MAYO CLINIC

American Association of Neuropathologists
Diagnostic Slide Session 2024
Case #3

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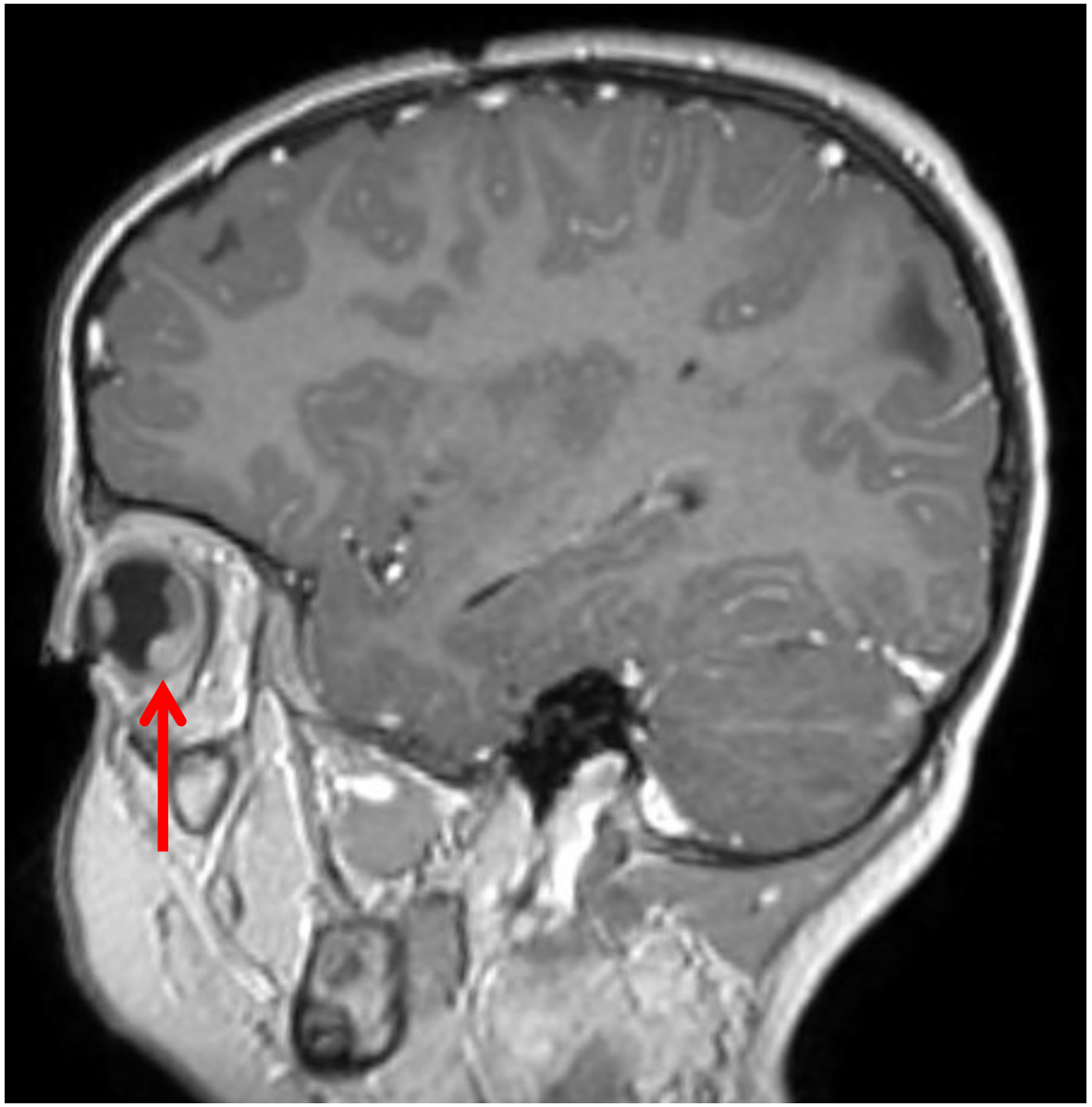
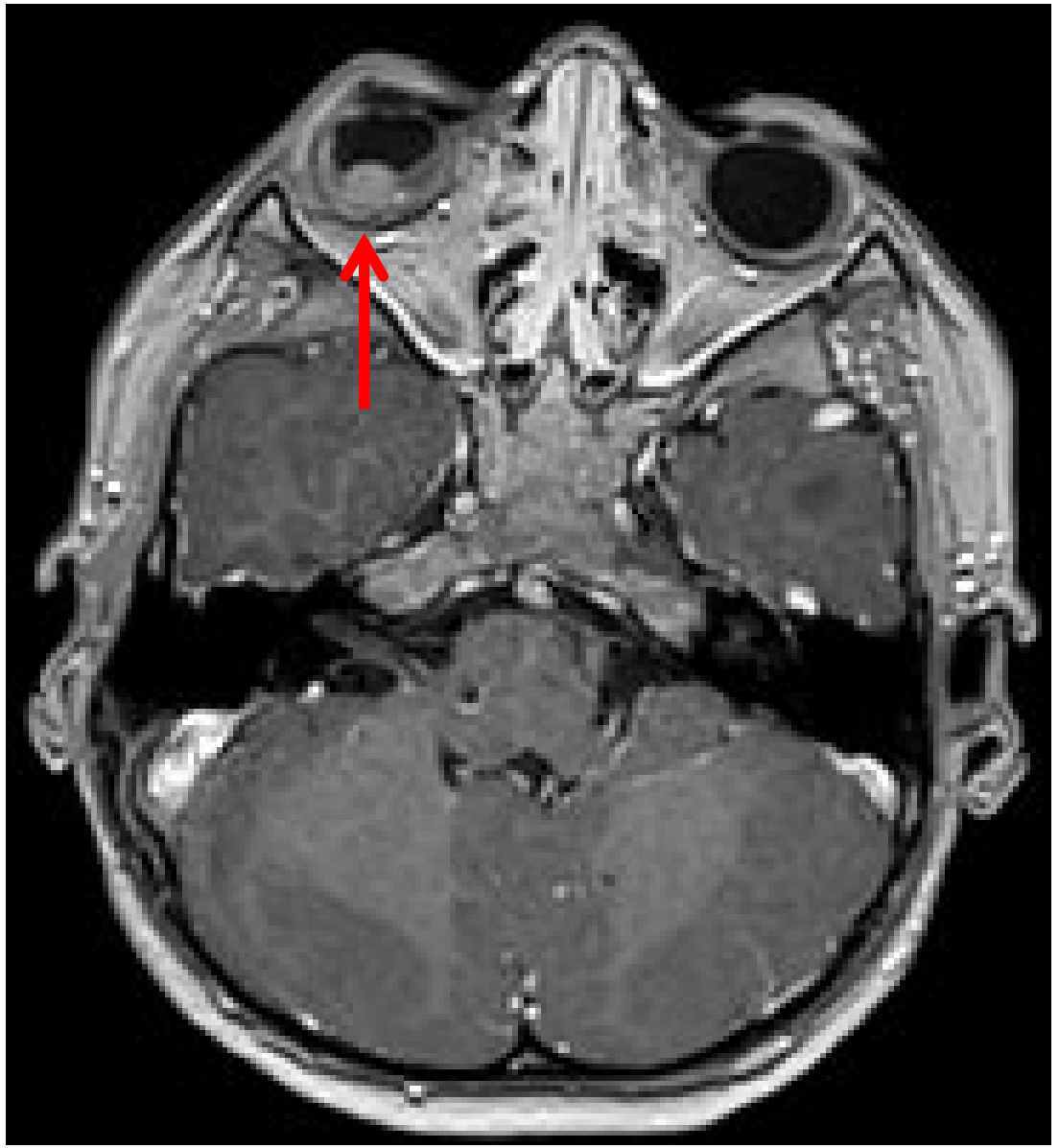
Clinical Summary

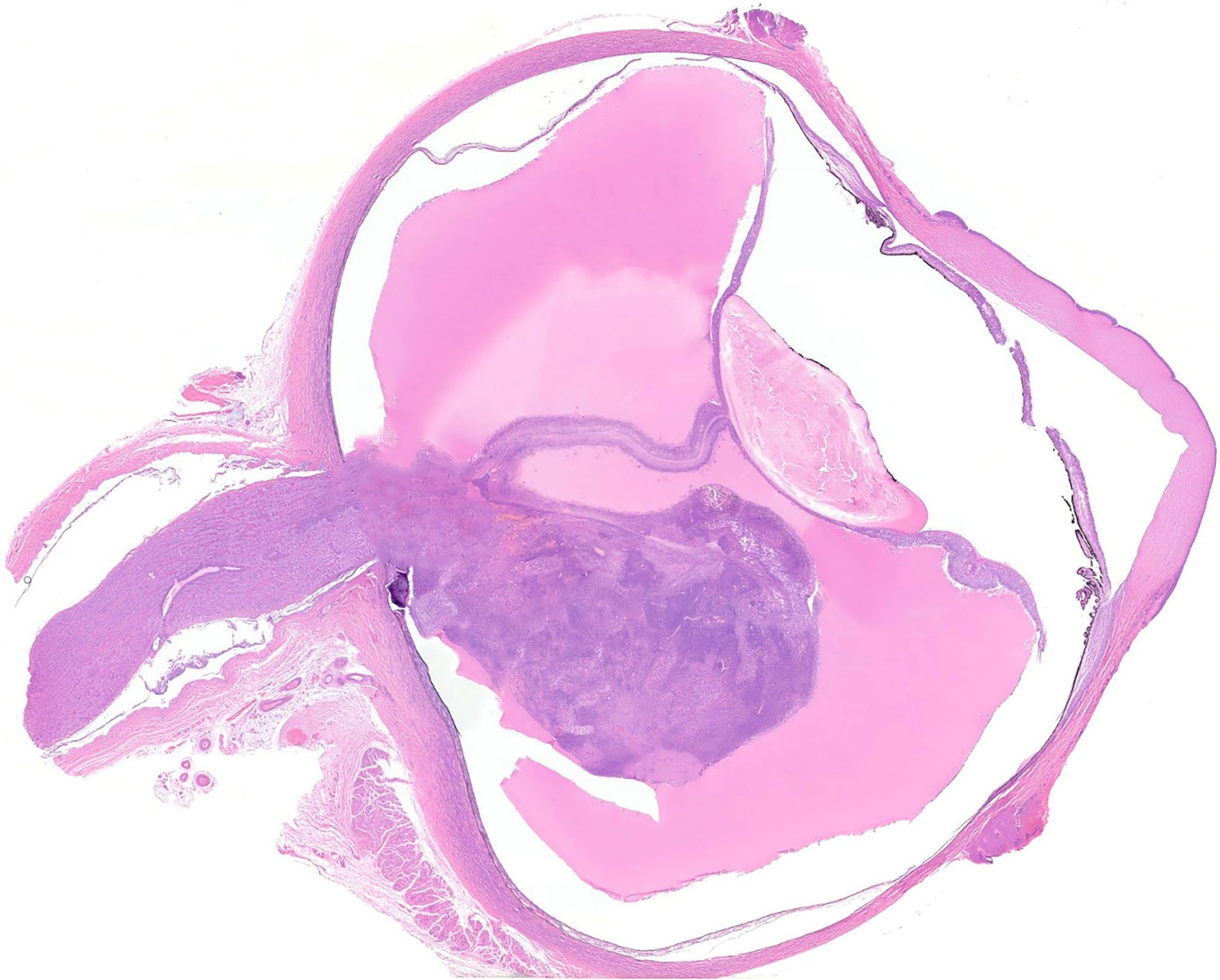
- 4-year-old-boy with a history of right eye retinal detachment and neovascular glaucoma which ultimately progressed to a blind, painful right eye.
- Prior history of a single seizure.

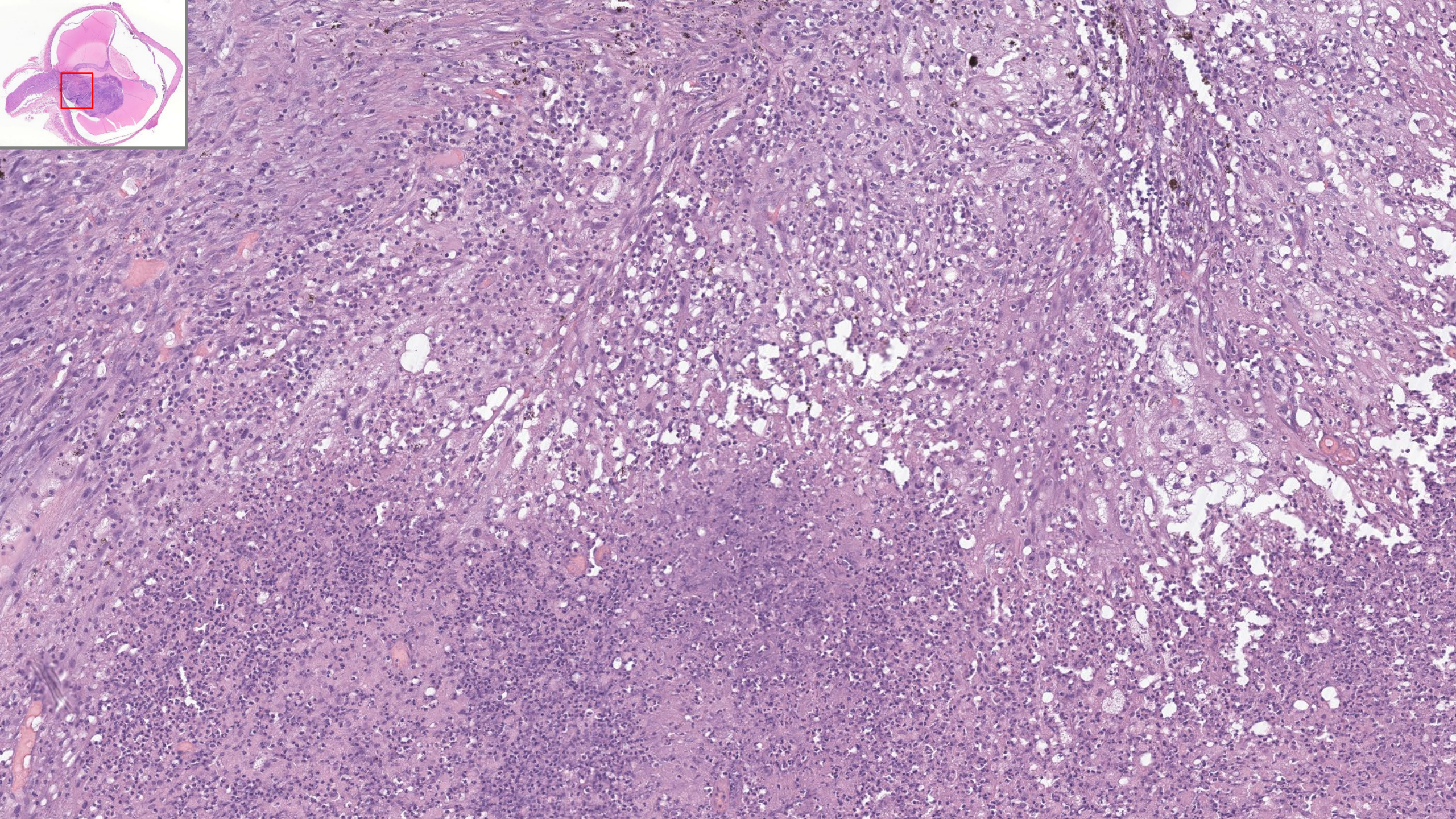


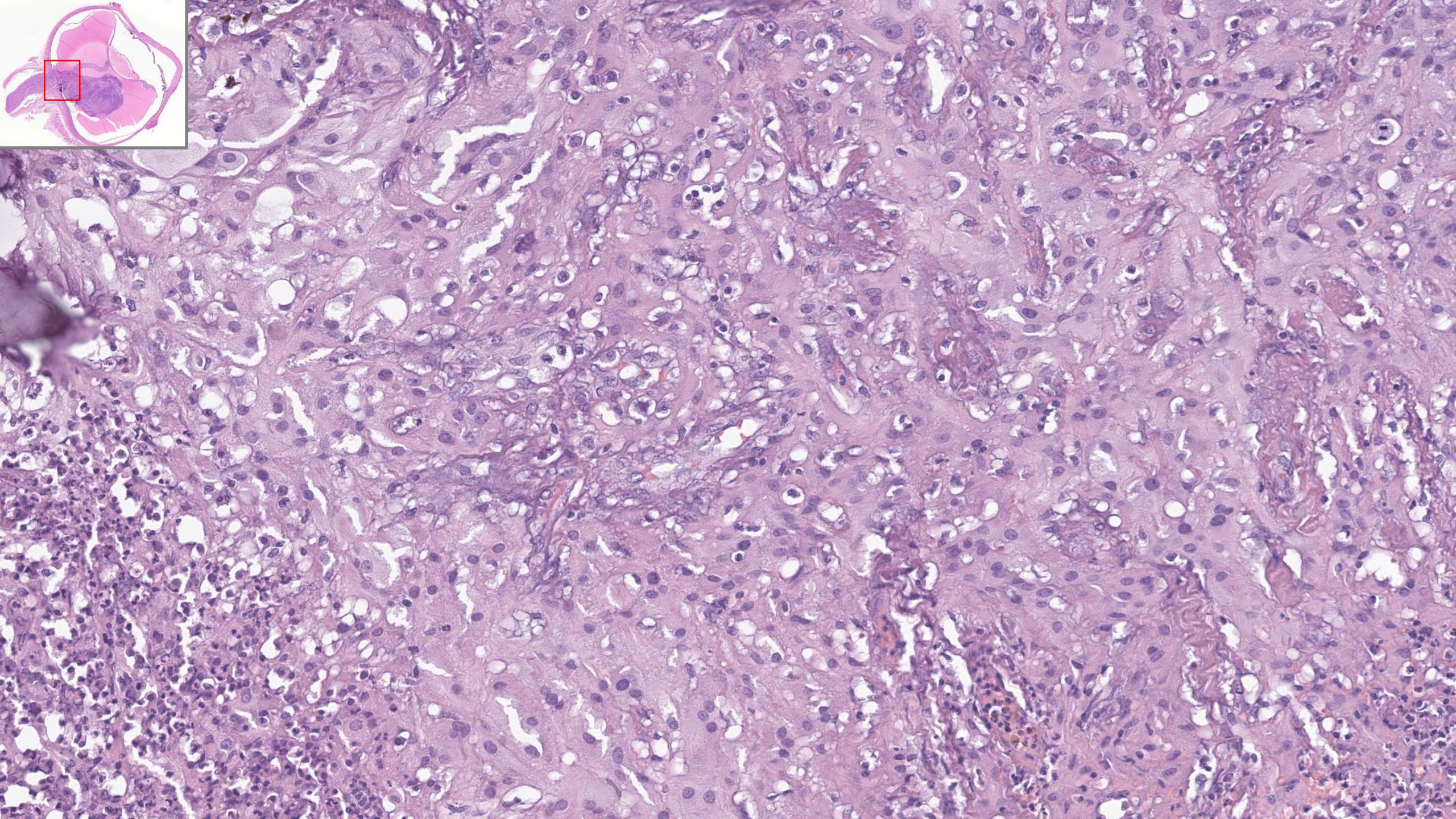
T1 Sagittal

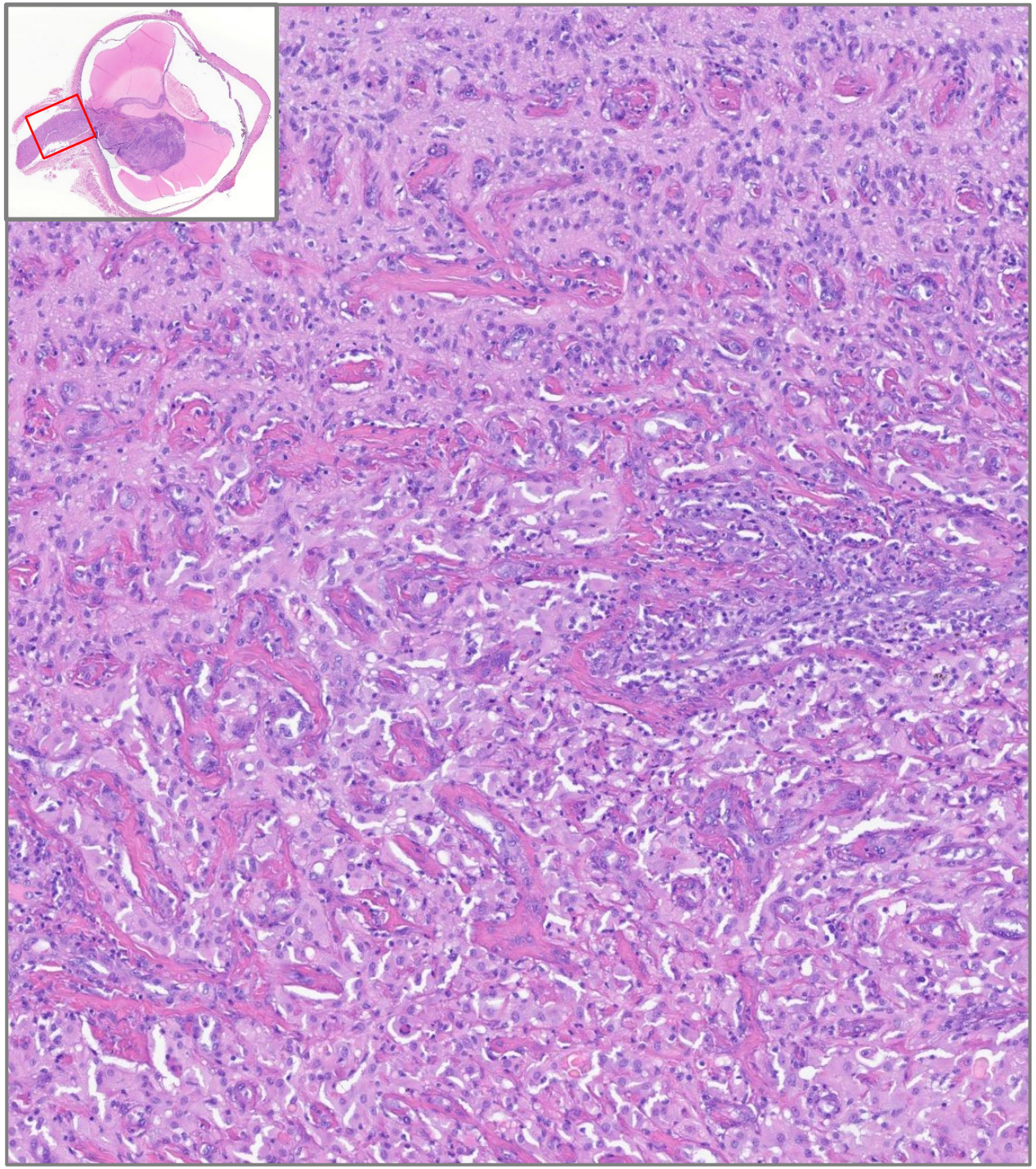


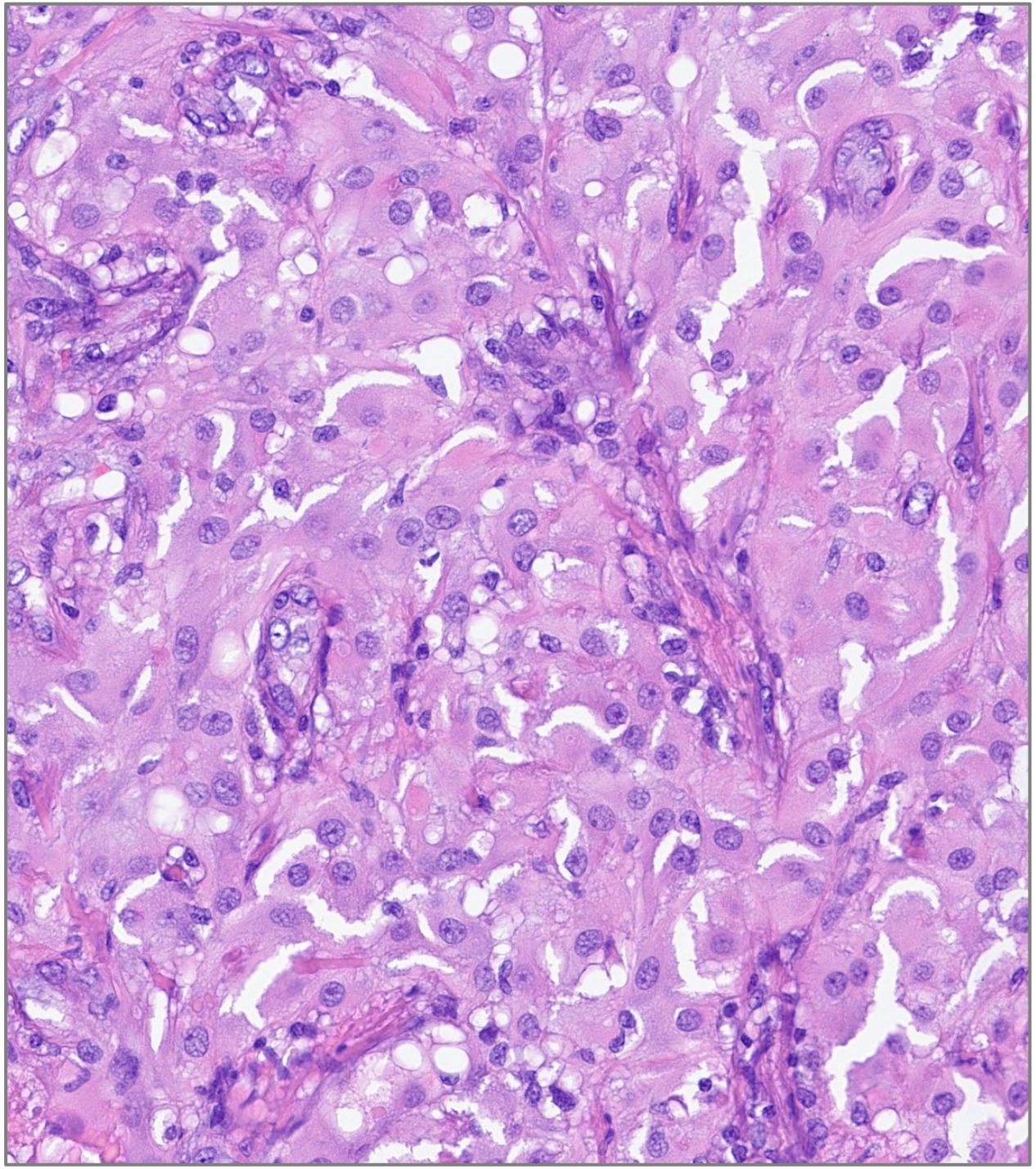
T1 Axial



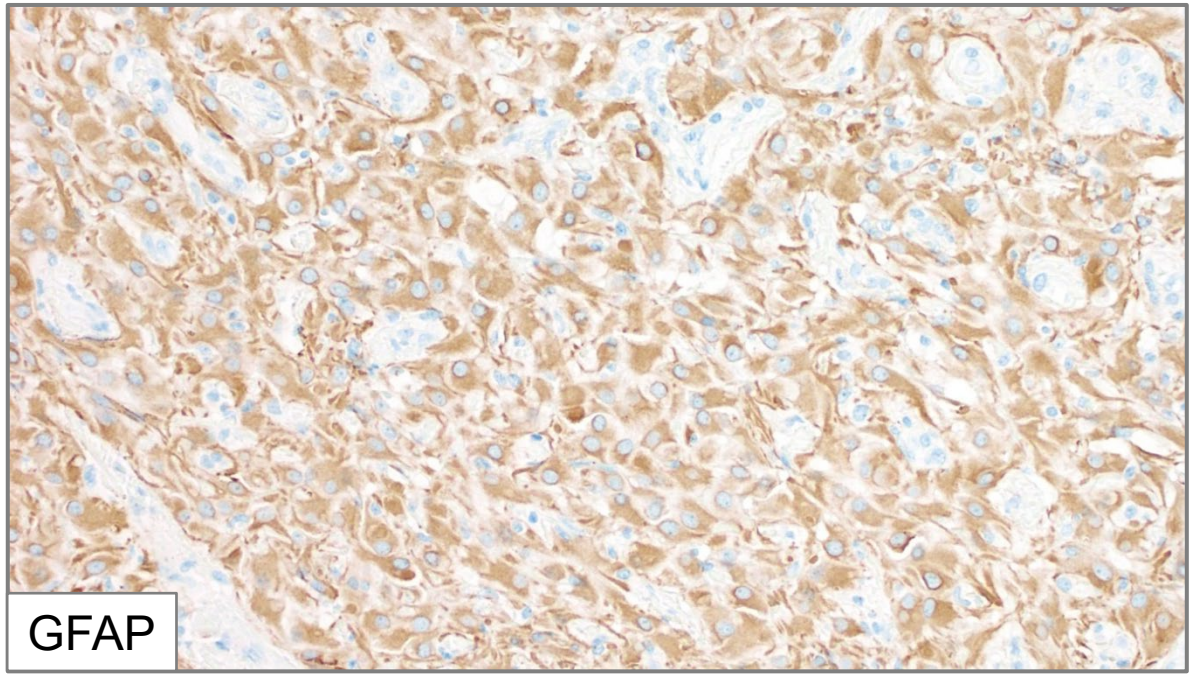


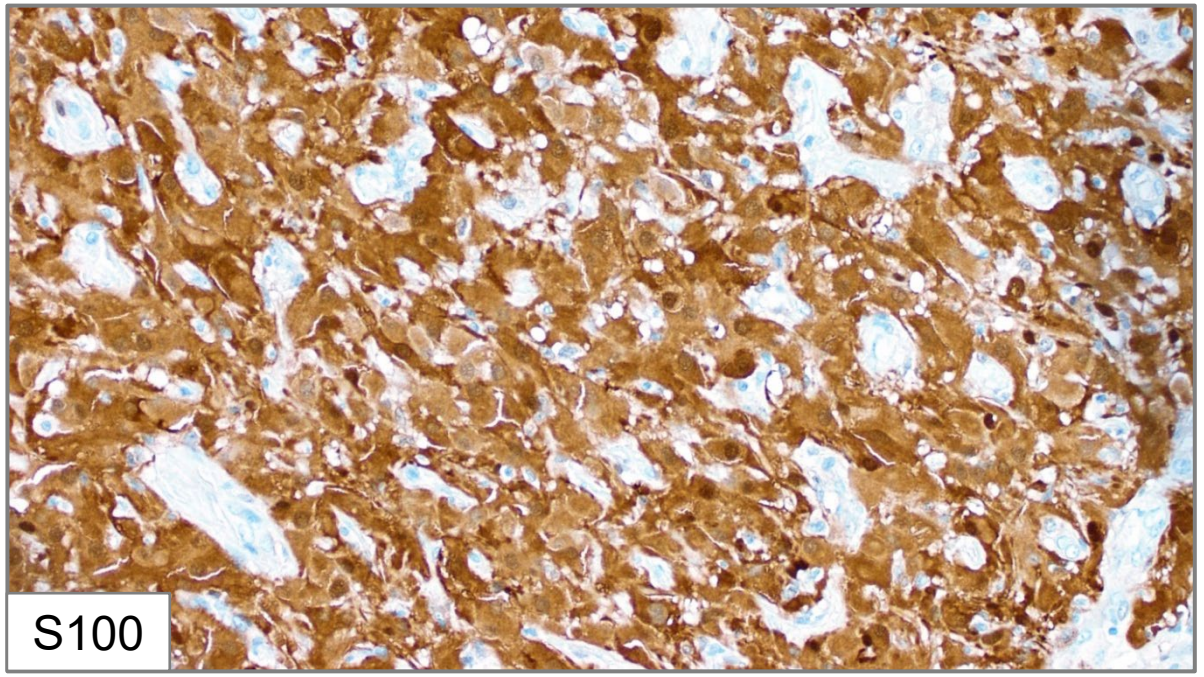


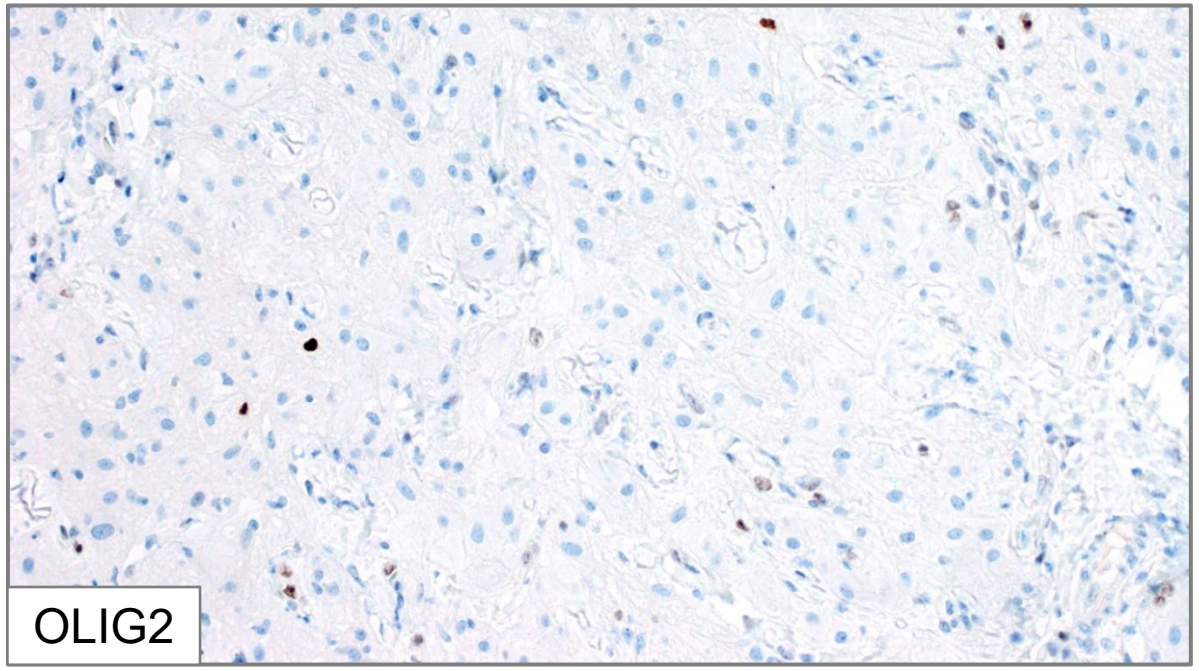


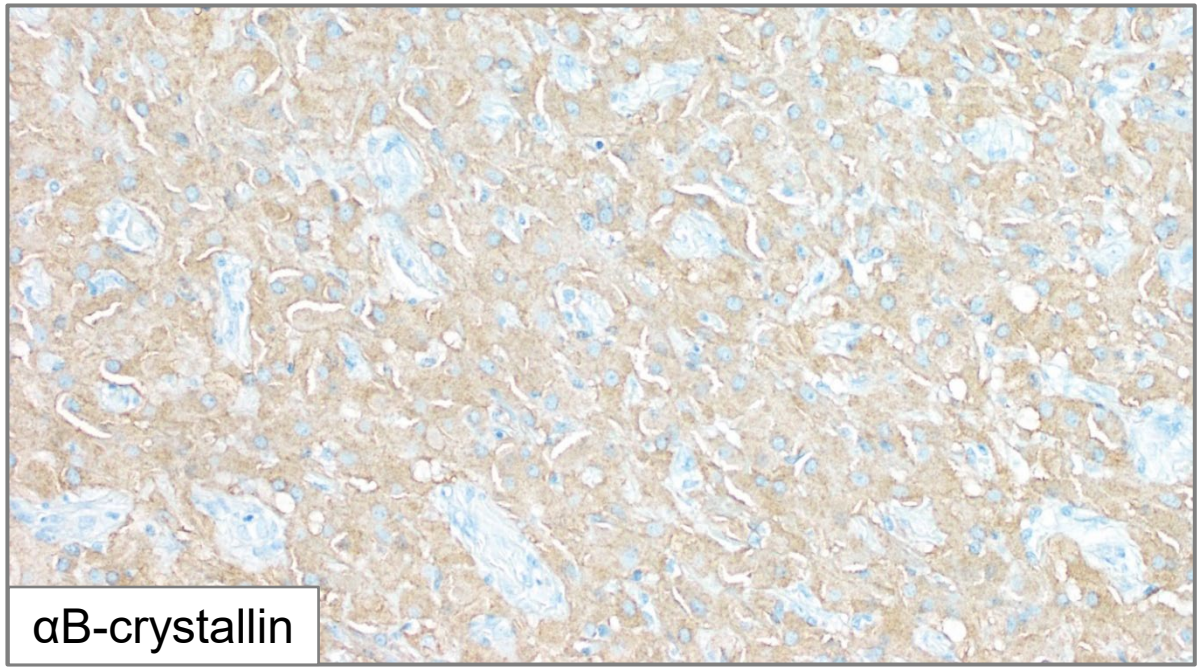


Differential diagnosis?

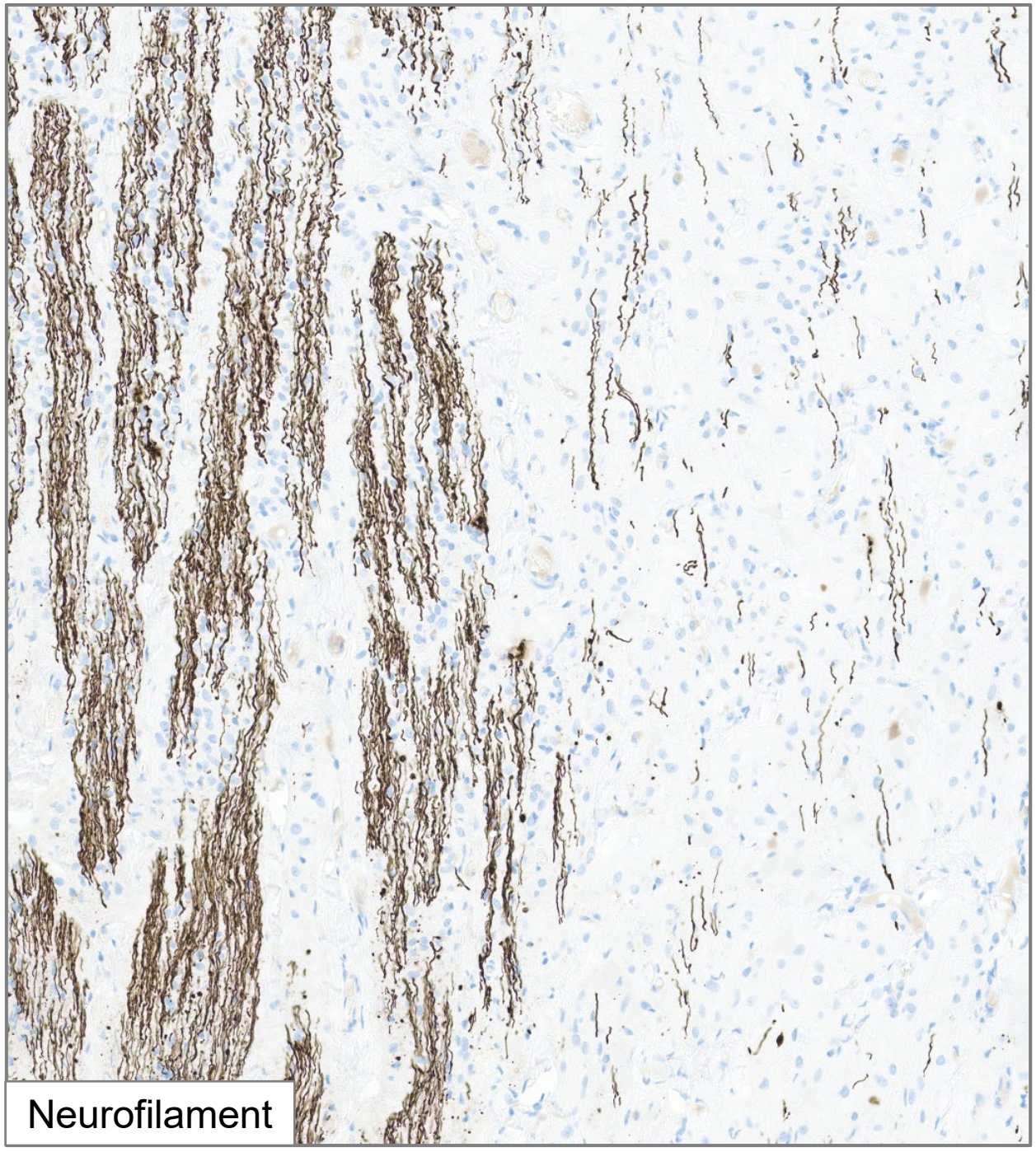


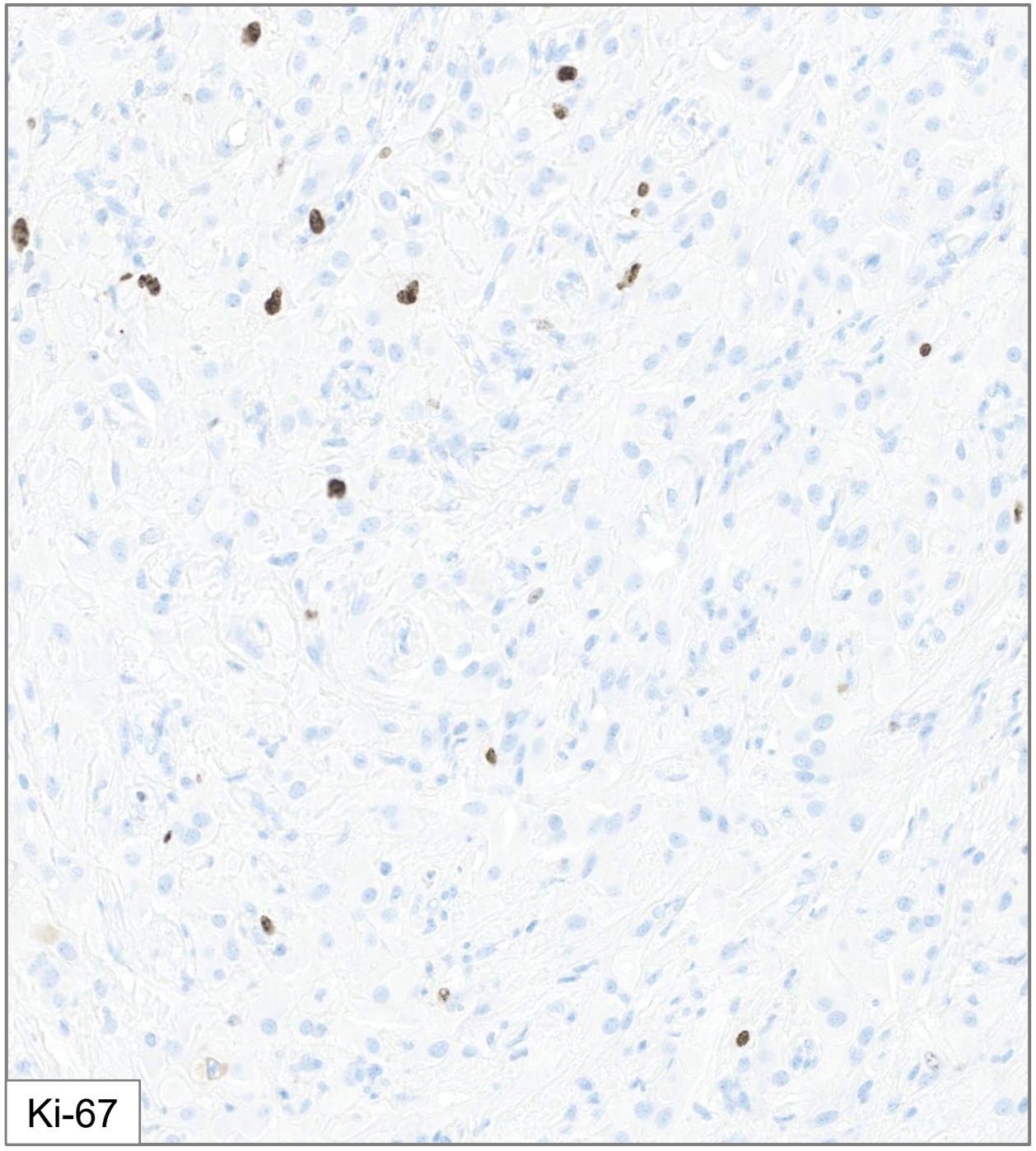






Synaptophysin: negative


Neurofilament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Differential Diagnosis

		Morphology	Genetics
Retina	Retinal astrocytic hamartoma (RAH)	Two histologic patterns: 1) Spindled astrocytes 2) Large tumor cells with abundant glass eosinophilic cytoplasm (gemistocytic / SEGA-like)	Tuberous sclerosis complex Neurofibromatosis 1/2 Retinitis pigmentosa mutation
	Nodular and massive retinal gliosis	Elongated spindled astrocytes with eosinophilic cytoplasm. Hyalinized/ sclerotic vascular channels and Rosenthal fibers	None
	Combined hamartoma of the retina and RPE	Disorganized retinal tissue intermixed with vessels and tubules of proliferating retinal pigment epithelium	Neurofibromatosis 2 Gorlin syndrome
Optic Nerve	Pilocytic astrocytoma / optic nerve glioma	Biphasic growth pattern and tumor cells with bipolar hair-like processes. Rosenthal fibers and EGBs.	Neurofibromatosis type 1 KIAA1549::BRAF fusions

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Modified from Poole Perry et al., 2013

Case 3: Additional Clinical Information

Neurologic:

- History of a single seizure and abnormal EEG
- Behavioral outburst night terrors, speech difficultly, sleep problems

Cardiovascular:

- Cardiac rhabdomyoma

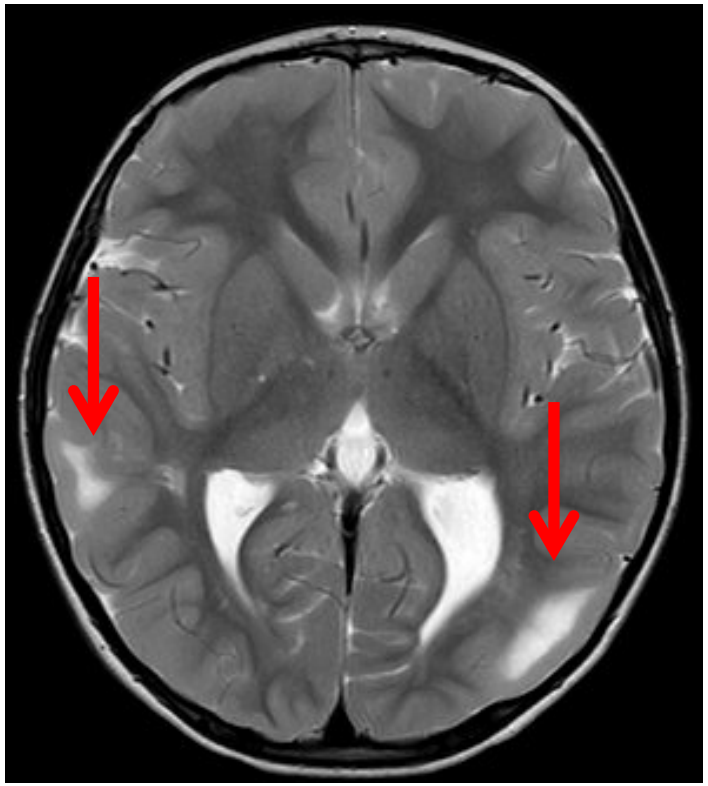
Skin

- Hypopigmented macules on skin (>3)

Diagnostic Genetic Testing:

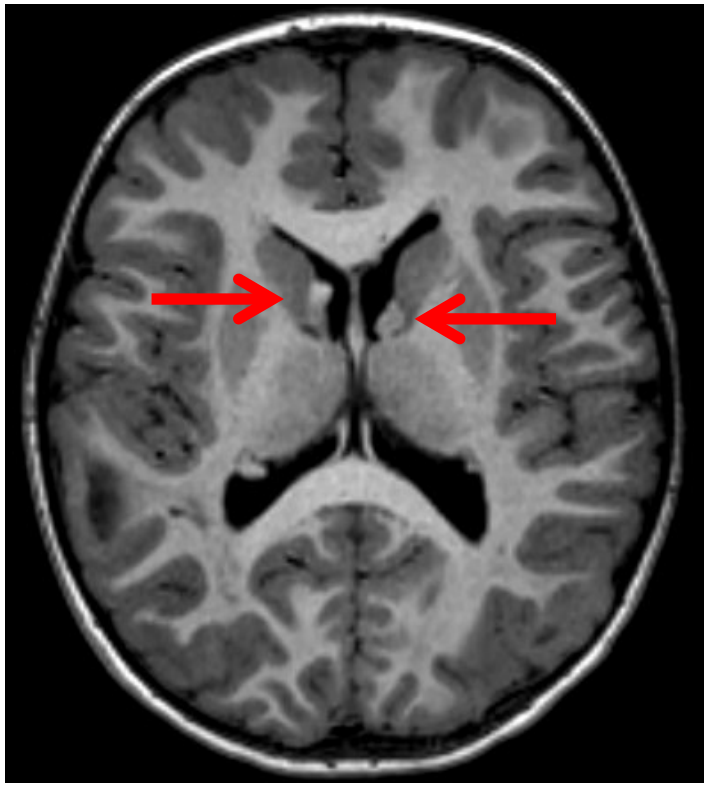
- TSC2 pathogenic mutation
  - c.2838-122G>A

Cortical tubers



T2 Axial

Subependymal nodules



T1 Axial

Final Diagnosis:

Retinal astrocytic hamartoma

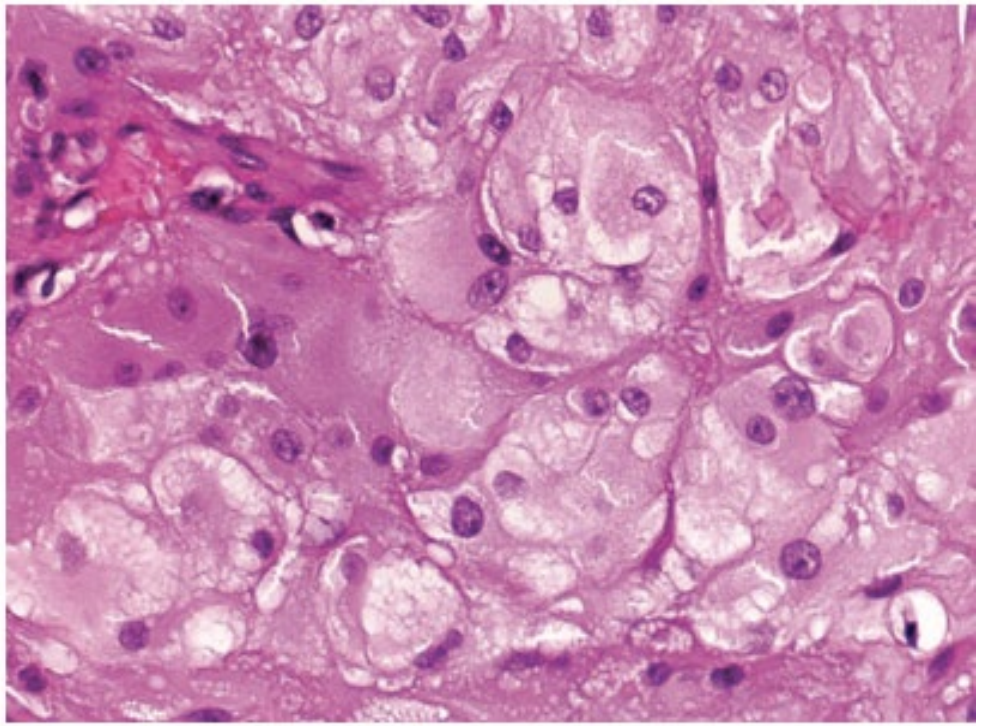
in a background of acute endophthalmitis

Retinal astrocytic hamartoma (RAH)

- Benign hamartomas typically involving the retina and optic disc, ranging from <1 to > 5 mm
- Typically arising in children or young adults
- Visual changes in a subset depending on location, hemorrhage, and proliferative retinopathy, or exudation
- Strongly associated with TSC, up to 20 – 50%

RAH Histologic Subtypes		
	Astrocytic hamartoma (RAH)	Giant cell astrocytoma of the retina
Morphology	Spindle-shaped cells with cytologically bland nuclei	Large polygonal cells with eosinophilic cytoplasm (SEGA-like)
Calcifications	+	++
IHC	GFAP, S100	GFAP, S100, +/- neuronal markers
Aggressive subtype	-	+

Giant cell astrocytoma subtype:



AGGRESSIVE RETINAL ASTROCYTOMAS IN FOUR PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX

BY *Jerry A. Shields MD,* Ralph C. Eagle Jr MD, Carol L. Shields MD*, AND *Brian P. Marr MD*

Clinical Ophthalmology

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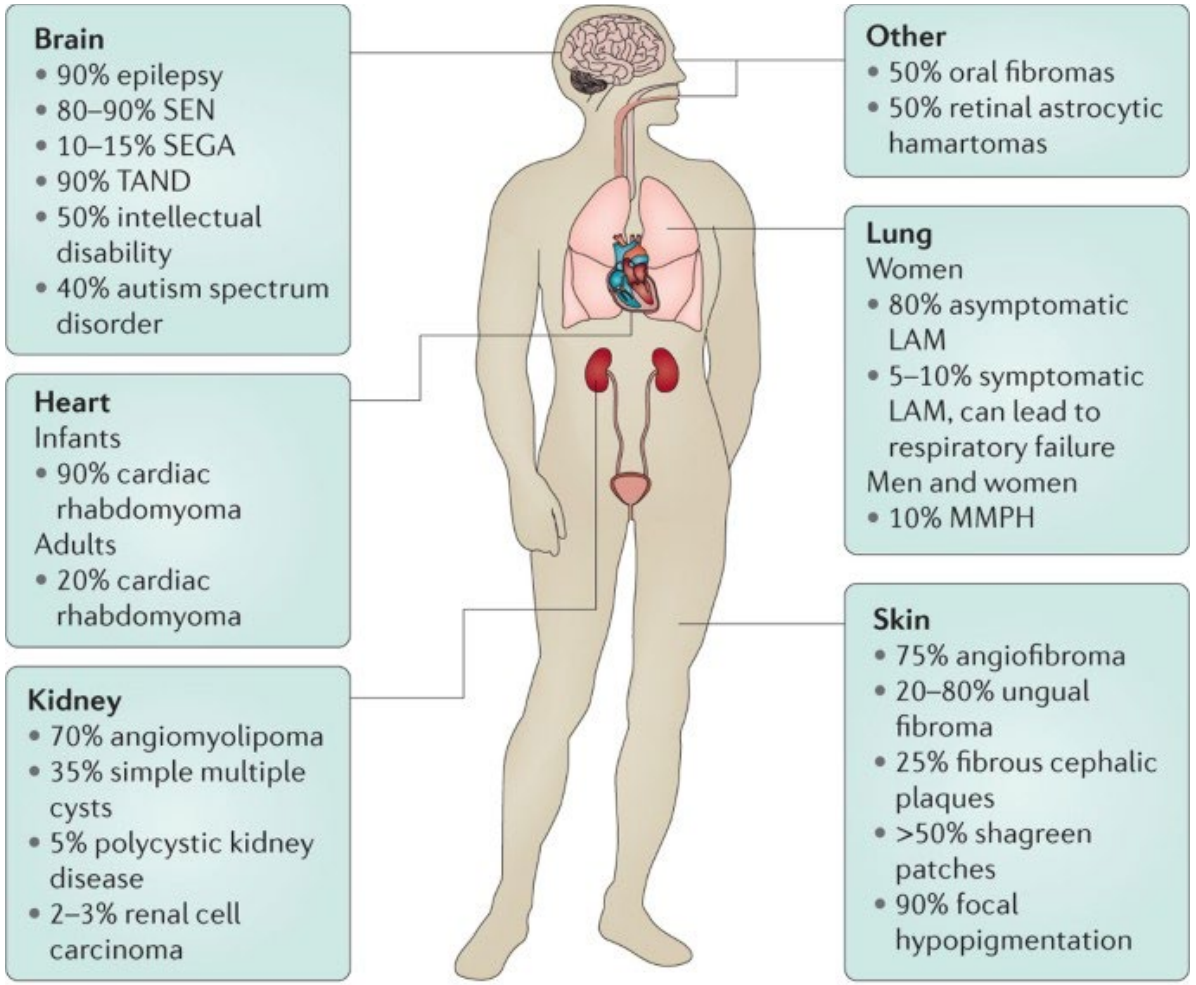
CASE REPORT

Aggressive retinal astrocytoma associated with tuberous sclerosis

Tuberous sclerosis complex diagnostic criteria (2021)

Autosomal dominant disorder caused by loss-of-function mutations in TSC1 or TSC2.



Tuberous sclerosis complex

Elizabeth P. Henske[1], Sergiusz Jóźwiak[2,3], J. Christopher Kingswood[4], Julian R. Sampson[5] and Elizabeth A. Thiele[6]

Nature Reviews | Disease Primers

Major Criteria	Minor Criteria
Hypomelanotic macules (≥3)	"Confetti" skin lesions
Multiple retinal hamartomas	Dental enamel pits (≥3)
Multiple cortical tubers and/or radial migration lines	Intraoral fibromas (≥2)
Subependymal nodule (≥2)	Retinal achromic patch
Cardiac rhabdomyoma	Multiple renal cysts
Subependymal giant cell astrocytoma	Nonrenal hamartomas
Angiofibroma (≥3) or fibrous cephalic plaque	Sclerotic bone lesions
Ungual fibromas (≥2)	
Shagreen patch	
Lymphangiomyomatosis	
Angiomyolipomas (≥2)*	

Definite TSC:

- 2 major features or 1 major feature with 2 minor features.

Possible TSC:

- Either 1 major feature or 2 minor features.

Genetic diagnosis criteria:

- A pathogenic variant in TSC1 or TSC2

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