence until February 1992, when he died of myocardial infarction. No autopsy was performed.

Tumor tissue removed at surgery was fixed in 10% formalin and embedded in paraffin. Paraffin sections were stained with HE. Light microscopy showed the

Fig. 1 *left*: Precontrast CT scan showing a large, marginally calcified mass mainly occupying the right lateral ventricle. *right*: Postcontrast CT scan showing dense enhancement of the lesion.

Fig. 2 Right carotid angiograms showing a large tumor stain fed through the anterior choroidal artery.

tumor was composed of uniform closely packed small cells with a fine fibrillary area (Fig. 3A). Prominent perivascular fibrillary areas resembled pseudorosettes. The tumor cells had central regular nuclei and clear cytoplasm, forming the so-called "perinuclear halo" (Fig. 3B). Patchy calcification was found, but no mitosis or necrosis. Immunohistochemical studies showed no staining for glial fibrillary acidic protein (GFAP), S-100 protein, neurofilament protein (68, 160, and 200 kd), and synaptophysin.

For electron microscopy, specimens were immediately fixed in cold 2.5% glutaraldehyde in phosphate buffer, post-fixed in 1% osmic tetroxide, dehydrated, and embedded in Epon. Ultrathin sections were stained with uranyl acetate and lead citrate. Electron microscopy revealed oval-shaped tumor cells with rich cytoplasm containing many mitochondria, Golgi apparatuses, and lysosomes (Fig. 4A). The cell

processes contained many dense-cored and clear vesicles (Fig. 4B), and also microtubules (Fig. 4D). Some lysosomes were vacuoles suggesting lipofuscin granules (Fig. 4C). Synapses similar to dendro-dendritic (Fig. 4E) or dendro-somatic synapses (Fig. 4F) were also abundant.

Discussion

The number of cases of central neurocytoma confirmed by electron microscopy has increased.^{1,6-8,10,12,16-20,22} The clinical features of this tumor have been gradually defined. Central neurocytomas characteristically occur in the supratentorial ventricular structures of young adults, and the prognosis is favorable. Light microscopy suggests a diagnosis of oligodendroglioma, but electron microscopy clearly shows the differentiated neuronal neoplastic cells. Abortive synapses and dense-cored and clear vesicles are common, but typical synapses are infrequent.

Jerdan *et al.*⁵ and Wilson *et al.*²⁴ previously termed intraventricular neurogenic tumors in adults as "differentiated neuroblastomas." These tumors were similar to those reported by Hassoun *et al.*,⁴ but lacked well-formed synapses. Nishio *et al.*¹⁰ considered that all these tumors belonged to the same category, and that the presence of synaptic structures indicated the degree of differentiation. Kubota *et al.*⁷ reported that central neurocytomas consisted of more differentiated tumor cells than those of cerebral neuroblastomas in young patients, and classified tumor cells of central neurocytomas into three different types according to the extent of differentiation.

We agree that these neuronal tumors belong to the

Fig. 3 Photomicrographs showing small round cells with trabecular connective tissue stroma (A: HE stain, $\times 360$), and tumor cells with perinuclear halo structure (B: HE stain, $\times 720$).

Fig. 4 Electron micrographs showing round tumor cells containing many mitochondria and Golgi apparatuses in the cytoplasm (A: bar = 1 μ m), cytoplasmic process containing dense-cored and clear vesicles (B), cytoplasm containing many lysosomes and lipofuscin granules (N: nucleus) (C), cytoplasmic process containing microtubules (arrowheads) (D), dendro-dendritic synapse-like structure (E), and dendro-somatic synapse-like structure (F) (B-F: bar = 10 μ m).

category of central neurocytoma, and consider that the present case of neurocytoma shows the most prominent neuronal differentiation of reported neurocytomas. Well-formed synapses like typical dendro-dendritic and somato-dendritic synapses were abundant and lipofuscin granules were obvious in the tumor cells. No previous descriptions of lipofuscin granules in neurocytomas have been given. Lipofuscin granules are related to aging in normal neuronal tissue, so this structure in neurocytoma may indicate the slow-growing nature of this neoplasm.

Immunohistochemical studies have detected neuron-specific enolase, S-100 protein, and Leu-7 in central neurocytomas.^{1,7,10,12,18,19} These factors occur in various non-neuronal elements^{9,13,21} and are not specific for neuronal cells. Diffuse GFAP staining in neurogenic tumors may be reactive astrocytes.^{4,7,8,10-12,14,17,19} Synaptophysin is an integral calcium-binding membrane protein of presynaptic vesicles.²³ Barbose *et al.*¹⁾ and von Deimling *et al.*²²⁾ reported the usefulness of synaptophysin in establishing the definitive neuronal nature of central neurocytoma. Immunohistochemical studies for GFAP, S-100 protein, neurofilament protein, and synaptophysin were negative

in our case, although loss of immunoreactivity may depend on tissue preservation. We could not obtain any conclusive results about the origin of this tumor from our immunohistochemical observations.

In most reported cases including ours, the origin of the tumors was the septum pellucidum or ventricular wall. Central neurocytomas may originate in the nests of primitive neuroectodermal cells in the septum pellucidum or of matrix layer cells in the ventricular wall.^{3,4,7,10,22)}

Further studies are needed to reveal the biological characteristics such as genesis and spectrum of differentiation of this tumor, and to confirm the validity of synaptophysin as a definitive marker for central neurocytomas or other neuronal neoplasms.

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