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Ectopic Intrasphenoidal Growth Hormone Releasing Pituitary Adenoma Associated with an Intracranial Aneurysm

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Abstract

Pituitary adenomas are a type of of the most frequent intracranial tumors. These tumors can extend outside the sella, but very rarely originate ectopically to the sellar region. A 71-year-old patient presented to our institution, with prior clinical history of noncontrolled arterial hypertension and new-onset high-intensity pulsatile headache. Upon suspicion of a hypertensive emergency with probable brain compromise, a nonenhanced computed tomography of the head was performed. A mass within the sphenoid sinus was found. Endocrinological workup demonstrated a significant elevation of the growth hormone. As an incidental finding, a brain aneurysm was evidenced, which was treated endovascularly prior to the mass treatment. Subsequently, the patient successfully underwent a gross total resection through an endonasal transsphenoidal approach. Histopathological results were consistent with a pituitary ectopic adenoma. A postoperative improvement in levels of somatomedin C was documented postoperatively.

Keywords
- adenoma
- pituitary gland
- ectopic
- sphenoid sinus
- acromegaly
- hypophyseal fossa

Introduction

Pituitary adenomas are one of the most prevalent intracranial tumors. Adenomas can extend outside the sella, but very rarely originate ectopically. Likewise, the production of growth hormone (GH) is also atypical in these cases. Only 16 case reports have been presented in the current medical literature to our knowledge. The following is a case of an ectopic Intrasphenoidal GH Releasing Pituitary Adenoma Associated with an Intracranial Aneurysm.

Case History

A 71-year-old female presented with a pulsatile high-intensity left hemicranial headache and blurred vision. Previous clinical antecedents included arterial hypertension as well as a noninsulin-dependent diabetes mellitus treated with metformin. On the admission, physical examination presented a blood pressure of 184/106 mm Hg. Additional findings included a thick voice, pronounced mandibular angles, as well as large nose and fingers. Neurological examination was

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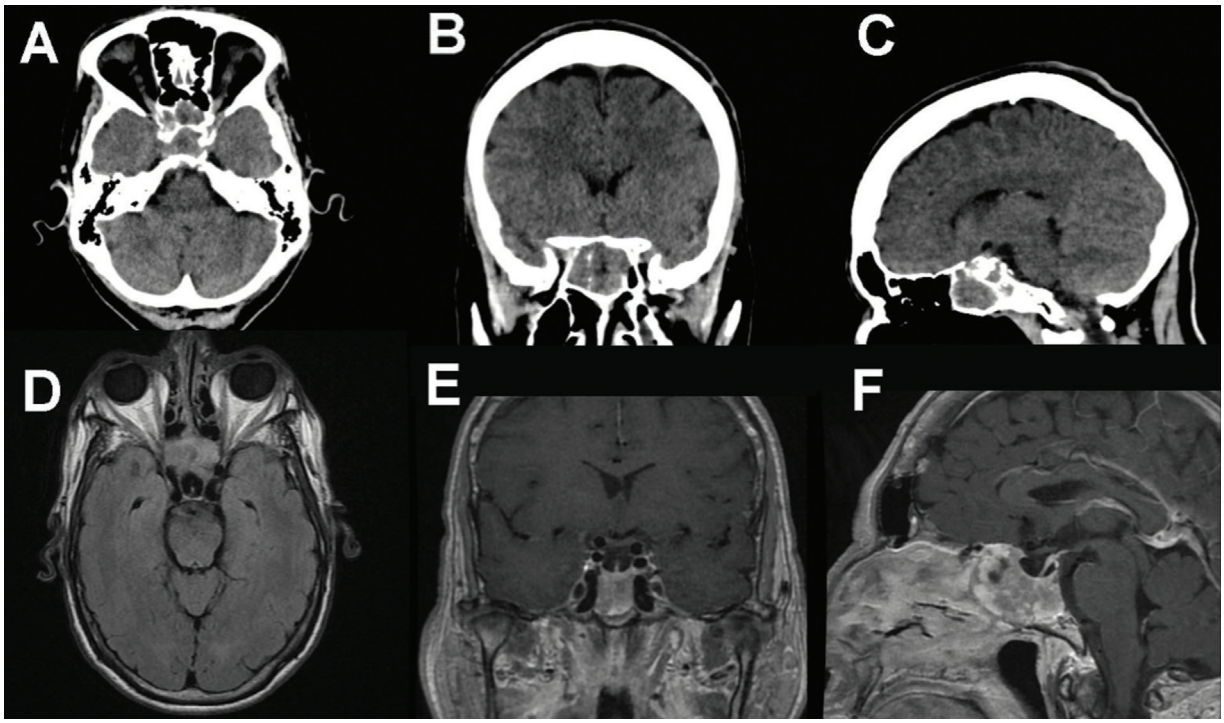

Fig. 1 (**A**–**C**) Computed tomography in axial, coronal, and sagittal cut, respectively, showing lesion with soft tissue density occupying the sphenoid sinus, with remodeling of the bone walls and partial erosion of the floor of the Turkish sella. There is no apparent intracranial extension. (**D**–**F**) Magnetic resonance contrasted in spin echo, fluid-attenuated inversion recovery, and T1, respectively, that evidences solid mass, neoplastic appearance, with few cystic changes, highly cellular and vascularized, with epicenter in the body of the sphenoid. There is no compression of the chiasm.

unremarkable. A nonenhanced head computed tomography (CT) scan of the head was performed showing a $4 \times 3 \times 3.3$ cm solid lesion with epicenter in the sphenoid sinus that remodeled its bony contours. No invasion to the sella or an extension to the intracranial compartment was observed. A complementary enhanced magnetic resonance imaging (MRI) showed discrete enhancement after gadolinium administration (►**Fig. 1**). The endocrinological workup demonstrated elevated insulin-like growth factor-1 (IGF-1) (426 ng/mL) and GH (5.6 ng/mL) levels, which were consistent with the diagnosis of acromegaly. The rest of the hormonal profile was within normal ranges. As part of the surgical planning, a CT angiography was performed, with an incidental finding of a saccular aneurysm of the anterior communicating artery, which was embolized preoperatively (►**Fig. 2**).

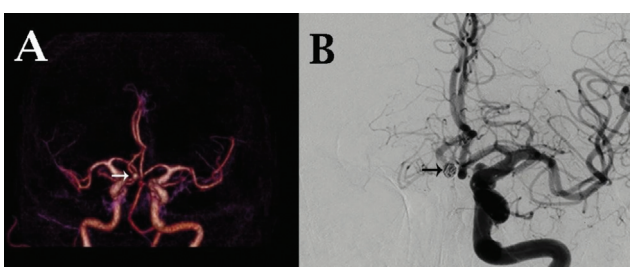

Fig. 2 Three-dimensional angio-computed tomography image and three-dimensional reconstruction that evidences aneurysmal disease at the level of AComA. (**A**, *left*) Aneurysm in anterior communicating segment (*arrow*). (**B**, *right*) Postoperative embolization with AComA aneurysm coils (*arrow*).

The patient underwent a transsphenoidal endoscopic resection of the tumor. Intraoperatively, the tumor was adhered to the cavernous sinus bilaterally, as well as to the dorsum sellae, with the evidence of scarce tumor adjacent to it, but not infiltrating the pituitary gland. A near-total resection (> 90%) was achieved. Usual fashion closure was performed, aided with a nasoseptal flap (►**Fig. 3**).

The immunohistochemistry demonstrated generalized positivity for GH and prolactin; these findings were consistent with a mamo somatotropic pituitary adenoma. (►**Fig. 4**).

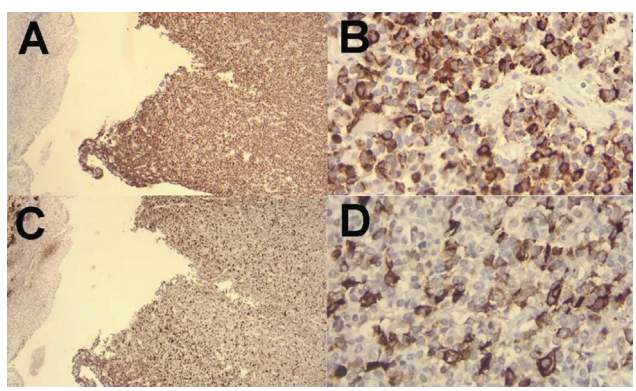

Fig. 3 Pituitary adenoma, volume of 9 cc. On the left, magnification is 10× and on the right is 40 × . (**A** and **B**) Immunohistochemical staining for growth hormone with generalized positivity. (**C** and **D**) Immunohistochemical stain for prolactin hormone with generalized positivity.

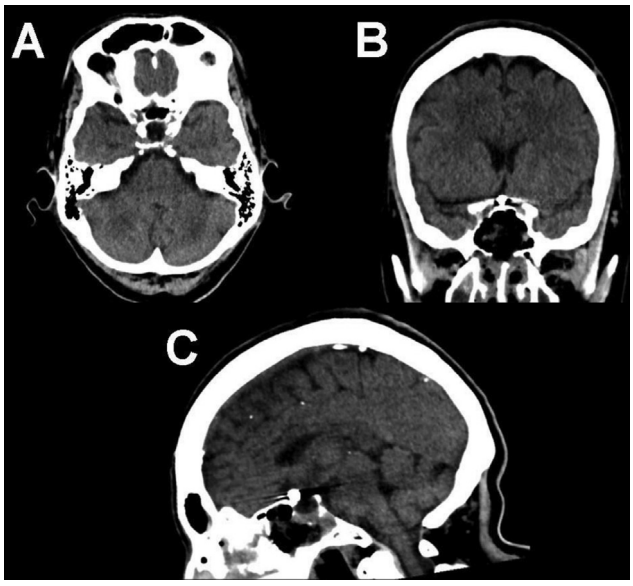

Fig. 4 (**A**–**C**) Postoperative computed tomography in axial, coronal, and sagittal cuts, respectively, where a resection of at least 90% of the lesion is evident. No areas of active bleeding.

A normalization of blood pressure and levels of IGF-1 (8.15 ng/mL) were observed postoperatively.

Discussion

Ectopic Pituitary Adenomas

Pituitary tumors correspond to 10 to 20% of intracranial tumors[1–3] EPAs are considered as very rare neoplasms. The most accepted theory about their origin suggests that they come from the migration path of the Rathke's pouch or craniopharyngeus duct, which is part of the ectoderm of the stomodeum. During this migration process, some aberrant pituitary cells of the future adenohypophysis will remain somewhere in this path giving rise to ectopic pituitary adenomas (EPAs).[3] EPAs are an extremely rare pathology. Until 2003, only 50 cases had been reported in the literature, mostly aged females.[4–6]

Diagnostic Challenges

In regard to location, most are usually found in the sphenoid sinus, followed by a suprasellar localization, clivus, and occasionally within the cavernous sinus.[7]

Classic symptoms are usually headache and constant nasal obstruction. Visual involvement is rare.[1–8] Endocrinologically, two thirds exhibit hormonal activity. Adrenocorticotropic hormone is the most commonly secreted (36%) hormone, followed by prolactin (28%), GH (22%), and less frequently thyroid-stimulating hormone (16%)[7] in our case the endocrinological workup demonstrated elevated IGF-1 (426 ng/mL). According to the consensus published in 2014 by the Endocrine Society, the acromegaly diagnosis should be made based on IGF-1 levels, and GH levels should not be used. Post-glucose load GH levels is recommended only in scenarios with inconclusive IGF-1 levels.[9,10] On the other hand, the imaging study is mandatory in all patients with suspected diagnosis of acromegaly, since GH-producing adenomas are the most frequent etiology of this pathology. The ideal study is the enhanced-MRI of the sella.[10,11]

Treatment

In terms of treatment, after the diagnosis of acromegaly is confirmed, the primary goal of treatment is the normalization of GH and IGF-1 levels, as well as reduction in the volume of the lesion, since these two factors are correlated with worse clinical outcomes in terms of impaired glucose metabolism and comorbidities such as diabetes mellitus, coronary heart disease, sleep apnea, cardiovascular disease, and arterial hypertension. In the case of our patient, adequate control of hypertension was achieved only after surgical resection of the tumor.

Surgical management has been considered the gold standard for the management of acromegaly, obtaining hormonal control rates approximately 65%, when a gross total resection is attempted endonasally. However, when a complete resection is not achieved due to a vascular invasion, debulking with partial volumetric resection has been shown to aid in decreasing hormone levels with complementary treatment with administration of a somatostatin receptor ligands (SRLs). Therefore, medical management is only indicated in cases of noncontrol of IGF-1/GH serum levels after surgical treatment. The use of ligands of the first-generation SRLs such as octreotide is recommended, obtaining success rates up to 55% after surgical management.[9,10]

In our review, less than 100 cases of EPAs have been published worldwide,[7–12] of which only 15 presented with GH-producing adenomas[6,13–25] (►**Table 1**), none with concomitant aneurysmal disease, as the case presented above. However, it has been observed that aneurysms can coexist with non-EPAs in up to 7% of cases. It is also known that patients with acromegaly have 4.4 times the risk of developing cerebral aneurism and, most frequently, they are located in the anterior communicating artery, representing a challenge when defining which pathology to treat first and the time of intervention. Some theories suggest that hypertension, added to endothelial remodeling and alteration in collagen genesis along with elevated levels matrix metalloproteinases and endothelial growth factor could explain the increase in the prevalence of aneurysm in this population.[26–30]

In our case, treatment of the AComA versus observation was chosen in consideration of high risk of rupture in the next 5 years due to a PHASES score of 9 points (4.3% bleeding at 5 years). The decision for clipping vs coiling was selected based on the risk of intraoperatively rupture due to sudden decrease in intracranial pressure and surgical limitation of management of a rupture complication by a transsphenoidal approach. Coiling technique was chosen because of a dome/neck ratio or greater than 2, an neck of the aneurism less than de 7 mm, which makes it technically

Table 1 Cases reported in the literature of producing ectopic adenomas as of November 1, 2021

Author	Biochemical diagnosis	Ectopic localization	Dura	Turkish sella base	IHC
Ramírezet al 2013[6]	GH 7.7 ng/mL	Sphenoid sinus	Intact	Intact	GH ++
	IGF-1 4.8 × ULN				PRL +
	PRL 12.7 ng/mL				
Corenblum et al 1980[13]	GH 46.8 ng/mL	Sphenoid sinus	Intact	Intact	GH ++
	PRL 5 ng/mL				
Warner et al 1982[14]	–	Sphenoid sinus	Intact	Erosion	GH ++
					PRL +
Madonna et al 2001[15]	–	Sphenoid sinus	Intact	Erosion	GH ++
					TSH +
Matsuno et al 2001[16]	GH 97 ng/mL	Sphenoid sinus	Intact	Absent	GH ++
	IGF-1 2.3 × ULN				PRL +
	PRL 140 ng/mL				α - SU +
Hori et al 2002[17]	GH 14.5 ng/mL	Sphenoid sinus	Defect	Absent	GH ++
	PRL 26.3 ng/mL				
Mitsuya et al 2004[18]	GH 133 ng/mL	Sphenoid sinus	Intact	Intact	GH ++
	PRL 73 ng/mL				PRL +
Gondim et al 2004[19]	GH 97 ng/mL	Sphenoid sinus	Intact	Absent	GH ++
	IGF-1 2.7 × ULN				
	PRL 17 ng/mL				
Chan et al 2005[20]	–	Sphenoid sinus	Intact	Intact	–
Bhatoe et al 2007[21]	GH 36 ng/mL	Clivus	Defect	Erosion	GH ++
					PRL +
					LH +
					FSH +
Guerrero et al 2007[22]	GH 12.3 ng/mL	Sphenoid sinus	Intact	Intact	GH ++
	IGF-1 1.9 × ULN				PRL +
	PRL 40.2 ng/mL				
Kurowska et al 2008[23]	GH 4.3 ng/mL	Sphenoid sinus	–	–	GH ++
	IGF-1 2.5 × ULN				
Appel et al 2012[24]	GH 6 ng/mL	Clivus	Intact	Intact	GH ++
	IGF-1 3.1 × ULN				PRL +
	PRL 26 ng/mL				
Hong et al 2012[25]	GH 18 ng/mL	Sphenoid sinus	Intact	Partially absent	GH ++
	IGF-1 3.6 × ULB				
Current case, 2021	IGF-1 426 ng/mL	Sphenoid sinus	Intact	Erosion	GH ++
	PRL 6.8 ng/mL				PRL +
					TSH +

Abbreviations: α-SU, α-subunit of glycoprotein hormones; FSH, follicle-stimulating hormone; GH, growth hormone; IGF-1, growth factor type 1; IHC, immunohistochemistry; LH, luteinizing hormone; PRL, prolactin; TSH, thyroid-stimulating hormone.

possible. Furthermore in the context of a patient who was aimed to be reoperated in less than 7 days, the need of antiplatelet therapy in flow diverters, was no ideal. The coiling conduct was reinforced by good results of ISAT trial, even knowing that this study only includes ruptured aneurisms.[31,32] A favorable outcome for both lesions was achieved with adequate hormonal control. No complications were observed.

Conclusion

We present the case of a patient with imaging, clinical picture, paraclinical and histopathological diagnosis compatible with a mamo somatotropic EPA, with an additional incidental finding of intracranial aneurysmal disease. No other cases like this had been presented in the literature available due to the coexistence of aneurysmal disease. This case represents valuable information for the analysis of this type of tumors, providing a high scientific and educational value for its approach and treatment.

In this case, multidisciplinary management—endovascular, neurosurgical, and endocrinological—was the key to success. That is why according to clinical practice guidelines, we consider that this type of pathology should be treated in centers of excellence of pituitary tumors.

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Conflict of Interest
None declared.

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