Sporadic Hemangioblastoma Arising from the Infundibulum

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ABSTRACT

Hemangioblastomas are rare vascular tumors most often found in the posterior fossa and cervical spinal cord and commonly associated with von Hippel-Lindau Disease. We report a case of sporadic hemangioblastoma in a patient without von Hippel-Lindau Disease. Imaging characteristics included a solid, suprasellar mass that was homogeneously enhancing. These findings most resembled a pituicytoma or choroid glioma because of the close association with the infundibulum and the homogeneous avid enhancement. Microscopically, the neoplasm was seen to be composed of vascular channels associated with foamy stromal cells, containing clear cytoplasmic vacuoles. Microscopic and immunohistochemical findings were consistent with hemangioblastoma. Hemangioblastomas are a rare form of vascular tumor most commonly associated with von-Hippel Lindau disease. Our finding of non-cystic hemangioblastoma arising from the infundibulum demonstrates that, while rare, hemangioblastomas should be considered on the differential diagnosis for an avidly enhancing suprasellar mass.

CASE REPORT

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A 38-year-old female presented with a 9-month history of headaches and amenorrhea. Laboratory workup revealed low luteinizing hormone LH and follicle stimulating hormone FSH. Her past medical history includes irregular menses, remote history of melanoma excision from her thigh, and surgical removal of an ovarian cyst as a child. MRI of the pituitary was performed.

Magnetic resonance imaging [MRI] exam of the pituitary found the pituitary gland to be within normal limits in appearance but relatively small in size with a maximum height of approximately 3 mm. For a woman in the childbearing years this pituitary size was considered small. Additionally, a 13 x 13 x 13.2 mm homogeneously enhancing spherical mass was seen in the upper half of the infundibulum, which appeared to arise from the infundibulum itself and impinge upon the undersurface of the optic chiasm and third ventricle. The mass was isointense relative to the cortex on T1- and T2-weighted images, and enhanced avidly and homogeneously after contrast administration (Figure 1). The lesion was not well appreciated on DWI or on ADC map (Figure 2).

The patient underwent endoscopic transsphenoidal resection of the mass using stereotactic navigation. Intraoperatively, a soft, fleshy, yellowish tumor with a vascular capsule was identified in the suprasellar space arising directly from the pituitary stalk, grossly reminiscent of a pituicytoma. Gross total resection of the primary lesion was obtained, and the pituitary stalk was sectioned as a component of tumor

removal. Partial resection of pituitary gland was also performed for better exposure to the lesion.

Gross inspection of the mass revealed a 6 x 3 x 3 mm fragment of red-tan soft tissue. Histopathologic analysis of hematoxylin and eosin [H & E] stained sections showed a neoplasm composed of vascular channels associated with foamy stromal cells, containing clear cytoplasmic vacuoles (Figure 3A). No necrosis or mitotic activity was seen. Immunohistochemical analysis revealed positive staining for S100 (Figure 3B), neuron-specific enolase [NSE] (Figure 3C) and galectin-3 (Figure 3D), with some weak staining for inhibin. The tumor was negative for meningioma and spindle cell oncocytoma marker epithelial membrane antigen [EMA], as well as chordoid glioma of the third ventricle and pituicytoma marker glial fibrillary acidic protein [GFAP]. Based on the microscopic and immunohistochemical findings, a diagnosis of hemangioblastoma was established.

DISCUSSION

Etiology & Demographics:

Hemangioblastomas are highly vascular tumors found in the central nervous system [CNS], most commonly detected in the posterior fossa and cervical spinal cord, but also seen in retina [1]. Hemangioblastomas are uncommon, accounting for approximately 3% of CNS tumors [2]. They are less commonly sporadic, and rarely occur outside of the posterior fossa. Only a small handful of cases have been reported of supratentorial hemangioblastoma without von Hippel-Lindau Disease [VHL] [3]. Of these, only four cases of hemangioblastoma arising from the pituitary infundibulum have been reported [4].

Clinical & Imaging Findings:

We report a case of suprasellar hemangioblastoma in a patient without VHL, which, based on close association with the infundibulum and avid enhancement, strongly resembled a pituicytoma.

While up to 83% of VHL patients may have cerebellar hemangioblastomas, solitary hemangioblastomas are associated with VHL disease in only 10-20% of cases [2, 3, 5-8]. VHL-associated hemangioblastomas are typically multiple, often recur after surgical resection, and present at age 20-30 years, whereas the sporadic form is commonly solitary, occurs at age 40-50 years, and does not recur after definitive treatment.

Hemangioblastomas of the CNS are best visualized on gadolinium-enhanced MRI. While MRI findings are not pathognomonic, hemangioblastomas are typically seen on MRI as a cystic mass with an enhancing mural nodule, most commonly in the posterior fossa. The nodule is dark on T1-weighted images, bright on T2-weighted images, and homogeneously enhancing [3, 7, 9]. Infrequently hemangioblastomas may be solid, with peripheral enhancement, or cystic with an enhancing wall. Neuroangiography reveals a highly vascular tumor within an avascular cyst, with feeding vessels from dural arteries [3].

The clinical presentation of hemangioblastomas depends on the site of the lesion. As hemangioblastomas are most commonly found in the posterior fossa, symptoms are typically related to cerebellar dysfunction and include ataxia and gait disturbance [10]. Headaches are also common and related to mass effect from the tumor resulting in increased intracranial pressure [10].

Hemangioblastomas can be divided into sporadic and familial syndromic forms. Familial forms are associated with von Hippel-Lindau Disease, an autosomal dominant condition characterized by a large variety of predominantly low-grade lesions (endolymphatic sac tumor, cystadenoma of epididymis and broad ligament, renal and pancreatic cysts), but also more aggressive (pheochromocytomas and neuroendocrine tumors of pancreas) and malignant (renal cell carcinoma) tumors. VHL is caused by mutations in tumor suppressing VHL gene resulting in altered signaling pathways that cause upregulation of vascular endothelial growth factor [VEGF] [9].

Histopathologically, hemangioblastomas are highly vascular tumors consisting of numerous capillaries and stromal cells [10]. They are seen as an extensive vascular network with neoplastic stromal cells featuring nuclear hyperchromasia and degenerative atypia [10]. They are commonly positive for CD34, NSE [7], S100 protein [11, 12], and galectin-3 [13].

Treatment & Prognosis:

Definitive management of CNS hemangioblastoma is by surgical resection of the enhancing nodule. If the location of the mass is not amenable to excision, then stereotactic surgery and radiation therapy are non-definitive alternatives. Additionally, as hemangioblastomas in VHL can often recur, surgery is reserved for symptomatic lesions.

Differential Diagnoses:

The differential diagnosis for a solid suprasellar enhancing mass includes meningioma, pituicytoma, chordoid glioma, germ cell tumor, aneurysm, sarcoidosis, Langerhans cell histiocytosis, metastases, and rarely hemangioblastomas. Meningiomas are typically isointense on T1 and T2 and less likely hypointense on T1 and hyperintense on T2 to grey matter, and contain calcifications. Pituicytomas are hypointense to gray matter on T2 weighted images. Chordoid gliomas are isointense to gray matter on T1 and T2-weighted images. Germ cell tumors are variable depending on the subtype, but are generally hypointense or isointense to gray matter on both T1 and T2 weighted images, and may demonstrate susceptibility artifact from small hemorrhages. Aneurysms are best seen on CT or MR angiography studies, where a vessel diameter greater than 3mm is highly suggestive. Unlike hemangioblastomas that demonstrate a T2 hyperintense cystic component, aneurysms will be dark on T2 due to flow

voids. Neurosarcoid typically causes hydrocephalus from ventricular outflow compression and is multifocal, whereas hemangioblastoma is typically solitary, particularly in the sporadic form. Although Langerhans cell histiocytosis may present as a slightly hyperintense mass compared to gray matter on T2-weighted images, it is often accompanied by multiple lytic bony lesions seen on CT, plain film, or MRI. Metastases are also typically in the differential diagnosis for any intracranial mass, however the infundibulum is an uncommon location for metastatic disease.

TEACHING POINT

We report a sporadic case of solitary, non-cystic hemangioblastoma arising from the infundibulum and appearing quite similar to a pituicytoma and chordoid glioma. This demonstrates that, while rare, hemangioblastomas should be considered on the differential diagnosis for an avidly enhancing suprasellar mass.

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FIGURES

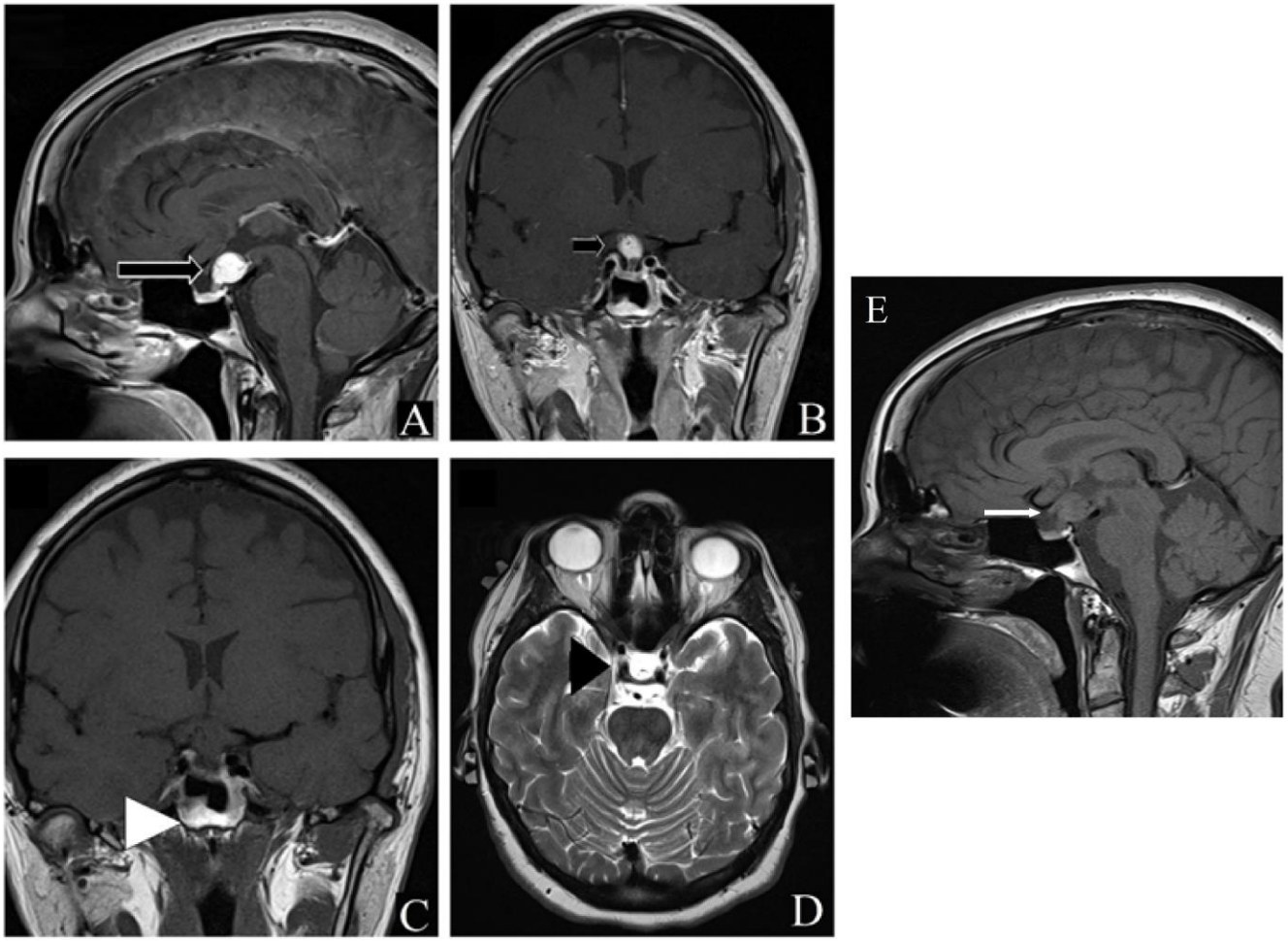

Figure 1: 38-year-old female with sporadic hemangioblastoma of infundibulum.
Technique: Gadolinium enhanced 3T MRI of the brain, pituitary protocol. Sagittal and coronal post-contrast T1 weighted images and axial T2 weighted image through the pituitary fossa.
Findings: (a)Homogeneously enhancing 13x13mm spherical mass seen in upper half of infundibulum (long arrow), (b) and impinging on the undersurface of the optic chiasm (short arrow). (c) The mass was isointense relative to cortex on both t1-weighted images (white arrowhead) (d) t2-weighted images (black arrowhead), and t1-weighted precontrast sagittal images.

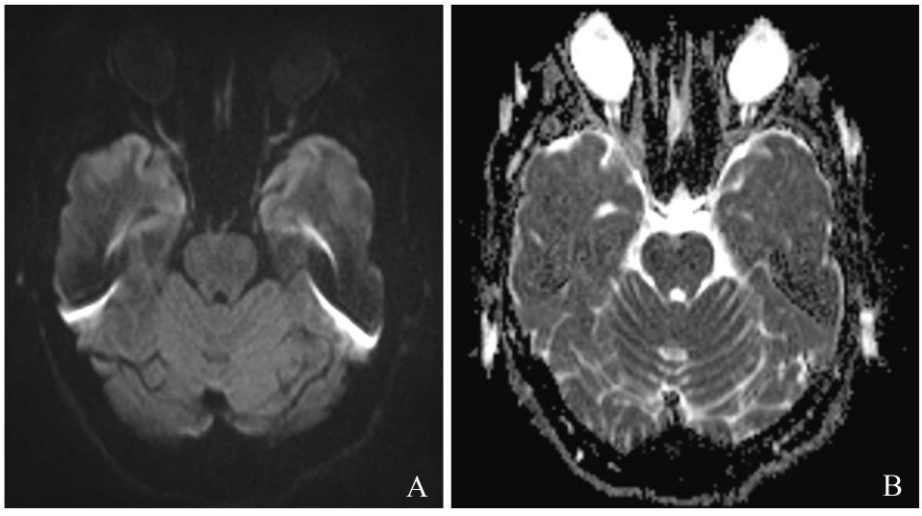

Figure 2: 38-year-old female with sporadic hemangioblastoma of infundibulum.
Technique: 3T MRI of the brain, pituitary protocol. Diffusion weighted images with ADC map.
Findings: No diffusion restriction is noted on the b1000 images (a) and there is no dark spot on the ADC map (b).

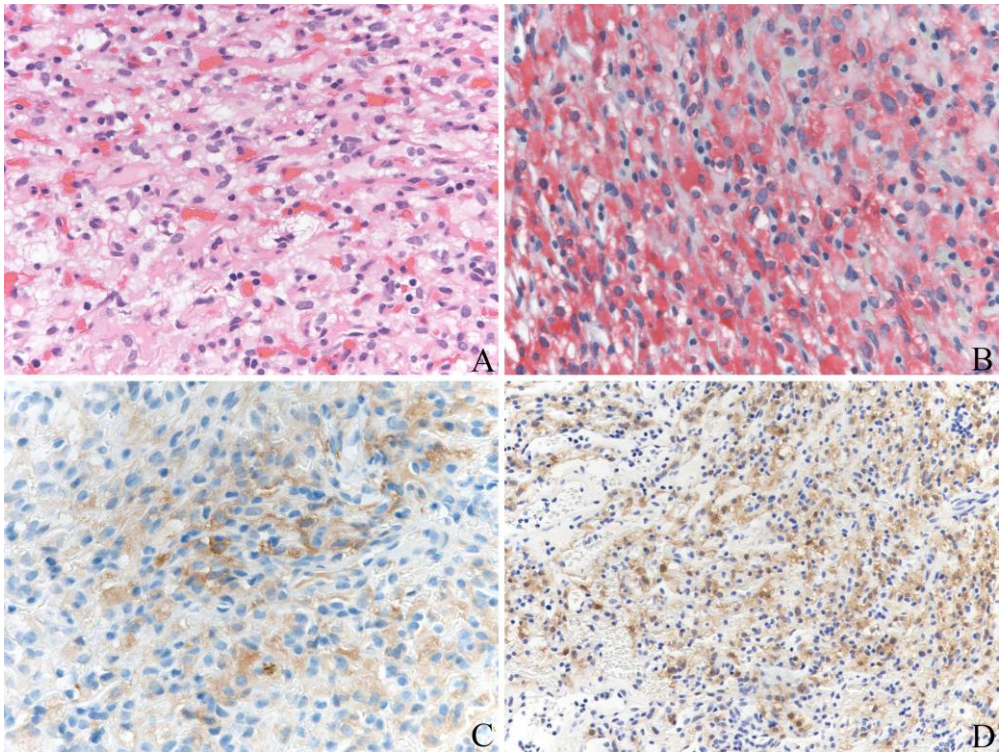

Figure 3: 38-year-old female with sporadic hemangioblastoma of infundibulum.
Technique: (a) H&E stained section 200x magnification, (b) s100 stained section 200x magnification, (c) NSE stained section 200x magnification, (d) galectin 3 stained section 100x magnification.
Findings: (a) H&E stained section disclose vascularized tumor with abundance of vacuolated foamy cells (*). (b) Positive red chromagen staining for s100 (**). (c) Positive red chromagen on NSE stain (***). (d) Positive red chromagen on galectin 3 stain (****).

Etiology	• Associated with von Hippel-Lindau Disease • Less commonly occur sporadically • Considered to be related to altered VEGF signaling.
Clinical Presentation	• Most commonly cerebellar dysfunction
Incidence	• 1:40,000. • Half of hemangioblastomas are associated with von Hippel-Lindau Disease. • Represents 1% of primary intracranial neoplasms.
Gender Ratio	• Slight male predominance.
Age Predilection	• VHL-associated: age 20-30 years • Sporadic Form: Age 40-50 years
Risk Factors	• Unknown
Treatment	• Surgical resection. Consider stereotactic surgery and radiation therapy for unresectable / multifocal lesions.
Prognosis	• Up to 20% recur, thus surgery is reserved only for symptomatic lesions.
Imaging Findings	• Cystic mass with an enhancing mural nodule, most commonly in the posterior fossa. • T1-weighted images: Dark • T2-weighted images: Bright and homogeneously enhancing

Table 1: Summary table for Hemangioblastoma.

	T1-weighted MRI	T2-weighted MRI	CT/Other imaging
Meningioma	• Isointense-to-minimally hyperintense to gray matter. • May have hypointense calcifications. • Strongly contrast enhancing dural-based mass with dural tails.	• Variable, most commonly iso/hypointense to gray matter.	• CT: Irregular calcified mass emerging from dura.
Pituicytoma	• Hypo/isointense to gray matter	• Heterogeneous, tends to be hypo/isointense	• CT: Solid mass within sella turcica.
Chordoid Glioma	• Isointense to gray matter. • Strong uniform contrast enhancement.	• Isointense to gray matter	• CT: Moderately hyperattenuating.
Germ cell Tumor (Germinoma is most common. Others include pineoblastoma, pineocytoma.)	• Hypo/isointense to gray matter	• Isointense to slightly hyperintense to gray matter	• CT: Heterogeneous density, contrast enhancing. • T2* GRE: Small hemorrhages cause susceptibility artifact
Aneurysm	• T1-weighted images: Acute hemorrhage is isointense to CSF.	• Flow voids indicative of blood vessel.	• CTA/MRA: Vessel diameter > 3mm.
Neurosarcoid	• Ventricular outflow compression may lead to hydrocephalus. • Dural and subarachnoid space lesions. • Isointense to gray matter.	• If in sella turcica, may be hyperintense and appear cystic	• CT: May be solid or multifocal masses. Hydrocephalus from ventricular outflow compression.
Langerhans Cell Histiocytosis	• Bright secondary to lipid-laden histiocytes. • Contrast-enhancing soft tissue masses.	• Slightly hyperintense to gray matter when in the infundibulum.	• CT: Lytic bone lesions and geographic skull base bone destruction. • Plain film: Multiple lytic bone lesions.
Metastases	• Contrast-enhancing soft tissue mass.	• Variable, may be isointense to gray matter.	• CT: Commonly solid-attenuating with contrast enhancement or possibly central necrosis.
Hemangioblastoma	• Hypointense cystic mass with an enhancing mural nodule.	• Hyperintense due to cystic component.	• CT: Primary mass enhances with contrast. Cystic component is low-attenuating. Most commonly found in the posterior fossa.

Table 2: Differential diagnosis table for Hemangioblastoma.

ABBREVIATIONS

CAN = central nervous system
EMA = Epithelial membrane antigen
GFAP = glial fibrillary acidic protein
H & E = hematoxylin and eosin
MRI = magnetic resonance imaging
NSE = neuron-specific enolase
VEGF = vascular endothelial growth factor
VHL = von Hippel-Lindau Disease

KEYWORDS

Hemangioblastoma; von-Hippel-Lindau disease; suprasellar mass; infundibulum; neuroradiology; MRI

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