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Case report

Subependymal giant cell astrocytoma in a genetically negative tuberous sclerosis complex adult: Case report

Sanjay Konakondla (MD)[a,*], Mayur Jayarao (MD)[a], Jami Skrade (MD)[b], Caterina Giannini (MD PhD)[c], Michael J. Workman (MD)[d], Chad J. Morgan (MD)[d]

[a] Division of Neurological Surgery, Department of Surgery, University of Missouri School of Medicine, Columbia, MO, United States
[b] Department of Pathology, Cox Health, Springfield, MO, United States
[c] Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, United States
[d] Springfield Neurological and Spine Institute, Springfield, MO, United States, United States

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ABSTRACT

Introduction: The well-described entity of Subependymal Giant Cell Astrocytoma (SEGA) in the setting of Tuberous Sclerosis Complex (TSC) is profound in current literature. It has been described in children as well as adults with or without identifiable clinical presentations of tuberous sclerosis. To our knowledge there has not been any report of a negative genetic workup of Tuberous Sclerosis Complex in an adult patient presenting with an isolated SEGA.
Case report: We present a case of a 25-year-old female with no medical history who presented to the emergency room for headaches. Further workup included gadolinium enhanced MRI of the brain which revealed a homogenously enhancing mass in the left lateral ventricle with eccentric calcification and resultant obstructive hydrocephalus. A left frontal craniotomy with an interhemispheric transcallosal approach was taken for complete removal of the mass.
Discussion: Final pathological diagnosis was SEGA with suggestive cell population, positive GFAP and positive synaptophysin. Genetic testing included TSC1 (MLPA, DNA Sequencing) and TSC2 (MLPA, DNA Sequencing), which were all negative. The panel did not identify mutations associated with Tuberous Sclerosis.
Conclusion: Rare cases of isolated SEGA have been reported in patients who do not have typical features of tuberous sclerosis, and may represent minimal penetrance of the disease with an attenuated phenotype. Negative genetic testing, as demonstrated, can be seen in adults with isolated SEGA. With a negative genetic workup of TSC, regular follow up may still be necessary; however this may prove to be low yield for identifying any TSC features in the future.

1. Introduction

Subependymal Giant Cell Astrocytoma (SEGA) is classically recognized in the setting of Tuberous Sclerosis Complex (TSC). It has been described in children and adults, more commonly in the 1st and 2nd decades of life, with or rarely, without identifiable clinical presentations of tuberous sclerosis [1–3]. Patients can also present with cortical tubers and subependymal nodules. These are most commonly supratentorial, and vary in size and number [4].

The treatment and time sensitive workup of TSC, especially its neurologic manifestations, are critical to acknowledge [1]. A subsequent diagnostic panel of studies and screening tests for TSC is important after establishing a diagnosis of TSC [4]. There has not been a report, to our knowledge, of an isolated SEGA in an adult who has a genetic workup negative for TSC. These patients, though, rare, must be identified as it has important implications to postoperative follow up and patient car..

2. Case report

A 25-year-old female presented to the emergency room with gradually worsening headaches for approximately 1 month. CT of the head was completed without contrast, which revealed a 1.5 cm × 1 cm hyperdense intraventricular mass with peripheral calcification in the left frontal horn of the lateral ventricle (Fig. 1). Also noted was unilateral dilation of the left lateral ventricle suggestive of obstructive hydrocephalus from direct obstruction of the foramen of Monro. Her headaches were bi-frontal without radia-

* Correspondence to: Department of Neurosurgery, Geisinger Medical Center, Danville, Pennsylvania, 100 N Academy Avenue, Danville, PA 17822, United States.
E-mail address: skonakondla@geisinger.edu (S. Konakondla).

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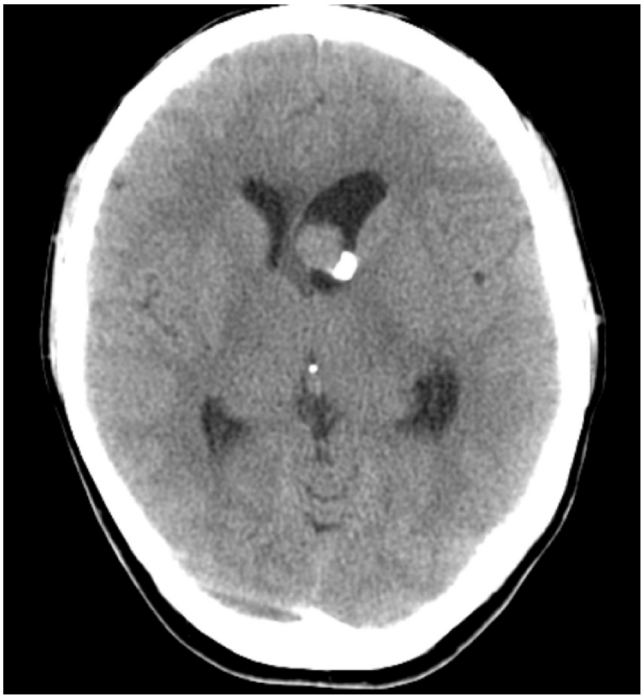

Fig. 1. Computed tomography of the head without contrast revealing a 1.5 cm × 1 cm hyperdense intraventricular mass with peripheral calcification in the left frontal horn of the lateral ventricle.

tion, and 9/10 in intensity. Her physical exam, including thorough neurologic exam was unremarkable.

2.1. Imaging and surgical intervention

MRI of the brain demonstrated a dense, 1.8 cm × 1.2 cm × 1.9 cm, partially calcified, homogenously enhancing mass in the left frontal horn of the lateral ventricle at the level of the foramen of Monro in close relation to the left basal ganglia, specifically the caudate. There was noted outflow obstruction and resultant unilateral dilation of the left lateral ventricle.

To achieve symptomatic relief and tissue diagnosis, a left frontal craniotomy for an interhemispheric transcallosal approach was completed for tumor resection. Intraoperative microscope was used and BrainLAB neuronavigation was used for preoperative planning and intraoperative navigation. The tumor was grossly a red, vascular lesion at the foramen of Monro. It did appear to have attachments to the lateral wall of the ventricle by the caudate nucleus. A small piece of the tumor was noted in the foramen of Monro, likely the cause of the CSF obstruction. The majority of the tumor was resected en bloc and sent to pathology. A plane was made along this attachment and this portion was also removed, representing a total excision. The foramen of Monro was widely patent after tumor removal. A fenestration of the septum pellucidum was also completed.

2.2. Diagnosis

Histologically, the tumor was a cellular glial neoplasm formed of cells with variable morphology. In areas, the cells had a spindle appearance with long processes running in fascicles, which were intersecting. Focally, the long processes seemed to acquire a "vague perivascular," arrangement. Pleomorphic cells, with multinucleation and abundant eosinophilic cytoplasm, formed the tumor. Only rare mitotic figures were seen. Extremely high vascularity was noted with thin walled vessels and fibrin thrombi, which was suggestive of organizing hemorrhage. A small fragment of the tissue also revealed extensive calcifications likely corresponding to the densely calcified areas seen on CT and MRI (Fig. 2). GFAP was positive and synaptophysin revealed scattered positive cells. Final pathological diagnosis was SEGA, WHO grade I, due to the suggestive cell population, positive GFAP and positive synaptophysin. Additional immunohistochemical staining for BRAFV600E, NeuN, CD34, and neurofilament were completed. CD34 staining was limited to vascular walls and not in the tumor cells. The remaining stains were negative. Silver stain demonstrated the presence of reticular fibers. IDH1/IDH2 pyrosequencing and MGMT methylation status were negative. P53 is weakly positive in tumor cells, and silver stain were both negative. Ki67 index was 4%. Further review of pathology specimens was completed at Mayo Clinic by a neuropathologist (CG). Genetic testing included complete sequencing of TSC1 (MLPA, DNA Sequencing) and TSC2 (MLPA, DNA Sequencing), which were all negative. The panel did not identify mutations associated with Tuberous Sclerosis.

2.3. Hospital course and follow up

Post-operatively, the patient was placed in the neuroscience ICU. CT of the head and MRI of the brain were completed which revealed total tumor resection. On post-operative day 4, the patient was discharged home with complete resolution of her preoperative symptoms.

Follow up imaging was completed 6 and 9 months post-operatively, which did not reveal any residual or recurrent mass and was without new abnormalities or masses.

3. Discussion

Tuberous Sclerosis Complex (TSC), also known as Bourneville-Pringle disease, is an autosomal dominant neurocutaneous disorder that predisposes patients to benign lesions in multiple organ systems. The full triad is only evident in approximately 29% of cases and 6% of TSC patients have none of these findings. The mandated consensus for establishing a definitive, probable, and possible diagnosis is also described [4]. It is the neurologic manifestations of TSC that represent the leading cause of associated morbidity and mortality [3].

SEGA is a benign, slow growing intraventricular lesion of mixed glioneuronal cells and giant cells. SEGA is, by itself, a major diagnostic criterion [3]. Two major criteria are necessary to establish a definite diagnosis of TSC. The pathophysiological mechanism for SEGA formation and the natural history of SEGA has not been clearly defined. SEGAs have been theorized to arise from subependymal nodules (SENs), however this remains in debate.

3.1. TSC and SEGA

The vast majority of the data elucidated about SEGAs result from investigations completed on TSC patients. Reports on the prevalence of SEGA in TSC patients have been described based on various diagnostic criteria [3]. According to the International Tuberous Sclerosis Complex Consensus Conference in 2012, the definition of a SEGA includes a lesion at the caudothalamic groove with a size of more than 1 cm in any direction or a subependymal lesion at any location that has shown serial growth on consecutive imaging regardless of size [3]. In one study, of 179 patients already diagnosed with TSC, a histopathologic diagnosis of SEGA was made after surgical intervention in 5.6% of the patients who were symptomatic [2].

There are currently no standardized guidelines or standardized expert opinion, regarding surveillance imaging vs operative