Subependymal giant cell astrocytoma

A WHO grade I tumor

Subependymal giant cell astrocytoma is a transformation lesion or benign intraventricular tumor, usually located near the foramen of Monro [1].

Epidemiology

They occur in 5%–20% of patients with tuberous sclerosis complex (TSC) [2] [3] [4].

Histology

Gross description

Circumscribed, often calcified.

Microscopic (histologic) description

Composed mainly of large polygonal to elongate cells resembling astrocytes or ganglion cells with abundant, finely granular eosinophilic cytoplasm, bright pink cellular processes, large round / oval nuclei, prominent nucleoli.

Perivascular pseudorosette formation is common.

Infiltration of mast cells and lymphocytes is common.

No Nissl substance in cytoplasm.

Presence of mitoses, vascular proliferation or necrosis does NOT indicate anaplastic progression [5].

Large cells with abundant cytoplasm and prominent nucleoli

NSE

Positive stains

Mixed glioneuronal phenotype

GFAP+, S100+, also neurofilament proteins, neuronal associated class III β-tubulin

Negative stains

HMB45 (unlike other tuberous sclerosis related lesions).

Clinical

The diagnosis of TSC is based on clinical features, but the variability of phenotype and age at symptom onset makes this challenging.

In the infant, the earliest finding is of “ash leaf” macules (hypomelanotic, leaf-shaped) that are best seen with a Wood’s lamp. Infantile myoclonus may also occur.

In older children or adults, the myoclonus is often replaced by generalized tonic-clonic or partial complex seizures, which occur in 70–80%. Facial adenomas are not present at birth but appear in > 90% by age 4 yrs (these are not really adenomas of the sebaceous glands, but are small hamartomas of cutaneous nerve elements that are yellowish-brown and glistening and tend to arise in a butterfly malar distribution, usually sparing the upper lip).

Retinal hamartomas occur in ≈ 50% (central calcified hamartoma near the optic disc or a more subtle peripheral flat salmon-colored lesion). A distinctive depigmented iris lesion may also occur.

Diagnosis

● Definitive diagnosis 2 major criteria, or 1 major AND ≥ 2 minor

● Possible diagnosis 1 major or ≥ 2 minor

Major criteria

≥ 3 hypomelanotic macules ≥ 5 mm diameter ≥ 3 angiofibromas or fibrous cephalic plaque ≥ 2 ungual fibroma shagreen patch

multiple retinal hamartomas

cortical dysplasias (including tubers & cerebral white matter radial migration lines) subependymal nodules

subependymal giant cell astrocytoma (SEGA)

cardiac rhabdomyoma

lymphangioleiomyomatosis

≥ 2 angiomyolipomas

Minor criteria

“confetti” skin lesions ≥ 4 pits in dental enamel ≥ 2 intraoral fibromas achromic retinal patch multiple renal cysts nonrenal hamartomas

Evaluation

Plain skull X-rays

May show calcified cerebral nodules.

CT scan

Intracerebral calcifications are the most common (97% of cases) and characteristic findings. Primarily located subependymally along the lateral walls of the lateral ventricles or near the foramina of Monro.

Low density lesions that do not enhance are seen in 61%. Probably represent heterotopic tissue or defective myelination. Most common in the occipital lobe.

Hydrocephalus (HCP) may occur even without obstruction. In the absence of a tumor, HCP is usually mild. Moderate HCP usually occurs only in the presence of a tumor.

Subependymal nodules are usually calcified, and protrude into the ventricle (“candle guttering” described the appearance on pneumoencephalography).

Paraventricular tumors (mostly giant cell astrocytomas; are essentially the only enhancing lesions in TSC.

MRI

Subependymal tubers are high on T2 and low on T1 and only ≈ 10% enhance.

Low signal in subependymal lesions may represent calcification. SEGA enhance intensely (enhancing subependymal lesions are almost always SEGAs).

Radial bands sign: abnormal signal intensity extending in a radial manner, representing cells of varying degrees of neuronal and astrocytic differentiation as well as difficult-to-classify cells.

Differential diagnosis

Subependymal Giant Cell Astrocytoma Differential Diagnosis.

Complications

They may obstruct cerebrospinal fluid (CSF) pathways. Rarely, they may secrete a protein-rich exudate, causing communicating hydrocephalus.

Complications include intraventricular hemorrhage, cognitive impairment, and inevitable recurrence if gross total resection is not achieved [6) 7) 8)].

A case is described of a subependymal giant cell astrocytoma that occurred as a mural nodule within a cyst in the parietal lobe. The tumor recurred twice over a period of 47 years despite two extensive surgical resections. Neither the patient nor any of his children suffered tuberous sclerosis [9)].

Subependymal giant cell astrocytoma in the absence of tuberous sclerosis complex

Kashiwagia et al. report a case of subependymal giant cell astrocytoma in a patient lacking clinical symptoms of tuberous sclerosis. The absence of any features of tuberous sclerosis initially dissuaded them from including subependymal giant cell astrocytoma in the differential diagnosis [10)].

Stavrinou et al report the second case of intraventricular and intratumoral hemorrhage complicating a Subependymal giant cell astrocytoma (SEGA) and the first case in which these complications occurred in an adult patient in whom there was no previous suspicion of systemic disease [11)].

Beaumont et al. report the case of a 14-year-old male with a subependymal giant cell astrocytoma (SEGA) that occurred in the absence of tuberous sclerosis complex (TSC). The patient presented with progressive headache and the sudden onset of nausea and vomiting. Neuroimaging revealed an enhancing left ventricular mass located in the region of the foramen of Monro with significant mass effect and midline shift. The lesion had radiographic characteristics of SEGA; however, the diagnosis remained unclear given the absence of clinical features of TSC. The patient underwent gross-total resection of the tumor with resolution of his symptoms. Although tumor histology was consistent with SEGA, genetic analysis of both germline and tumor DNA revealed no TSC1/2 mutations. Similarly, a comprehensive clinical evaluation failed to reveal any clinical features characteristic of TSC. Few cases of SEGA without clinical or genetic evidence of TSC have been reported [12)].

Treatment

see Subependymal giant cell astrocytoma treatment.

Case series

2017

Three patients with TSC and a large intracranial SEGA received oral rapamycin (0.5 mg/day) or everolimus (2.5 mg/day) before surgery for tumor resection. After mTOR inhibitor therapy, computed tomography scans and magnetic resonance imaging revealed tumor reduction. Tumor bleeding was easy to control during surgery, and the border between tumor and surrounding brain tissue was clearly differentiated. Analysis of postsurgical tumor specimens showed low blood density and focal necrosis.

Preoperative mTOR inhibitors could be a potentially novel treatment modality in large TSC-SEGA with hydrocephalus. In this series, mTOR inhibitors were not only safe and well tolerated, but also beneficial for tumor resection [13].

Case reports

Subependymal giant cell astrocytoma case reports.

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