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Ectopic Pituitary Adenomas Presenting as Sphenoid or Clival Lesions: Case Series and Management Recommendations

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Abstract

Background An ectopic pituitary adenoma presenting as a clival or sphenoid mass is a rare clinical occurrence that may mislead the clinician and result in unnecessary interventions or potential medicolegal consequences. Here, we present one of the largest multi-institutional case series and review the literature with an emphasis on radiological findings and critical preoperative workup.

Methods Retrospective chart review.

Results Nine patients were identified with ectopic pituitary adenomas of the sphenoid or clivus. There were four females and five males. Median age was 60 years old (range, 36–73 years). The most common presenting symptom was headache (56%). Five (56%) patients presented with a mass arising from the clivus while four (44%) presented with a mass in the sphenoid. Six (67%) patients demonstrated biochemical evidence of hypersecretion on full endocrinology panel. All masses showed evidence of enhancement with gadolinium with a propensity for adjacent bone involvement. Lesions also had a predilection for growth toward the cavernous sinus, carotid artery, or sellar floor. Surgical intervention was performed in eight patients (89%). In eight patients (89%), tumors demonstrated immunoreactivity to prolactin.

Conclusions Pituitary adenomas can rarely present as an isolated sphenoid or clival mass. Lesions displayed similar magnetic resonance imaging findings with an erosive growth pattern toward the sellar floor, cavernous sinus, or adjacent carotid artery. Patients with clival or parasellar lesions with comparable features should have a preoperative workup which includes prolactin level and alert the physician to consider an ectopic pituitary adenoma in the differential to prevent unnecessary surgery and potential complications.

Keywords
- pituitary adenoma
- ectopic pituitary tumors
- sphenoid tumors
- clival tumors

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Introduction

Pituitary adenomas most commonly present as an intrasellar tumor. Ectopic pituitary adenomas (EPAs) arise when an adenoma occurs without any obvious continuity with the normal pituitary gland.[1] Due to its rarity, ectopic pituitary tumors may often be diagnosed in a delayed fashion after extensive surgical resection. Early clinical suspicion is necessary to avoid unnecessary interventions.

Here, we present one of the largest multi-institutional case series of patients presenting with EPAs of the sphenoid or clivus with emphasis on clinical presentation, radiographic findings, and pathology. The findings in this article may increase awareness of this rare entity and aid the clinician in formulating the most appropriate management approach.

Methods

The study was approved by the institutional review board at all involved tertiary care centers. The pituitary databases at each center were accessed and queried for EPAs. Pituitary adenomas were considered ectopic if they presented as isolated clival or sphenoid masses with a normal appearing sella and pituitary gland. Nine patients meeting criteria were identified and their clinical records were accessed for chart review. The clinical presentations, histological diagnosis, hormonal levels, and imaging were extracted from the medical records.

Results

Nine patients were identified and included in this study. Patient information including demographic information, imaging characteristics, and histopathology are illustrated in ►**Table 1**. There were four females and five males. Median age was 60 years old (range, 36–73 years). The most common presenting symptom was headache (56%) followed by decreased libido (33%). Five (56%) patients presented with a mass arising from the clivus while four (44%) presented with a mass in the sphenoid. Six (67%) patients demonstrated biochemical evidence of hypersecretion on full endocrinology panel most commonly to prolactin. On imaging, all masses showed evidence of enhancement with gadolinium. In seven of nine patients (79%), masses abutted the inferior margin of the sella. In five patients (56%), there was evidence of extension to the carotid artery. The pituitary gland, stalk, and sella turcica were normal in all cases. Surgical intervention was performed in eight patients (89%). In eight patients (89%), tumors demonstrated immunoreactivity to prolactin.

Discussion

EPAs are a rare clinical entity with the majority of the literature comprised of case reports. Various sites for EPAs have been described including the cavernous sinus, sphenoid, clivus, and nasopharynx.[2–5] In each instance, there is no discernable connection with the normal pituitary gland and the intrasellar anatomy is within normal limits.

Pathogenesis and Clinical Manifestation

It is hypothesized that the embryological development of the anterior pituitary is likely responsible for the formation of EPAs in characteristic locations.[6] The adenohypophysis originates from the upper mucous membranes of the buccopharyngeal membrane. As the sphenoid develops, an infolding of the buccopharyngeal membrane, referred to as Rathke pouch, denotes the beginnings of the adenohypophysis. Rathke pouch will eventually push upward through the developing sphenoid and into the sella turcica where it meets the neurohypophysis.[7] Remnants of Rathke pouch can reside along its course from the upper pharynx to the sella. Adenomatous change of these remnant cells can theoretically result in EPAs of the nasopharynx, sphenoid, and clivus.

Symptom presentation in our series was nonspecific and was most commonly headache. Four (44%) patients presented with obvious symptoms of the endocrine disorder, which included three patients with fatigue and decreased libido from prolactin oversecretion and one patient with acromegaly from growth hormone excess. Four (44%) patients presented with sphenoid sinus EPAs and five (56%) patients presented with clival EPAs. Hou et al performed the largest literature review of cases and identified 65 cases of EPAs in the literature.[8] According to their systematic review, approximately 36.9% of EPAs arise in the sphenoid sinus and 7.2% in the clivus. They report that among EPAs, 30.9% were corticotropin (ACTH)-secreting tumors, 28.1% were prolactinomas, 27.4% were endocrine-inactive, 6.8% were growth hormone secreting, and 3.4% stained positive for thyrotropin.[8] In our series, the majority of patients (89%) presented with EPAs demonstrating prolactin immunoreactivity. Despite the high incidence of prolactin immunoreactivity in this series, only three patients demonstrated prolactin oversecretion on the endocrine panel.

Imaging Features

Few studies have explored the computed tomography (CT) and magnetic resonance imaging (MRI) characteristics of EPAs with emphasis on identifying salient features that may alert the physician to consider the entity preoperatively. Yang et al performed the largest study characterizing CT and MRI findings in a series of eight patients presenting with sphenoid EPAs.[9] In their study, EPAs were isodense to gray matter, rarely showed calcification, and commonly caused adjacent bone remodeling, sclerosis, or erosion. Bone involvement was evident in 62.5% of EPAs. MRI lesions were isointense to gray matter, showed mild-to-moderate enhancement and were usually heterogeneous on T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI) sequences. EPAs also showed a preferentially growth pattern that involved the cavernous sinus and encased the adjacent carotid artery. Additionally, they noted an association with an empty sella in 62.5% of patients.[9]

Similar to the study of Yang et al, EPAs of the clivus and sphenoid demonstrated distinctive features in our series (►**Figs. 1** and **2**). CT most commonly exhibited an expansile mass with adjacent bone erosion seen in 89% percent of patients. MRI demonstrated an enhancing mass in all cases

Table 1 Patient information including demographic information, imaging characteristics and histopathology

Patient	Age (y)	Sex	Presenting symptoms	Location	Imaging (CT/MRI)	Pathology
1	73	F	Headache	Sphenoid	Expansile enhancing mass in the right sphenoid with dehiscence of the posterior wall of the sphenoid, thinning of the right cavernous carotid artery plate, bordering the anterior margin of the sella turcica, normal pituitary gland, and stalk	Pituitary adenoma, immunoreactive to prolactin
2	60	F	Headache	Clivus	Expansile enhancing mass centered in the left clivus with erosive changes extending to the posteroinferior margin of the sella and cavernous sinus encasing the cavernous ICA, normal pituitary gland, and stalk	Pituitary adenoma immunoreactive to prolactin
3	67	M	None	Clivus	Enhancing mass of the right clivus with extension to the vertical clival ICA and posteroinferior margin of the sella, normal pituitary gland, and stalk	Pituitary adenoma immunoreactive to prolactin
4	36	M	Headache, decreased libido	Clivus	Enhancing mass centered in the anterior clivus, normal pituitary gland, and stalk	Pituitary adenoma immunoreactive to prolactin, prolactin level 26 ng/mL
5	66	F	Headache and gait disturbance	Sphenoid	Enhancing expansile mass centered in the floor of the sphenoid sinus, normal pituitary gland, and stalk	Pituitary adenoma immunoreactive to prolactin and TSH
6	60	M	Postcoital amnesia	Sphenoid	Enhancing expansile mass in the left sphenoid extending to the left cavernous sinus and floor of the sella. Normal pituitary gland and stalk	Pituitary adenoma immunoreactive to ACTH
7	72	M	Neck pain, dizziness, decreased libido, lethargy	Clivus	Enhancing mass involving the body of the clivus with extension to the bilateral cavernous sinuses and sellar floor. Normal pituitary gland and stalk	No pathology, prolactin level 469.9 ng/mL
8	50	F	Headache, fatigue, joint pain, acromegaly	Clivus	Mildly enhancing mass of the upper anterior clivus abutting the sellar floor, normal pituitary gland and stalk	Pituitary adenoma immunoreactive to prolactin and GH, IGF-1 level 937 ng/mL
9	49	M	Decreased libido, nasal airway obstruction	Sphenoid	Enhancing expansile mass of the sphenoid sinus floor extending inferiorly to the nasopharynx, normal pituitary gland, and stalk	Pituitary adenoma immunoreactive to prolactin, prolactin level 630 ng/mL

Abbreviations: ACTH, corticotropin; CT, computed tomography; F, female; GH, growth hormone; ICA, internal carotid artery; IGF-1, insulinlike growth factor 1; M, male; MRI, magnetic resonance imaging; TSH, thyrotropin.

with a heterogeneous appearance on T1WI and T2WI sequences. Around 56% of patients showed lesions with extension to the cavernous sinus or encasement of the adjacent carotid artery. In 67% of patients, lesions abutted the sellar floor. Interestingly, no patients presented with an empty sella as is commonly reported in the literature.[1,4,10]

Management

Management of EPAs is similar to their intrasellar counterpart and is dependent on hormone profile, symptoms of mass effect, and patient health. Surgical adenectomy is indicated in patients presenting with acromegaly, Cushing disease, thyrotropinomas, and nonfunctioning macroadenomas with symptoms of mass effect. Medical therapy with dopamine agonists such as bromocriptine or cabergoline is indicated for patients with prolactinomas as first-line therapy.[6,11–13] Patients that are poor surgical candidates or have unresectable tumors can be considered for radiotherapy.[14]

When evaluating patients with suspected EPAs, a careful history and physical examination are critical to assess for endocrinological dysfunction as the large majority of EPAs present with hormone immunoreactivity, particularly

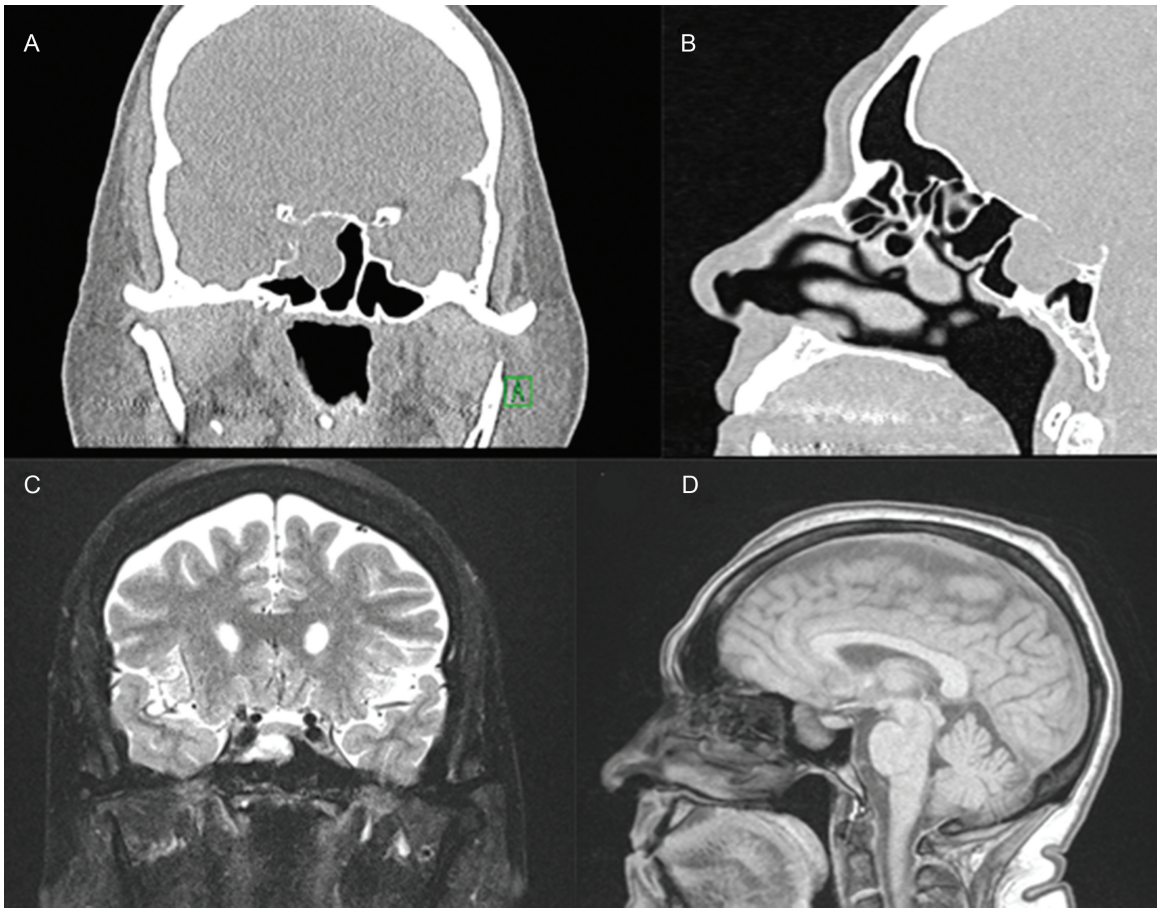

Fig. 1 CT and MRI of patient presenting with isolated sphenoid mass. CT reveals an expansile well-circumscribed soft tissue mass projecting into the right sphenoid sinus with dehiscence of the posterior wall of the sphenoid sinus and thinning of the adjacent right cavernous carotid artery plate (**A, B**). MRI shows a complex lesion of the right sphenoid with low T1, high T2 signal bordering the anterior margin of the sella turcica with a normal appearing pituitary gland (**C, D**). CT, computed tomography; MRI, magnetic resonance imaging.

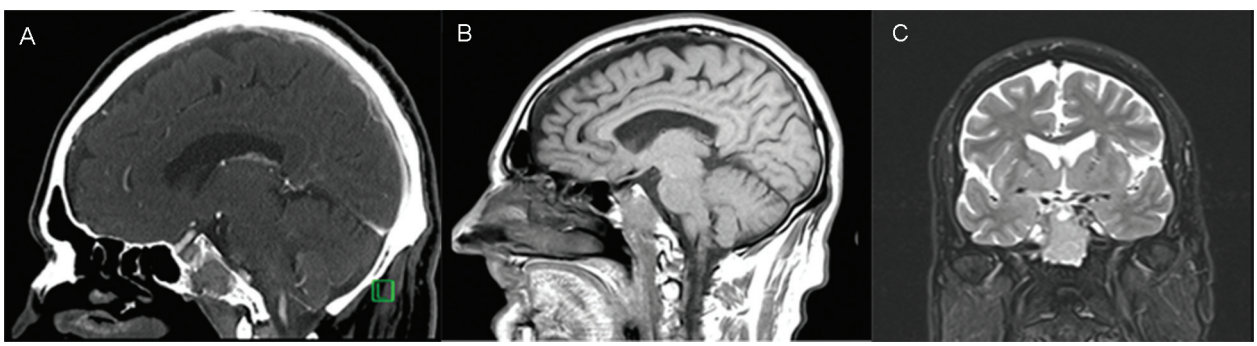

Fig. 2 CT and MRI in one of the patients presenting with a clival lesion. CT demonstrates an erosive lesion centered in the clivus (**A**). MRI reveals a T2 bright lesion of the clivus abutting the sellar floor and intimately involving the right petrous carotid artery (**B, C**). CT, computed tomography; MRI, magnetic resonance imaging.

symptoms of prolactin and ACTH excess. CT and MRI are complementary and should both be attained. CT should be critically assessed for the presence of adjacent bone involvement and MRI should assess for the presence of an enhancing mass with preferential growth pattern toward the cavernous sinus, carotid artery, or sellar floor. An empty sella can provide additional support. Once EPA is suspected, a complete endocrine panel should be completed and managed accordingly with medical therapy or surgery if indicated. Surgical intervention should begin with initial frozen section analysis to narrow the differential.

Conclusion

Here, we report one of the largest multi-institutional series of EPAs of the sphenoid and clivus. Lesions displayed similar CT and MRI findings with an erosive growth pattern toward the sellar floor, cavernous sinus, or adjacent carotid artery.

Patients presenting with similar findings should have a full endocrine panel and alert the physician to consider an EPA in the differential to prevent unnecessary surgery and potential complications.

Note

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