Atypical and Rare Variants of Central Neurocytomas

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KEYWORDS

• Anaplastic • Atypical • Central neurocytoma • Ganglioneurocytoma • Liponeurocytoma • MIB-1

KEY POINTS

- Central neurocytomas (CNs) can be variable in terms of location, histology, and imaging, and can be morphologically similar to oligodendrogliomas, ependymomas, pineocytomas, and neuroblastomas.
- CNs are seen in the ventricular system and extraventricular locations, and rarely in usual locations such as the spinal cord, retina, and pons.
- Atypical central neurocytomas are defined as having a high proliferative index (MIB-1 index >2%) with or without vascular proliferation, increased mitotic figures, and necrosis.
- Atypical CNs have higher recurrence and lower disease-free survival rates.
- Other rare histopathologic variants of CNs include ganglioneurocytoma, liponeurocytoma, myoneurocytoma, and pigmented neurocytoma, which have a similar clinical course to classical CNs and need to be differentiated from other primary central nervous system tumors.

INTRODUCTION

Central neurocytomas (CNs) are benign intraventricular tumors that occur most often in young adults and constitute 0.1% to 0.5% of all primary brain tumors. First described by Hassoun and colleagues[1] in 1982, CNs were believed to have a cellular origin from the septum pellucidum.[2,3] Recent investigations suggest that they derive from neuroglial precursor cells in the subependymal plate of the lateral ventricles and circumventricular organs with characteristics of dual differentiation along glial or neuronal lines (predominates). The neurocytes composing these neurocytomas are similar to cells in the dentate layer of the hippocampus or internal granular layer of the cerebellum. Their neuroectodermal origin allows them to differentiate along neurocytic or glial lineage.[4]

Although primarily described as an intraventricular tumor, numerous cases of extraventricular neurocytoma (EVN) locations have been reported, namely cortex,[5,6] cerebellum,[7,8] olfactory bulb, insula,[9] thalamus,[6] pineal gland,[10] retina[11] and spinal cord.[12] Under light microscopy, tumor cells have a honeycomb-like arrangement, small round or oval nuclei, scant cytoplasm, and a perinuclear halo, all of which can resemble oligodendroglioma, and large fibrillary areas resembling pineocytoma. Straight-line arrangement of cells and pseudorosette formation can give the appearance of clear cell ependymoma in some samples. CNs were probably historically misdiagnosed because of these similarities.[2,3,13]

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Determining the neuronal origin of tumor cells is crucial to definitively diagnose CNs. This assessment is accomplished using immunohistochemistry for synaptophysin or neuron-specific enolase and electron microscopy.[2,3,5,14]

Although classic CN is present in the ventricles, occurs in young adults, and has uniform sheets of cells with neuronal differentiation, its clinical presentation, anatomic location, and cytopathologic characteristics and outcomes can vary. This review highlights the extent of variation and atypia seen in CN cases and how these factors could potentially affect their management.

VARIATION IN LOCATION: NEUROCYTOMAS

CNs are primarily intraventricular tumors (lateral ventricle, third ventricle, or near the foramen of Monro) that present with increased intracranial pressure and symptoms secondary to obstructive hydrocephalus.[2] Rare variants, however, can occur in various sites of the central nervous system (CNS). EVNs are a well-known atypical subset of neurocytomas, and can be present in both supratentorial and infratentorial cortical locations. Cortical neurocytomas have been reported in frontal,[5] parietal,[5,9,15] temporal,[5] and occipital[6] lobes and in the insula.[9] In a series of 6 patients, Sgouros and colleagues[6] reported 2 cases of neurocytoma arising from the thalamus and extending to the ventricles. In a report on radiologic features of these tumors, Ng and colleagues[10] introduced a case arising from the pineal gland. Rarely, EVNs have been reported to arise from the spinal cord.[12,16] These variations in location are detailed elsewhere in this issue. EVNs can also occur in the cerebellum.[8,17]

HISTOPATHOLOGIC VARIATION

Tumors Mimicking Neurocytomas: Neurocytic Features

CNs overlap morphologically with oligodendrogliomas, neuroblastomas, pineocytomas, ependymomas, and dysembryoplastic neuroepithelial tumors (DNETs) (**Figs. 1–3**). These tumors all share histology with sheets of uniform round cells. True CNs, however, are neuroepithelial tumors with neuronal differentiation, thus differentiating them from oligodendrogliomas, neuroblastomas, pineocytomas, and ependymomas, which have oligodendroglial, neuroblastic, pineocytic, and ependymal differentiation pathways, respectively. Neuronal markers, such as synaptophysin (predominantly in fibrillary zones and perivascular nuclei-free cuffs) and NeuN (nuclear staining), are specific for CNs in almost all cases. Rarely, variants may be encountered with staining for multiple cell lines, including neurocytes, oligodendrocytes, and neuroblasts.[18] Other rare neurocytoma variants may demonstrate a pseudopapillary pattern with hyalinized vascular cores but maintain synaptophysin positivity.[19] Hassoun and colleagues[1] considered these overlaps with

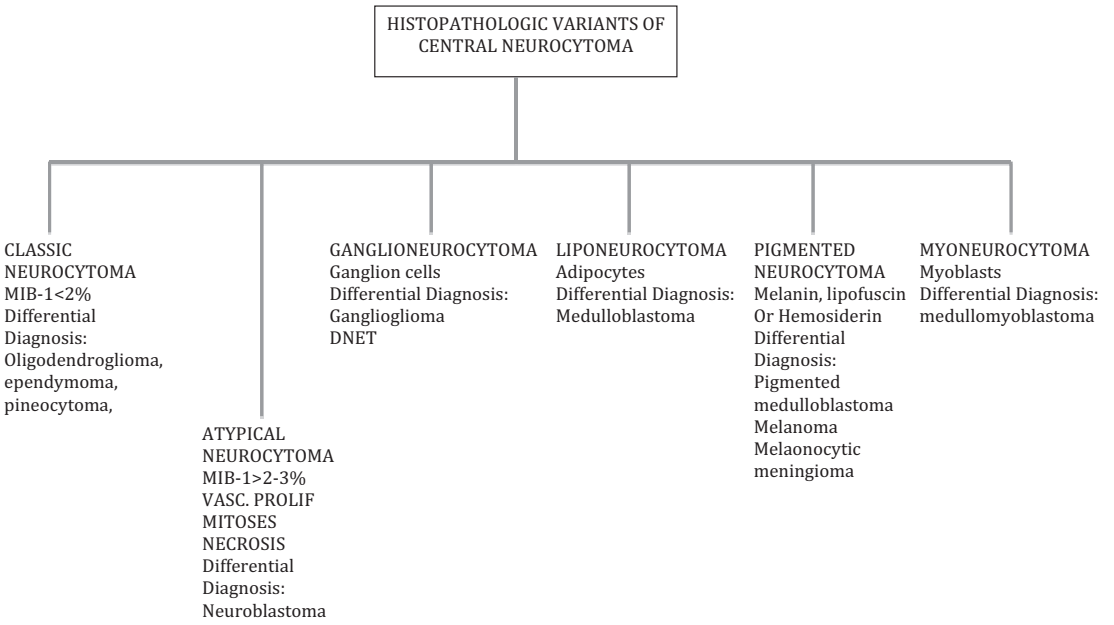

Fig. 1. Histopathologic variants of CNs. Chart demonstrating the different known histopathologic variants of CNs.