Giant pituitary macroadenoma of stem cell origin: illustrative case

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BACKGROUND Giant pituitary macroadenomas with a diameter >4 cm are rare tumors, accounting for only about 5% of pituitary adenomas. They are more difficult to maximally resect safely owing to limited access as well as encasement of adjacent structures. Acidophil stem cell adenomas are rare immature neoplasms proposed to derive from common progenitor cells of somatotroph and lactotroph cells. These adenomas comprise about 4.3% of surgically removed pituitary adenomas. No previous reports have described acidophil stem cell adenomas that grow to the size of giant macroadenomas. This rare entity poses special challenges given the need for maximal safe resection in an immature neoplasm.

OBSERVATIONS The authors report a 21-year-old female who presented with 3 years of progressive visual decline and a giant macroadenoma. She underwent endoscopic transsphenoidal surgery for decompression. Given the tumor size and involvement of adjacent critical structures, gross-total resection was not achieved. The authors review the literature on giant pituitary adenomas and provide a discussion on clinical management for this rare entity.

LESSONS The authors present a very rare case of a giant pituitary adenoma of acidophil stem cell origin and discuss the technical and management challenges in this rare entity.

Illustrative Case

A 21-year-old right-handed female presented in 2017 with headaches and progressive visual decline in the left eye. She was evaluated by a primary care physician and was diagnosed with a brain mass. She gradually developed right-sided visual field deficits. She presented to our center in 2020. Ophthalmological examination demonstrated acuity at 1/200 in the right eye and no light perception in the left eye. Visual field testing showed a right temporal visual field defect with relatively preserved central acuity nasally and superior-temporally. Optical coherence tomography (OCT) showed dramatic nerve fiber layer dropouts with loss of ganglion cells. Detailed endocrine evaluation revealed no abnormalities. She had no stigmata of Cushing’s disease or acromegaly.

Magnetic resonance imaging (MRI) of the brain showed a large enhancing sellar/suprasellar mass measuring approximately 6.4 × 6.1 × 7 cm with prominent vascular flow voids (Fig. 1A–C). The adenoma was histologically confirmed to be an acidophil stem cell adenoma on electron microscopy.

ABBREVIATIONS ACA = anterior cerebral artery; CTA = computed tomography angiography; DWI = diffusion weighted imaging; ICA = internal carotid artery; MCA = middle cerebral artery; MRI = magnetic resonance imaging; OCT = optical coherence tomography.

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tomography angiography (CTA) showed the absence of the right A1 segment with distal reconstitution, as well as superior-lateral displacement of bilateral A2 segments (Fig. 1D). She underwent digital subtraction angiography for possible preoperative embolization. The tumor’s vascular supply was from multiple small branches of the bilateral internal carotid arteries (ICAs) and middle cerebral arteries (MCAs) (Fig. 1E–F). No suitable endovascular targets were identified.

She underwent endonasal transphenoidal resection in collaboration with an otorhinolaryngology specialist (S.C.P.). Seventy-degree reverse post scopes and retroflexed navigation suction instruments were used to maximize tumor visualization and extirpation. Intraoperative MRI demonstrated the extent of resection (Fig. 2). A craniotomy was not pursued.

Histopathological evaluation revealed loss of acinar architecture with sheets of pleomorphic cells possessing abundant acidophilic cytoplasm (Fig. 3A). Scattered cells were seen with cytoplasmic vacuoles and occasional mitotic figures (Fig. 3B). Immunohistochemical staining showed strong diffuse Pit-1 nuclear staining (Fig. 3C) and moderately elevated Ki-67 immunoreactivity (Fig. 3D). Fibrous bodies were stained for low-molecular-weight cytokeratin (CAM 5.2, Fig. 3E). Electron microscopy showed numerous dilated and giant mitochondria (Fig. 3F), confirming the diagnosis of acidophil stem cell adenoma.

MRI on postoperative day 1 showed small bilateral diffusion weighted imaging (DWI) abnormalities in the anterior cerebral artery (ACA) distribution (Fig. 4), from which she was asymptomatic. Postoperative CTA showed mild vasospasm of the left intracranial ICA and the left A1 segment. She was started on a steroid taper postoperatively. A detailed ophthalmological examination revealed no new

FIG. 1. A–C: Sagittal, coronal, and axial contrasted MRI showing giant pituitary macroadenoma with vascular proliferation. D: CTA showing lateral displacement of the left A1 segment and dropout of the right A1 segment with distal reconstitution. Digital subtraction angiography with anteroposterior views of the right ICA (E) and left ICA (F) injections showing vascular supply arising from multiple small branches originating from the bilateral ICA and MCA. Lateral view showed faint contrast extending to the anterior circulation (not shown). No suitable target was identified for preoperative endovascular embolization.

FIG. 2. A–C: Sagittal, coronal, and axial postoperative contrasted MRI studies showing residual tumor anteriorly.
deficits but no immediate improvements in her vision. The remainder of her course was relatively unremarkable. She was discharged home on postoperative day 8 with plans for outpatient radiation therapy once the tumor cavity maximally consolidated.

FIG. 3. Histopathological evaluation. A: Original magnification ×100. Hematoxylin and eosin (H&E) stain showing loss of acinar architecture with sheets of monomorphic cells. B: Original magnification ×400. Higher power H&E showing abundant acidophilic cytoplasm and scattered cells with cytoplasmic vacuoles and occasional mitotic figures. C: Original magnification ×100. Pit-1 immunohistochemistry showing strong diffuse nuclear staining. D: Original magnification ×400. Ki-67 immunohistochemical stain showing a moderately elevated proliferative index. E: Original magnification ×100. CAM 5.2 immunohistochemical stain for low-molecular-weight cytokeratin. Globular cytoplasmic positivity is consistent with fibrous bodies. F: Original magnification ×8000. Electron microscopy showing numerous dilated and giant mitochondria.

Discussion

Pituitary morphogenesis involves a complex interplay between several signaling molecules early in development. Selective expression of Pit-1 on mouse embryonic day e13.5–e17.5 gives rise to Pit1+ GATA2+ cells, which terminally differentiate to somatotrophs and lactotrophs expressing growth hormone and prolactin, respectively. Acidophil stem cell adenomas derive from residual undifferentiated Pit1+ precursors in adults. These rare tumors are defined by misplaced exocytosis, fibrous bodies, mitochondrial alterations, and oncocytic transformation. They represent only about 4.3% of adenomas and display a more aggressive clinical profile with variable expression of growth hormone and prolactin.

Given their aggressive growth pattern, acidophil stem cell adenomas typically come to medical attention early due to mass effect on adjacent structures. However, to our knowledge, no other reported cases have shown growth to the extent of forming a giant macroadenoma.

Observations

Despite its giant size and moderately elevated Ki-67 proliferative index, the tumor demonstrated limited invasiveness and appeared to remain within the tumor capsule. This is in contrast to other cancer stem cells that show more aggressive proliferation. This tumor retained the ability to recruit robust blood supply from bilateral ACA and MCA branches. Asymptomatic DWI changes are seen in up to 25% of patients after routine diagnostic cerebral angiography and are likely due to small silent emboli, especially given their higher frequency in patients with vascular risk factors (44% vs 13%, p = 0.03). Our patient was similarly asymptomatic from her DWI changes.

A combined endonasal–transcranial approach was considered in this case. However, given the extent of endonasal resection achieved and the vascularity of the tumor, it was deemed safer to treat her residual tumor using radiation therapy. Her postoperative vision did not immediately improve. Patients with thin preoperative retinal nerve fiber layers measured by OCT often fail to improve at 6 weeks postoperatively, and this effect can persist up to 1 year. Earlier identification and treatment of patients with lesions abutting the chiasm may help decrease the risk of long-term deficits postoperatively.

Lessons

Here, we report the first known case of an acidophil pituitary stem cell adenoma presenting as a giant macroadenoma with profound visual deficits. We identify clinical and operative challenges unique to this rare tumor, as well as postoperative visual and functional status. Our study limitation is that this is a retrospective review of a single patient’s data.

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Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Conception and design: Jane, Asuzu, Payne. Acquisition of data: Asuzu, Hakim, Payne. Analysis and interpretation of data: Asuzu, Hakim, Coss. Drafting the article: Asuzu, Hakim. Critically revising the article: Jane, Asuzu, Burke, Park. Reviewed submitted version of manuscript: Asuzu, Burke, Park, Payne. Created photomicrographs: Coss.

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