

## CASE REPORT

# Nonfunctioning Ectopic Pituitary Adenoma Presenting as Epistaxis: A Report of Two Cases

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## ABSTRACT

Ectopic pituitary adenomas are uncommon lesions and are found along the migratory pathway of the Rathke's pouch. Sites reported include suprasellar region, clivus, sphenoid sinus, nasopharynx, third ventricle, petrous temporal bone, hypothalamus, etc. Compared to intrasellar adenomas, a higher proportion of the ectopic examples are functional and most commonly produce adenocorticotrophic hormone (ACTH). The authors report two cases of ectopic pituitary adenoma in the sphenoid sinus in two male patients 36 and 40 years old, presenting with epistaxis. Both the patients did not have any endocrine abnormalities. The clinical and imaging findings were suggestive of sinonasal malignancy. The final diagnosis was made after histopathological examination and immunohistochemistry for cytokeratin, chromogranin and pituitary hormones. The diagnosis of ectopic pituitary adenomas is difficult especially in those tumors that are nonfunctioning. After extensive literature search, we could find only six cases of nonfunctioning adenomas reported in the sphenoid sinus and in all these cases the correct diagnosis could be made only by histopathology.

**Keywords:** Adenocorticotrophic hormone adenoma, Cytokeratin, Ectopic pituitary, Paraganglioma, Sphenoid sinus.

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## INTRODUCTION

Pituitary adenomas are common tumors in the sellar region. But a location outside this region is a rare occurrence. Ectopic pituitary adenomas have been described in

the suprasellar region, sphenoid sinus, petrous temporal bone, clivus, hypothalamus, parapharyngeal area parasellar region and third ventricle.<sup>1</sup> Many of these tumors were hormone secreting and a preoperative diagnosis of pituitary adenoma could be made. We present two cases, one in a 36-year-old man and the other in a 40-year-old man, with epistaxis as the presenting symptom. Imaging revealed lesion in the sphenoid sinus and clinical impression was that of a sinonasal malignancy. The correct diagnosis of ectopic pituitary adenoma could be made only by histopathological examination and immunohistochemistry.

## CASE REPORTS

### Case 1

A 40-year-old male presented with history of two episodes of epistaxis. He had headache for 5 months. Visual field and acuity were normal. Neurological examination was within normal limits. Ear, nose and throat examination revealed a pinkish to black colored mass along the middle turbinate in the left nasal cavity and enlarged middle turbinate in the right nasal cavity. Posterior rhinoscopy showed a pinkish mass in the right choana. Direct nasal endoscopy showed a mass coming out of the right sphenoidal recess. Sphenoid sinus ostium was widened with erosion of floor of sella. The mass was filling the right sphenoid sinus. There was a similar mass in the left sphenoidal recess. Hematological and biochemical investigations were within normal limits.

Cranial computed tomography (CT) scan revealed an isodense lesion in the sphenoid sinus with erosion of sellar floor. MR imaging showed a 3.8 × 3.6 × 2.4 cm T1 isointense, T2 and Flair slightly hyperintense lesion involving whole of the sphenoid sinus roof with extension into sella and parasellar region (Fig. 1A), anteroinferiorly the lesion extended to posterior ethmoidal cells, left choana and nasopharynx. The lesion showed moderate homogenous contrast enhancement (Fig. 1B). Clinical impression was that of a sinonasal malignancy. Since, the pituitary gland was seen separately (Figs 1C and D), there was no suspicion of a pituitary adenoma. A biopsy of the lesion was done. Histopathological examination revealed a cellular neoplasm composed of cells arranged in nests

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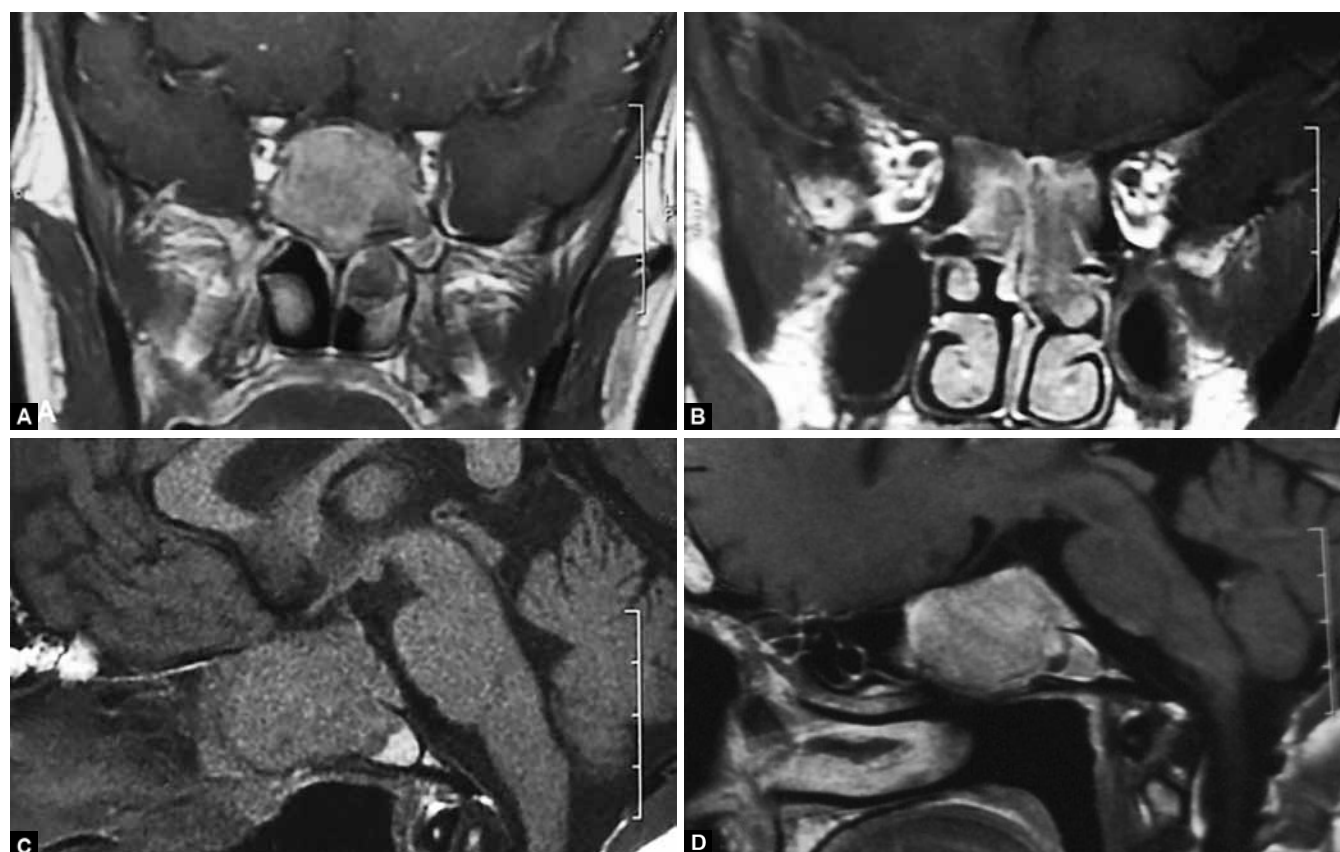
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**Figs 1A to D:** Case 1—Cranial MR images: (A) Coronal T1-W images showing an isointense lesion involving the sphenoid sinus reaching upto the sellar floor, (B) moderate contrast enhancement of the lesion and (C and D) the lesion is seen separately from the pituitary gland

separated by fibrovascular septae (Figs 2A and B). The cells were polygonal with moderate amount of eosinophilic cytoplasm and round to oval vesicular nuclei with fine powdery chromatin (Fig. 2C). There was no pleomorphism or increased mitotic activity. A provisional diagnosis of pituitary adenoma was made.

Endoscopic transnasal transsphenoidal surgery was performed. Peroperatively there was a large polypoid mass in the sphenoid sinus with erosion of sellar floor. The sellar floor was removed and the dura was found to be intact. On opening the dura, there was no evidence of intradural tumor and the pituitary gland appeared normal.

Histopathological examination showed a picture similar to the previous biopsy. With a differential diagnosis of paraganglioma immunohistochemistry was performed for confirmation of the diagnosis. The cells were positive for cytokeratin (Fig. 2D) and chromogranin (Fig. 2E). Tests with the entire panel of pituitary antibodies consisting were also performed. The cells expressed adenocorticotrophic hormone (ACTH) confirming the pituitary origin of the tumor (Fig. 2F). So the final diagnosis was an ACTH expressing ectopic pituitary adenoma of the sphenoid sinus. The patient is well at a follow-up of one and a half years.

## Case 2

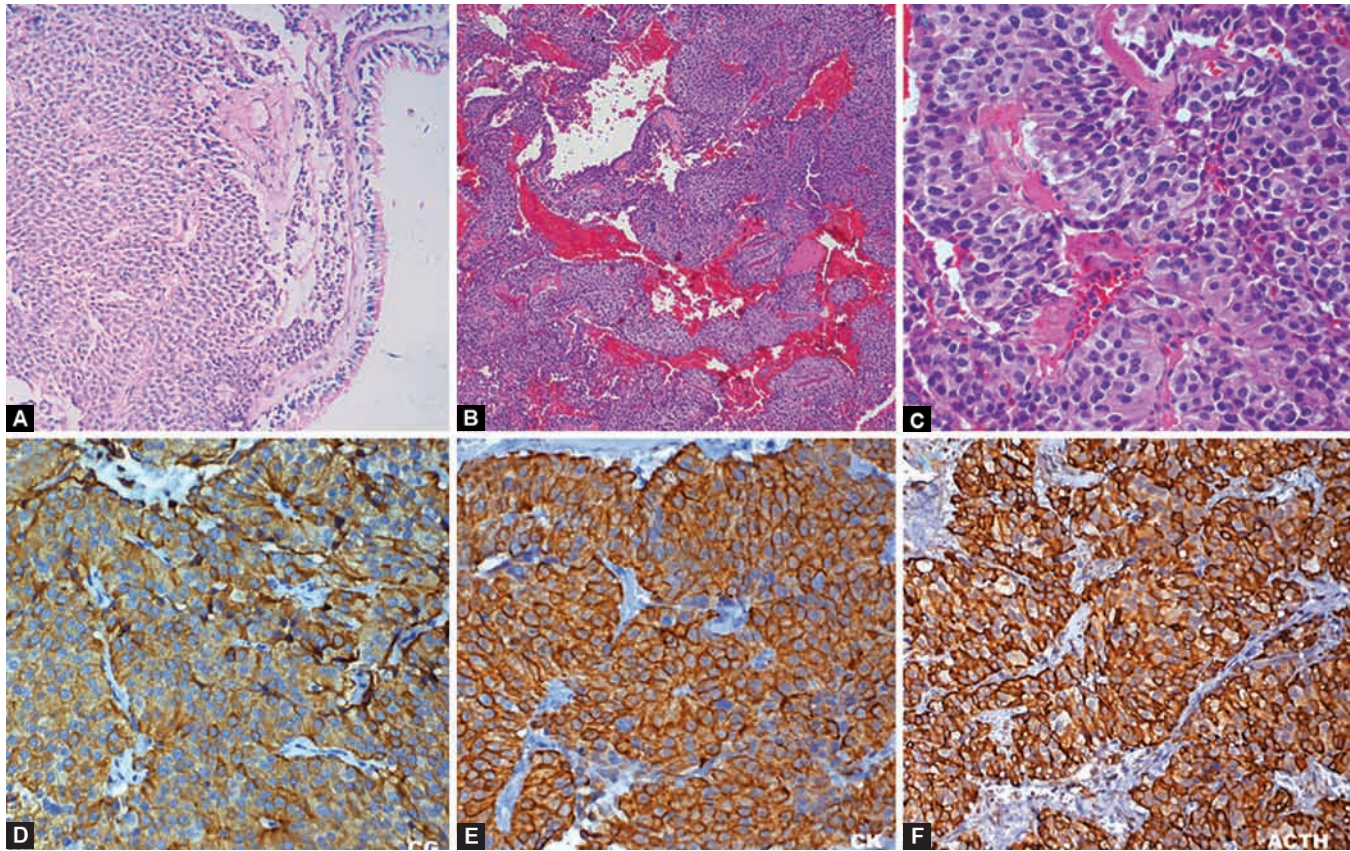
A 36-year-old man presented with complaints of two episodes of epistaxis with associated headache and vomiting. There was no history of nasal obstruction or hormonal disturbances. On examination, there was a mild proptosis of the left eye. A mass was seen posteriorly in the left nasal cavity. Hormonal evaluation was within normal limits.

Cranial magnetic resonance imaging showed a soft tissue density mass lesion seen occupying the sphenoid sinus with sellar floor erosion and extension into sella (Figs 3A and B). There was also extension into left ethmoid sinus, left nasal cavity, left choana and medially into the left orbital apex. With a clinical diagnosis of sinonasal malignancy a biopsy was taken.

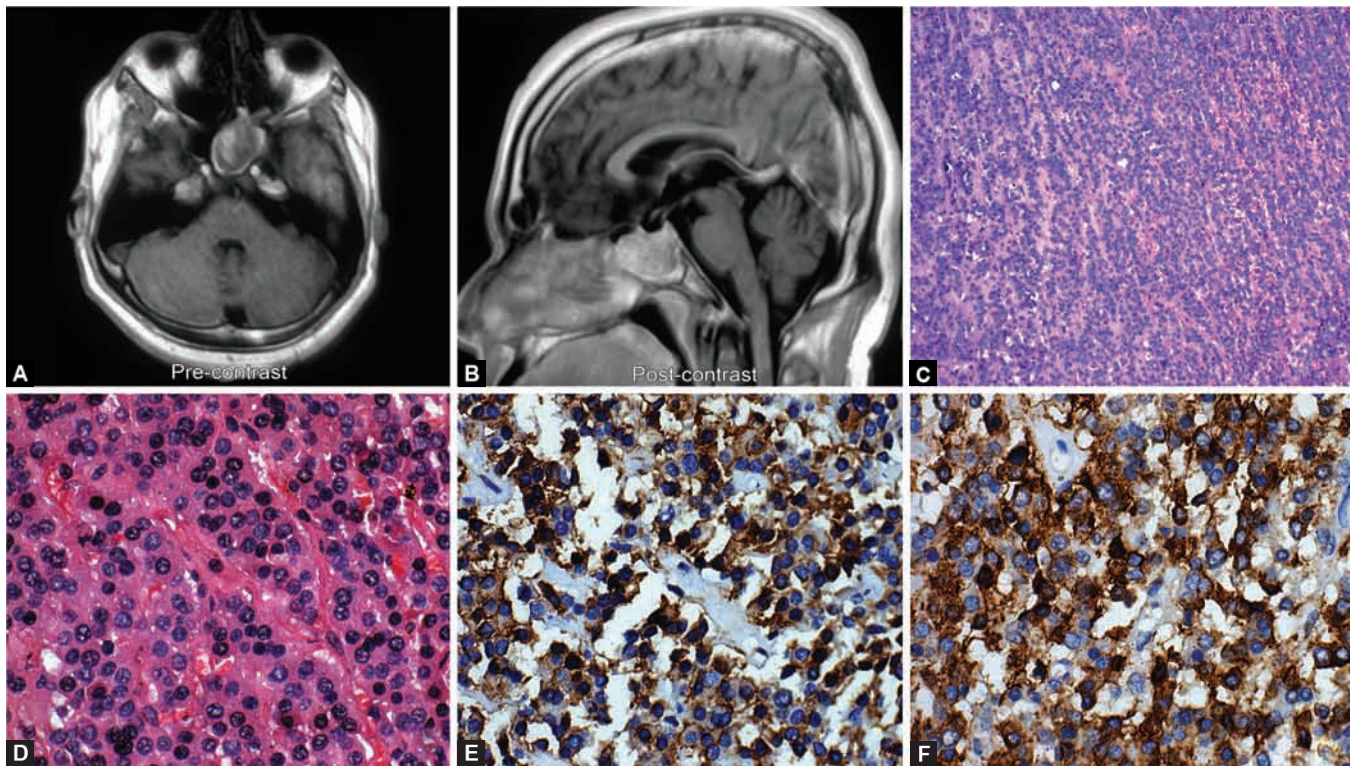
Histopathological examination revealed a pituitary adenoma with similar findings to the previous case (Figs 3C and D). Immunohistochemically, the cells were positive for chromogranin (Fig. 3E) and prolactin (Fig. 3F). So, the final diagnosis was an ectopic pituitary adenoma of the sphenoid sinus expressing prolactin.

## Review of Literature with Discussion

Ectopic pituitary adenomas are those which are located outside the sella turcica without any continuity with the



**Figs 2A to F:** Case 1—Histopathology: (A) Tumor beneath the sphenoid sinus mucosa (100x), (B) low-power view showing a highly vascular tumor with cells arranged in nests (100x), (C) high-power view showing nests of polygonal tumor cells with eosinophilic cytoplasm and powdery chromatin separated by fibrovascular septae (200x), (D) cytokeratin positivity in tumor cells (200x), (E) chromogranin positive tumor cells (200x) and (F) strong ACTH positivity in the tumor cells (200x)



**Figs 3A to F:** Case 2—A and B: Cranial MR images: (A) Tumor filling the sphenoid sinus, (B) contrast enhancing tumor is seen separate from the pituitary, (C and D) microscopy of the tumor showing the arrangement of cells in sheets and nests separated by fibrovascular septae (C—HE: 100x, D—HE: 400x), (E) tumor cells showing immunohistochemical positivity for chromogranin (400x) and (F) strong positivity for prolactin in the tumor cells (400x)

intraseptal normal pituitary tissue. The entity was first described by Erdheim in 1909. Common locations include: suprasellar region, sphenoid sinus, nasopharynx, clivus and parasellar region.<sup>1</sup> There are many postulations as to the origin of these tumors. They may be derived from residual cells of the Rathke's pouch persisting along the migratory pathway in the nasopharynx or sphenoid sinus or from the cells of the supradiaphragmatic portion of the pars tuberalis in the suprasellar region or from aberrant migrating cells of the craniopharyngeal duct in the third ventricle.<sup>2</sup> The continuity between the tumor and the normal pituitary should be evaluated by imaging and preoperatively to confirm origin from ectopic pituitary tissue. Radiologically, they may mimic other skull base lesions like nasopharyngeal carcinoma, chordoma or metastasis. The intraseptal pituitary gland tends to be normal or it may be associated with the empty sella syndrome. Preoperative diagnosis of ectopic pituitary adenomas of the skull base is difficult, because imaging suggests other neoplasms as in the present case. The diagnosis may not be difficult even with a normal sellar gland at imaging if the tumor is functioning. Two-thirds of the ectopic tumors are hormonally active and one-third is inactive. Most of the functioning tumors produce ACTH.<sup>3</sup> Sellar pituitary adenomas can present with epistaxis if there is apoplexy in a giant adenoma extending into the nasopharynx. Other cases in which epistaxis has been reported include an aggressive TSH adenoma and a large prolactinoma with an intratumoral aneurysm.<sup>4</sup> Twenty-five cases of ectopic pituitary adenomas involving the sphenoid sinus have been reported.<sup>5,6</sup> Most of these were functioning and the majority produced ACTH. Others were growth hormone or prolactin secreting. Only six nonfunctioning tumors have been reported in the literature.<sup>3,5,7-10</sup> In a review of 16 sphenoid sinus ectopic pituitary adenomas by T Horiuchi et al, 12 were functioning and five out of these were ACTH producing and four were prolactin producing.<sup>9</sup> In the present cases, the tumors were nonfunctioning and so pituitary adenoma was not considered in the differential diagnosis. The diagnosis of an endocrine tumor could be made only by histopathological examination. At microscopic examination, a close differential diagnosis was a paraganglioma which is again a tumor that is rare in the

sphenoid sinus. The pituitary origin of the tumor could be confirmed only by immunohistochemistry which showed expression of chromogranin, cytokeratin and ACTH. Paragangliomas are positive for chromogranin but negative for cytokeratin. Treatment of choice for ectopic pituitary adenomas is surgical excision. Radiotherapy is done when the resection is incomplete. This case illustrates the importance of histopathological examination with immunohistochemistry in the diagnosis of nonfunctioning ectopic pituitary adenomas and the need to consider ectopic pituitary adenomas in the differential diagnosis of sphenoid sinus lesions with sellar floor erosion and presenting with epistaxis.

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