

Sphenoidal Ectopic ACTH-secreting Pituitary Adenoma

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ABSTRACT

Ectopic pituitary adenoma occurs outside the sella without any continuity with the normal pituitary gland. We present a case of sphenoidal ectopic pituitary adenoma presenting as Cushing's syndrome. Imaging studies revealed a normal, compressed pituitary gland, a partial empty sella, and a sphenoidal mass initially suspected to be a

mucocele. At surgery, sellar floor was intact and adenomatous lesion was completely resected from the sphenoid sinus. Biochemical remission was achieved post-operatively. Histopathology revealed pituitary adenoma cells in the center of a mucocele sac. A detailed review of the literature is included.

Key words: Ectopic pituitary adenoma, Sphenoidal ectopic pituitary adenoma, ACTH secreting ectopic pituitary, Empty sella

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INTRODUCTION

Ectopic pituitary adenoma is defined as adenoma that occurs outside the sella without any continuity with the normal pituitary gland [1]. Since its description for the first time in 1909 by Erdheim in the vomero-sphenoidal region, about 75 cases have been reported in literature [2-12]. Sphenoid sinus followed by the suprasellar region remains the most common site for these adenomas[6]. Prior to our case report, literature review identified only 5 cases of sphenoidal ACTH secreting adenomas with a partial or complete empty sella [6, 13, 14]. Here, we present a case of sphenoidal ectopic pituitary adenoma presenting as Cushing's syndrome in association with a partial empty sella.

CASE REPORT

A 16-year old female presented to our endocrinology department with 4-year history of unexplained weight gain of approximately 15 kg as the primary complaint. On further questioning she gave a history of irregular menstrual cycles for the past 3 years, episodes of facial flushing and two episodes of poor wound healing. She also complained of intermittent, mild degree, non-specific headaches lasting 1-2 hours. She was diagnosed with diabetes mellitus 2 years prior to presentation and was started on oral hypoglycemics, with which her sugars were

partially controlled. On examination, she had moon-like face, hirsutism, and abdominal obesity. She weighed 70 kilograms. Systemic examination and nervous system examination were unremarkable. With the above features, a clinical diagnosis of hypercortisolic state (Cushing's syndrome) was made and further tests were directed towards confirming it and finding the possible source of cortisol hypersecretion. Her serum cortisol estimations at 8 am, 8 pm and 12 midnight revealed values of >50 µg/dl, 20.4 µg/dl and 21.4 µg/dl respectively, all elevated beyond the normal range. A low dose dexamethasone suppression (Liddle1) test showed serum cortisol to be 12 µg/dl two hours after the last dose of 0.5 mg of dexamethasone. A late evening (4 pm) plasma ACTH level was >10 pg/ml (elevated). Further, an 8 mg Dexamethasone suppression test (administering 8 mg of dexamethasone at 11 pm and estimating serum cortisol at 8 am the next day) revealed a value of 6.2 µg/dl (suppressed by >50%, thus signifying a positive test). The above results confirmed hypercortisolic state, showed that it was ACTH dependent and suggested pituitary to be the source. As indicated, she was investigated with an MRI of brain (Fig. 1 & 2), which showed the sella to be normal in size and shape, a partial empty sella with the pituitary gland being displaced posteriorly within the sella and no

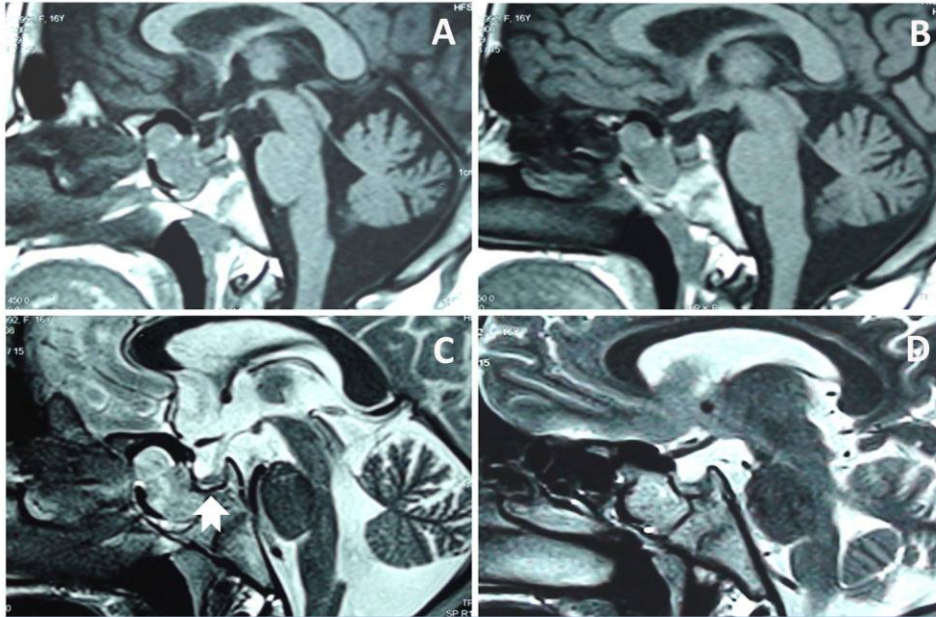


Figure 1: Sagittal T1W (A & B) and T2W (C & D) showing a normal sized sella, with partial prolapse of arachnoid and a compressed, posteriorly displaced pituitary gland (white arrow in C). A well-defined lesion in the sphenoid sinus could also be made out. Sellar floor appears to be intact.

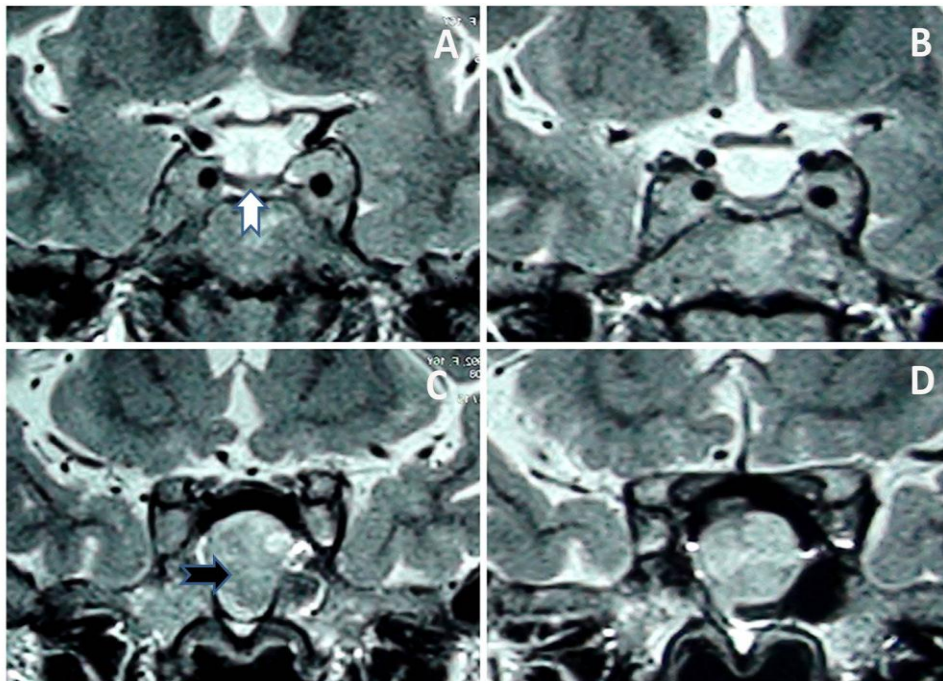


Figure 2: Coronal T2W images showing prolapse of arachnoid into the sella (B), a normal looking pituitary gland and pituitary stalk (white arrow in A) with a sphenoidal lesion (black arrow in C & D)

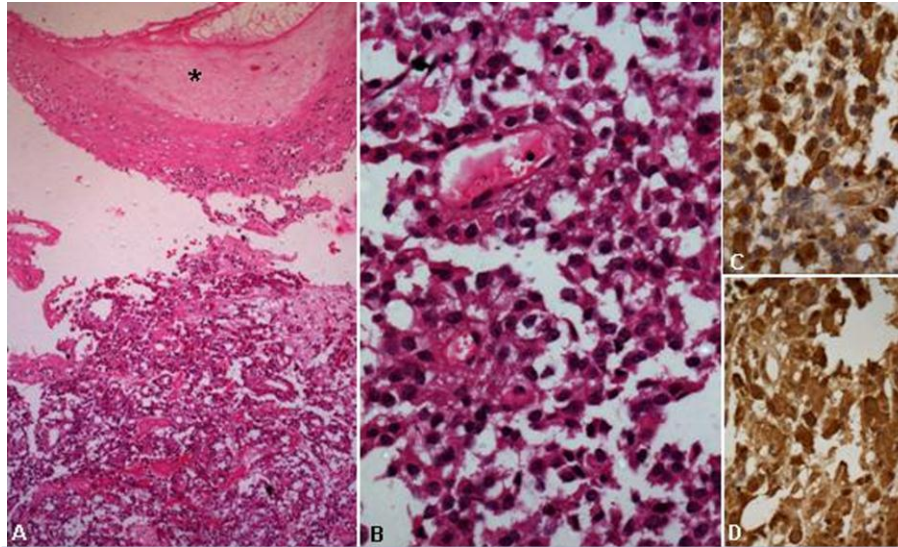


Figure 3: Low magnification view shows circumscribed highly vascular tumor in submucosal region (A). Note overlying mucosal lining of sinus with mucinous fluid beneath (asterix, A). The tumor cells are composed of cells with acidophilic cytoplasm in perivascular papillary arrangement (B). Tumor cells are seen expressing cytokeratin (C) and ACTH (D).

[A:H&ExObj.5, B:H&ExObj.20, C,D:ImmunoperoxidasexObj.40]

evidence of any pituitary micro/macro-adenoma. In addition there was a well-defined lesion in the sphenoid sinus, distinct from the sella and separated from it by an intact sellar floor. This lesion was isointense on T1W, and heterogeneously hyperintense on T2W with patchy contrast enhancement. A provisional diagnosis of partial empty sella syndrome with a sphenoidal mucocele was made. Here, we had a case of hypercortisolemia confirmed to be from a pituitary source. However her imaging revealed a normal sella and pituitary. She therefore needed an Inferior Petrosal Venous Sinus Sampling (IPSS) for further evaluation¹⁵. On IPSS, her ACTH values were as follows: IVC (Inferior vena cava) – 7.4 pg/ml; Left IJV (internal jugular vein) – 24 pg/ml; Right IJV – 12 pg/ml; Left IPS (inferior petrosal sinus) – 45 pg/ml; Right IPS – 5 pg/ml. These values confirmed pituitary to be the source of elevated ACTH levels, although the sella was normal on imaging, she was planned for a transsphenoidal exploration of the sella with the hope to identify a microadenoma not picked up on MRI, and to remove the (presumed) sphenoidal mucocele en route. She underwent an endonasal endoscopic transsphenoidal surgery. Intra-operatively, there was an intra-sphenoidal, well encapsulated grey-red, soft, suckable, vascular lesion (akin to a pituitary tumor) with mucosal attachment. The sphenoidal mass was

completely excised. The lateral wall of sphenoid sinus and more importantly, the sellar floor was intact. With the sphenoidal lesion now ruled out to be just a mucocele, possibility of an ectopic pituitary tumor was considered at this point and sella was not entered. Post-operatively, she recovered well. Cortisol replacement was given post-operatively, and a post-op cortisol estimation done on the 10th post-op day after withdrawal of cortisol replacement therapy for 48 hrs, revealed a value of 4 µg/dl (normal range; biochemical cure). Histological examination of resected tissue revealed mucocele lined by sinus mucosal lining with underlying mucinous fluid, with circumscribed tumor in submucosal region (Fig. 3A). The tumor was composed of neoplastic cells with deeply eosinophilic cytoplasm and vesicular nuclei arranged in papillary pattern around thin walled vessels (Fig. 3B), and nests in a highly vascular stroma. The tumor cells expressed cytokeratin (Fig. 3C) and ACTH hormone (Fig. 3D) confirming origin from adenohypophyseal cells. The patient is on a regular follow-up with biochemical remission at 3 months follow-up.

DISCUSSION

Ectopic pituitary adenomas are rare with about

75 cases reported in the literature thus far [2-4]. Among these, the most common site of an ectopic pituitary adenoma has been the sphenoid sinus (37% of all ectopic pituitary adenomas, fewer than 40 reported cases) followed by the suprasellar region (28% of all ectopic pituitary adenomas, fewer than 30 reported cases). Other sites include the clivus (7.7%), the nasal cavity (6.2%), the cavernous sinus (6.2%), the parasellar region (6.2%), and the sphenoid wing (3.1%) [2, 3, 14, 16]. Single cases of ectopic pituitary adenomas have also been reported in places such as the petrous temporal bone, the superior orbital fissure, the cavernous sinus, the third ventricle, and the temporal lobe [2, 17].

The exact reason for the origin of pituitary adenomas in ectopic sites remains uncertain, though several theories have been proposed for each site. Sphenoidal sinus ectopic adenomas are presumed to originate from embryonic cells that lag behind in the sinus during the formation of cartilaginous sellaturcica [1, 2, 4, 6, 7, 14, 17, 18]. This theory also explains the association of an empty sella with a sphenoidal ectopic pituitary adenoma. Because most of the anterior pituitary precursors of nasopharyngeal origin are left behind in the sphenoid sinus during migration, only a small number of cells would actually constitute the pituitary gland in the sella, leading to the appearance of a partial or a complete empty sella [1, 14, 19]. Yet, not all cases of sphenoidal ectopic pituitary adenomas are associated with an empty sella. It has also been speculated that sphenoidal ectopic adenomas were at one time the invasive portion of a sellar adenoma that extended to the sphenoid sinus with the intrasellar portion later undergoing apoplexy to leave behind only the sphenoidal portion with an empty sella [7, 19]. In such cases, however, one would not find an intact sellar floor and dura, a pre-requisite for the diagnosis of an ectopic adenoma. An intact sellar floor was visualised intra-operatively in our case. ACTH secreting adenomas account for 10-15% of all cases of pituitary adenomas. Interestingly however, among ectopic pituitary adenomas, almost 40-50% of the adenomas are ACTH secreting, making it the most common type of adenoma at any ectopic site [2, 6]. The reason for this is not known. In terms of hormonal activity, prolactinomas, non-functioning adenomas and growth hormone secreting adenomas, in that order are next in frequency to ACTH-secreting ectopics [2, 20].

The pre-operative diagnosis of an ectopic pituitary adenoma requires a very high index of

suspicion, especially so in the case of ACTH secreting tumors. The limited sensitivity of MRI in detecting microadenomas combined with the possibility of a visualised pituitary lesion being an incidentaloma makes definitive pre-operative diagnosis and localisation of Cushing's disease all the more inconclusive. In these situations, visualisation of a lesion at an altogether different site, like in our case, should prompt one to consider the possibility of an ectopic pituitary adenoma.

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