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Objectives

- Ectopic pituitary adenomas are a rare entity of adenoma formation which are extrasellar and/or without direct involvement of the pituitary gland, and can often present diagnostic challenges.
- We describe a rare presentation of a patient presenting with left ophthalmoplegia and ptosis, with an extrasellar / left lateral cavernous sinus mass extending towards V2/V3, initially concerning for malignancy.
- Transcranial biopsy revealed a corticotroph pituitary adenoma, which subsequently underwent spontaneous regression and symptom resolution.
- A literature review was conducted to review the presentation and characteristics, and management, of ectopic pituitary adenomas.
- Additionally, factors which predict the probability of regression of pituitary adenomas after transsphenoidal surgery are discussed.

Case Description

- A 48-year-old female with PMH of type 2 diabetes presented with headaches, left eye lid lag, blurry vision, and flu-like symptoms. Exam was notable for dense left eye ptosis, mydriasis, and complete ophthalmoplegia.
- MRI brain demonstrated expansile mass of the left cavernous sinus with extension towards foramen spinosum and ovale (Fig. 1A), and a normal pituitary gland. Leading differential diagnoses included malignant primary tumor such as lymphoma, metastatic tumor, inflammatory disease.
- Hypercortisolemia was noted during workup, but considered secondary to acute stress response from influenza pneumonia.
- A transcranial biopsy of the extradural tumor extending along V2/V3 was performed, as well as subtotal resection of tumor within the lateral cavernous sinus (Fig. 1B). While frozen pathology returned as a spindle cell tumor, final pathology returned as a corticotroph pituitary adenoma.
- Subsequently over the next six months, symptoms of ptosis and ophthalmoplegia resolved, cortisol normalized, and MRI imaging demonstrated involution and complete resolution of the tumor (Fig. 1C).

Pre- and Post-operative Imaging

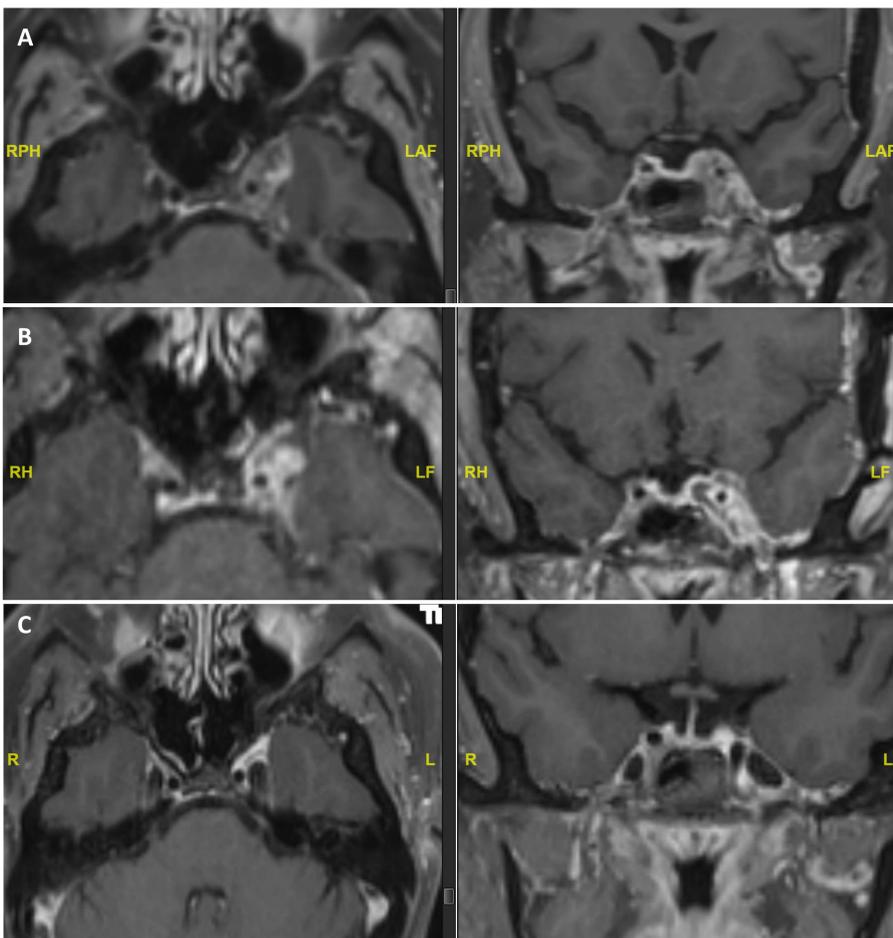


Figure 1: MRI T1 sequence with gadolinium demonstrating a heterogeneously enhancing left cavernous sinus mass with extension along V2 and V3. A) Preoperative imaging. B) Immediate postoperative imaging. C) Eight months postoperative imaging.

Ectopic / Extrasellar Pituitary Adenomas

- Prior studies showed ectopic pituitary adenomas are a rare entity, with the sphenoid sinus being the most common location (30-50%), and a small number (~13% in meta-analysis) within the cavernous sinus.¹
- Majority (80-90%) of ectopic pituitary adenomas we identified were functional tumors.
- Resection rates vary from 45-89%.^{1,3} Radiotherapy was commonly employed for subtotal resection.^{6,11} Recurrence rates were not consistently reported but were uncommon in the literature
- There were no previous case reports of involution after subtotal resection or biopsy, highlighting the rarity of this phenomenon.

Ohnishi et. al 2000² : 4 patients with suspected ectopic cavernous sinus adenoma	All four patients underwent EEA, subsequently 3 of 4 patients underwent radiation therapy to the cavernous sinus, all of which had effective response.
Knappe et. al 2017³ : 3 patients with ectopic cavernous sinus enhancement and symptoms of Cushing's Disease	Two patients had complete symptom resolution after resection; one patient continued to have hypercortisolism despite negative MRI, requiring bilateral adrenalectomy.
Agely et. al 2019⁴ : 1 patient, 44F	Complete symptom resolution after transsphenoidal resection of tumor.
Zhu et. al 2020⁵ : 1 patient, 22F, Cushing's Disease	Partial remission after resection, followed by complete resolution after radiation treatment.
Tucci et. al 1999⁶ : 1 patient, 54F	Underwent bilateral adrenalectomy and transsphenoidal hypophysectomy prior to MRI, which identified a cavernous sinus mass. Radiation therapy led to a delayed clinical response.
Koutourousiou et. al 2017⁷ : 1 patient, 36F, Cushing's Disease	Complete response after transsphenoidal resection.
Oldfield et. al 2013⁸ : 1 patient, 26F, Cushing's Disease	Complete response after transsphenoidal resection.
Koizumi et al 2011⁹ : 1 patient, 40F, Cushing's Disease	MRI negative but with cavernous sinus sampling localizing to left cavernous sinus. Complete resolution after removal of 3mm cavernous sinus adenoma.
Kim et. al 2003¹⁰ : 1 patient, 61F, Cushing's Disease	MRI negative; total hypophysectomy performed without cavernous sinus exploration. Died postoperative day 17 due to myocardial infarction; postmortem exam revealed right cavernous sinus adenoma.
Hata et. al 2003¹¹ : 1 patient, 24F presenting with left CN3 palsy without endocrinopathy	MRI with left cavernous sinus mass, underwent craniotomy and stereotactic radiosurgery with complete resolution of symptoms.

Regression of Residual Pituitary Adenoma

- The rate of regression or predictors of regression following subtotal resection of ectopic pituitary adenoma is not well studied.
- Regression of tumor residual can occur frequently after transsphenoidal surgery for subtotal resection of intrasellar pituitary adenoma, e.g. ~50% of cases.¹¹ The mechanism may be due to surgical manipulation causing tumor necrosis and/or devascularization of the tumor.
- Cavernous sinus involvement is a negative predictor of postoperative shrinkage of intrasellar pituitary adenomas¹¹, with may have potential implications for ectopic tumors within the cavernous sinus. Other negative predictors include history of previous pituitary surgery, larger tumor volume, preoperative panhypopituitarism.

Conclusions

- We demonstrate a rare presentation of ectopic pituitary adenoma fully within the cavernous sinus, in which a resective biopsy precipitated regression of the tumor and resolution of preoperative symptoms.
- This case highlights a diagnostic challenge in the broad differential for lateral cavernous sinus masses, which includes malignant primary tumor and metastases, inflammatory lesions, pituitary adenoma.
- For similar such cases where there is residual ectopic pituitary adenoma after subtotal resection, we would advocate for an initial postoperative period of close monitoring rather than immediately initiating radiation or medical treatment, as spontaneous involution of the residual tumor can obviate the need for additional treatment.
- Further studies are necessary to identify factors that predict the likelihood of regression of ectopic pituitary adenoma following subtotal resection.

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