

## Case Report

### Growth Hormone Secreting Ectopic Pituitary Adenoma: Case Report and Literature Review

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#### Abstract

**Background:** Pituitary adenomas are common primary brain tumors that occur in the sella turcica where the pituitary gland resides. However, rare condition where separate hormone secreting ectopic pituitary tissue can be present elsewhere in the brain.

**Case:** A 68-year-old female patient presented to our institution with growth hormone secreting pituitary adenoma. MRI showed normal sellar pituitary gland. A lesion was later identified eroding the sella, sphenoid bone, clivus, and dorsum sellae. Histopathological studies showed growth hormone secreting pituitary tissue.

**Conclusion:** Hormone secreting ectopic pituitary tissue can be present elsewhere in the brain and should be suspected in any patient with abnormally high levels of pituitary hormones with normal sellar MRI images.

#### Introduction

Pituitary Adenomas (PA) represent 10% to 15% of all reported brain tumors, being among the most prevalent intracranial growths [1]. They are seen in 1 out of 865 to 2688 individuals [2].

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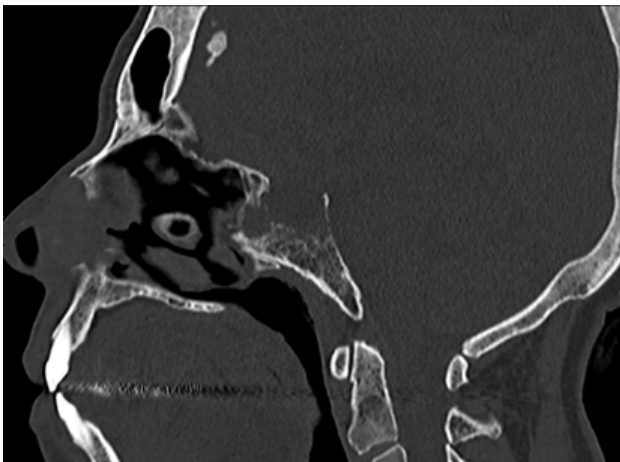
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Embryologically, the pouch of Rathke proliferates to form the anterior pituitary lobe, which, in turn, may abnormally replicate and grow into PA [3]. According to their size, pituitary adenomas fall under two categories. When the tumor size is 10 mm or more, PAs are called macroadenomas and they account for about 50% of all PAs, while the other half are microadenomas [4]. Another classification is based on their glandular function. About 44% of PAs are called functional PAs due to their hormonal secretion ability [5]. Normally, PA are found in the Sella Turcica (ST). A quite rare form of pituitary adenomas with roughly 100 cases documented in the literature are called EPA, or ectopic pituitary adenomas. EPA are not connected in any way to the normal pituitary gland and are always found outside the ST [6]. In previous studies, it has been shown that females are at risk of developing EPA twice as frequently as males [7,8]. A large percentage of EPA are benign, although a minority of cases can develop into malignant tumors [9]. Ectopic pituitary adenomas can produce any type of major pituitary hormones [10]. They can be GH, ACTH, PRL or TSH secreting tumors. Growth hormone secreting ectopic pituitary adenomas are extremely rare. Excessive GH secretion by sellar pituitary adenomas account for 98% of all cases. Less than 2% is secreted by NET and the rest are produced by EPAs [11]. Only 11 cases of GH-secreting ectopic pituitary adenomas have been confirmed by histopathology and reported in the literature so far [12].

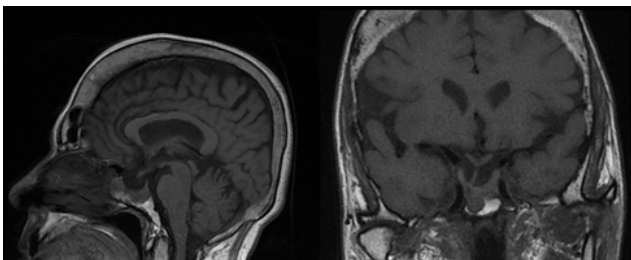
In this article, we report an additional rare case of growth hormone-secreting ectopic pituitary adenoma in the sphenoid sinus with a review of the literature.

#### Case Description

We present the case of a 68-year-old female patient who is known to have paroxysmal atrial fibrillation who presented to our institution with acromegaly symptoms. History goes back to 5 months prior to her presentation when the patient started complaining of fatigue and shortness of breath. Investigations were done which showed paroxysmal atrial fibrillation, hyperthyroidism and cardiomyopathy. MRI brain showed a sphenoid lesion extending to the sellar floor. The patient noticed an increase in shoe size and size of her hand and fingers. On exam, wide MCP joints were apparent. Hormonal profile showed elevated IGF levels. CT sinuses, done as part of pre-op planning, showed soft tissue mass eroding the floor of the sella, sphenoid bone and clivus. There is soft tissue mass in the right aspect of the sella, measuring approximately 1.2cm and the rest of the sella is seen empty (Figure 1). There is soft tissue lesion eroding the floor of the sella, eroding the sphenoid bone, the clivus and dorsum sellae, it is measuring approximately 3.2cm in its AP diameter and 1.4cm in its supero-inferior dimension (Figure 2). Anteriorly there is erosion of the anterior wall of the sella, significant thinning of the left sphenoid sinus. Intra-op, the tumor was apparent in the sphenoid sinus and the arachnoid membrane was bulging into the sinus. A grayish friable lesion was identified. Using ring curette and suction, the lesion was smoothly suctioned and dissected in all directions. Pathology showed growth hormone secreting pituitary adenoma.



**Figure 1:** CT brain bone window showing soft tissue lesion eroding the floor of the sella, eroding the sphenoid bone, the clivus and dorsum sellae, it is measuring approximately 3.2cm in its AP diameter and 1.4cm in its supero-inferior dimension.



**Figure 2:** Soft tissue mass in the right aspect of the sella, measuring approximately 1.2cm and the rest of the sella is seen empty.

Discussion

Only a few previous studies have tackled the origin of ectopic pituitary adenomas. Normally, the main pituitary gland divides into Sellar and pharyngeal sections around the eighth week of pregnancy. A pharyngosellar pituitary is an uncommon pituitary deformity that is caused by the disruption of this division. Many individuals often have a Pharyngeal Pituitary (PhP) as part of their anatomy. However, compared to the Sellar pituitary, PhP produces pituitary hormones around 4 to 10 weeks later. Pharyngeal pituitary can manifest as extracranial pituitary adenomas originating in the nasopharynx, clivus or the sphenoid sinus. These adenomatous pituitary masses may also result from the remaining pituitary tissue fragments in the craniopharyngeal canal that is present in 0.42% of asymptomatic people [13]. Sphenoid sinus is the most common site of EPA. In the past 26 years, ectopic pituitary adenomas of the sphenoid sinus have been reported in 7 out of 15 cases that we have collected for the literature review (Table 1). The finding of a pituitary mass inside the sphenoid sinus does not necessarily indicate the presence of an ectopic pituitary adenoma. It can be explained by a tumor inside the sella eroding the sellar wall and protruding to the sinus with the dura extending downwards [12,14]. Alternatively, a diagnosis of EPA cannot be excluded if there is invasion of the Sella Turcica [15]; although most of the cases reported previously demonstrated an intact sella and dura (Table 1). In our patient, MRI imaging revealed a mass occupying the sphenoid sinus, eroding the clivus and the sellar wall. The mass was not found to be

occupying the sella or protruding inferiorly into the sinus; thus, the diagnosis of ectopic pituitary adenoma was made based on the imaging and intra-op findings where part of the tumor was encountered inside the sphenoid sinus independently of the sellar pituitary. Furthermore, the patient presented to our hospital with signs of acromegaly, therefore, GH-secreting EPA was confirmed by high levels of serum IGF-1 along with the pathology results. Growth hormone secreting ectopic pituitary adenoma in the sphenoid sinus was first written about by Erdheim [16]. Through the review of literature (Table 1), we have identified 6 GH-secreting ectopic pituitary adenomas out of 15 cases reported in the past few years. Ectopic pituitary adenomas can stem from various sites including sphenoid sinus, superior orbital fissure, temporal lobe, third ventricle, and nasal cavity [17].

Literature reviews of EPA by Kepes and Fritzlen in 1964 identified a case of nonfunctional ectopic pituitary adenoma in the sphenoid sinus [18]. In 1975, Ortiz-Suarez and Erickson reported a case of ACTH-secreting EPA in the superior orbital fissure [19]. From 1909 until 1993, ectopic pituitary adenomas were most reported inside the SS [17]. 0.48% of all cases of ectopic pituitary adenomas are seen in the SS of which 25% are necrotic [17]. A case was described by Neilson and de Chadarevian in 1987 shows an ectopic pituitary adenoma in the temporal lobe [20]. Another case was identified in the third ventricle in 1990 by Kleinschmidt [21]. In 2004, a case of EPA was discovered in the cavernous sinus and reported by Mitsuya and Nakasu [22]. Ectopic pituitary adenoma in the sphenoid sinus extended to the nasal cavity through the craniopharyngeal canal was first reported by Kaushik in 2010 [23]. In addition, a case of parapharyngeal space was first documented in 2014 by Xiaofeng Wu using CT brain [10]. Despite highly developed imaging techniques, ectopic pituitary adenomas are still often misdiagnosed or diagnosed after some delay due to their rarity and complexity, therefore, can resemble many tumors of the skull base. However, EPA should always be kept in the differential diagnoses in patients with abnormally elevated levels of one of the major anterior pituitary hormones with an intact Sella turcica on MRI.

Author	Age / Sex	Associated Signs and Symptoms	Type of EPA	Location	Imaging Findings	Management
Li et al. [9]	47/F	Hematuria Epistaxis Headache Dizziness	ACTH-secreting	Sphenoid sinus and clivus	Non-contrast CT: Hypodense mass in the sphenoid sinus and clivus with intact Sella	Surgical removal followed by radiation therapy
Wu et al. [10]	59/F	Gradually enlarging painless lump on the neck No neurological or endocrine symptoms	GH-secreting	Right parapharyngeal space	Contrast-enhanced CT: Heterogenous density mass in the carotid sheath area	Tumor resection from the parapharyngeal space. The mass was totally removed along the vagus nerve inside the carotid sheath

Ramirez et al. [11]	45/F	Menstrual abnormalities Feet and hands enlargement Fatigue Sleep apnea Dental spacing Acanthosis nigricans	GH-secreting	Sphenoid sinus	Gadolinium enhanced T1W: Hypointense mass in the sphenoid sinus with an intact Sellar turcica and dura	Octreotide-LAR 20 mg for 4 months followed by surgical resection Trans-sphenoidal approach
Appel et al. [12]	50/F	Generalized muscle and joints pain Headache Enlargement of face, hands and feet	GH and PRL secreting	clivus	Gd-enhancing T1W: hypointense lesion on the right side of PG	Endoscopic transsphenoidal surgery confirmed a mass inside the clivus with an intact Sellar floor, dura and PG
Mitsuya et al. [22]	55/F	Enlargement of the hands, feet and hands	GH-secreting	Cavernous sinus	Gd-enhanced T1W: Mass surrounding the right ICA in the right cavernous sinus with an intact pituitary gland	Trans-sphenoidal surgery. Bromocriptine Gamma-knife surgery since bromocriptine treatment was unsuccessful
Kaushik et al. [23]	76/M	Right upper extremity weakness	PRL-secreting	Sphenoid sinus	TW1: Hypointense mass in the sphenoid sinus extending to the nasopharynx with intact Sella	Endoscopic transsphenoidal resection
Pojksic et al. [24]	65/F	Headache Nasal stuffiness	ACTH-secreting	Sphenoid sinus	Gadolinium-enhanced T1W: heterogeneously enhancing lesion in the sphenoid sinus with intact Sellar turcica	Trans-sphenoidal resection
Wang et al. [25]	66/M	Double vision Right proptosis	Inactive	Sphenoidal region	Gadolinium-enhanced T1W: Enhancing tumor in the sphenoidal region with intact pituitary gland inside the Sellar Turcica	Frontotemporal craniotomy with total tumor resection
Mudd et al. [26]	78/M	Blurry vision Leftward gaze double vision Headache	Inactive	Clivus	T2W: Lytic lesion inside the clivus with central enhancement. Intact Sellar turcica	Trans nasal endoscopic resection
Ferreira-Filho et al. [27]	30/F	Signs and symptoms of acromegaly	GH-secreting	Clivus and Sphenoid Sinus	T1/T2W: Enhancing mass in both Sphenoid sinus and clivus with an intact pituitary gland in the Sellar Turcica	Only pharmacological (Octreotide) since the patient refused surgery
Erdogan et al. [28]	50/F	Breathing difficulties	TSH and PRL secreting	Nasopharynx	Gd-enhanced T1W: Heterogeneously enhancing mass in the nasopharynx with a normal PG in the ST	Endoscopic surgery through the nasopharynx
Bobeff et al. [29]	64/F	Left-sided hearing loss	GH-secreting	Sphenoid Sinus	Gd-enhanced T1W: Irregularly enhancing lesion in the Sphenoid Sinus protruding to the left Choana	Subtotal resection via transnasal approach

Hata et al. [30]	24/F	Double vision Unable to open her left eye Mydriasis Absence of light reflex Fixed downward and lateral ocular position on the left side No signs of endocrinological abnormalities	ACTH-secreting	Cavernous sinus	TIW: well-enhancing mass in the left CS extending to the adjacent subdural space with intact PG inside the ST	Left orbito-zygomatic approach. Total resection through the Parkinson's triangle.
Horiuchi et al. [31]	75/M	Double vision on the left lateral gaze	ACTH-secreting	Sphenoid sinus	CT: Mass in the posterior wall of the SS with left clivus destruction	Trans-sphenoidal approach. Removal of 80% of the tumor. Sellar floor, dura and PG were intact
Aykel et al. [32]	2/M	Diminution of vision	—	Persistent cranio-pharyngeal canal near the mammillary body	TIW: hyperintense Lesion at the median eminence, anterior to the mammillary body	—

**Table 1:** Ectopic pituitary adenomas of the sphenoid sinus have been reported in 15 cases.

Conclusion

Pituitary adenomas represent 10-15% of all brain tumors and are normally found in the sella turcica. However, the presence of ectopic pituitary gland tissue was reported in other areas of the brain and was found to be a separate entity from the original pituitary gland with hormone secreting capabilities. Ectopic pituitary adenomas are twice more common in females than males with a large percentage being benign adenomas. Therefore, due to the capability of such tumors to be located elsewhere, normal sellar CT or MRI scans in a patient with elevated pituitary hormones should be suspected of having ectopic pituitary adenoma.

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