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Intra-Nasal Mass Presenting with Cushing's Syndrome and CSF Rhinorrhea: A Case Report

Timothy Josef L. Lao, MD and Michael N. Sabalza, MD, FAFN

Section of Neurosurgery, Department of Neurosciences, Makati Medical Center

This is a case of a 47 year-old female presenting with typical Cushingoid appearance and CSF rhinorrhea. MRI revealed a 4.4 cm x 2.9 cm x 4.5 cm enhancing intranasal mass with evidence of erosion of the left cribriform extending to the left anterior cranial fossa. Dexamethasone suppression test yielded elevated cortisol level. Endoscopic nasal biopsy done showed a round cell tumor positive for ACTH, synaptophysin, chromogranin A, and S-100. Patient subsequently underwent endoscopic endonasal excision of left intranasal mass with creation of pericranial flap for repair of CSF leak. This report is presented to discuss a rare case of ACTH secreting esthesioneurblastoma including its diagnostic challenges and surgical options for repair of anterior cranial fossa defect to address CSF leak particularly by means of a vascularized pericranial flap.

Key words: Esthesioneuroblastoma, olfactory neuroblastoma, Cushing's syndrome, ectopic ACTH production, CSF leak

Esthesioneuroblastoma, also known as olfactory neuroblastoma, is a rare neoplasm arising from undifferentiated tumors of neuroectodermal origin derived from the olfactory epithelium.[1] Since first described by Berger and Luc in 1924, approximately 1000 cases have been reported[2] with an estimated incidence of 4 cases per 10 million individuals accounting for approximately 5% of all sinonasal tumors.[3] Of these cases, around 9 have been reported to be ACTH producing tumors.[4-11]

Presented is a local case of this rare tumor presenting with ectopic ACTH production causing Cushing's syndrome.

The Case

Patient was a 47-year-old female admitted December 17, 2015 presenting with a 5 month history of CSF rhinorrhea associated with increasing central fat distribution, hyperglycemia, bipedal edema, and swelling on the left lateral aspect of the nose. MRI done as outpatient revealed an enhancing left nasal cavity mass approximately 4.4 cm x 2.9 cm x 4.5 cm extending to the left anterior cranial fossa with a normal appearing pituitary gland (Figure 1).

On admission, patient was noted to be hypertensive at 150/70 with moon facies, truncal obesity, skin hyperpigmentation, and bipedal edema. She was likewise noted to have elevated blood glucose and the following endocrine studies: ACTH of 1119.27 pg/mL (N.V.

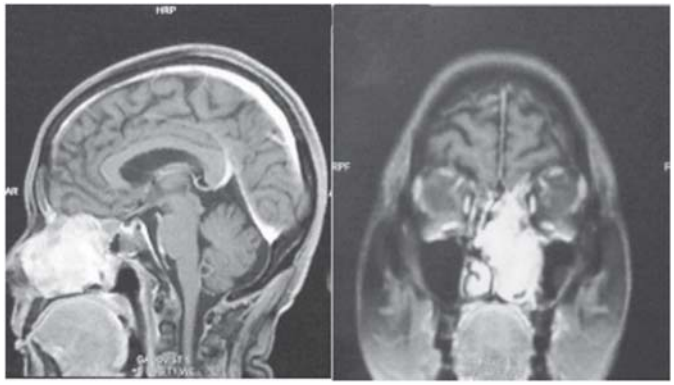


Figure 1. Sagittal and coronal MRI showing an enhancing left nasal cavity mass extending to the left anterior cranial fossa in this case of a patient with Cushing's syndrome secondary to esthesioneuroblastoma.

<50pg/mL) and cortisol of 2571.5 nmol/L (Figure 2). High dose dexamethasone suppression test with 8 mg Dexamethasone was done and cortisol measured the following day revealed non-suppressed levels at 2172 nmol/L.

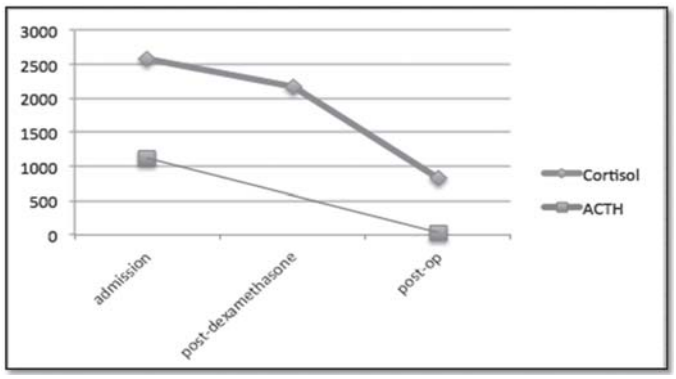
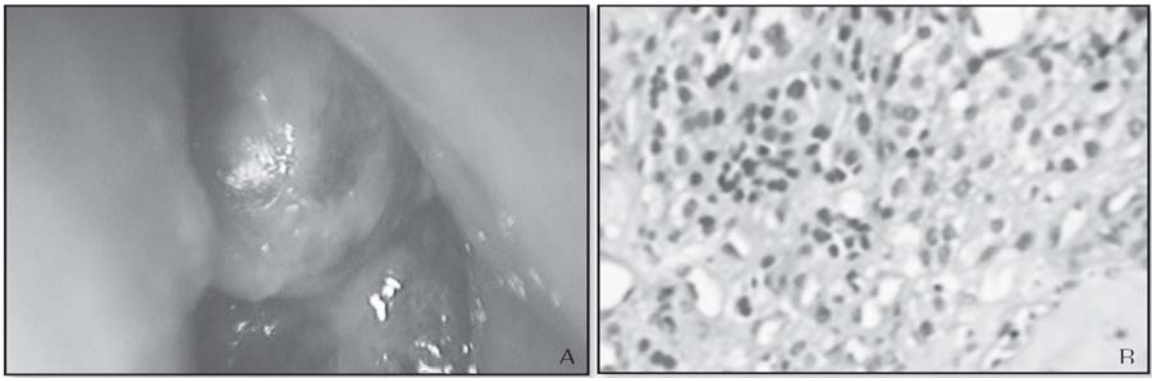


Figure 2. Cortisol (nmol/L) and ACTH (pg/mL) trend in this case of a patient with Cushing's syndrome secondary to esthesioneuroblastoma.

Endoscopic endonasal biopsy of the left nasal mass was subsequently done yielding several cream-tan, soft tissue fragments. Microsections of the specimens showed a tumor composed of sheets of fairly uniform round cells with hyperchromatic, round nuclei surrounded by proteinaceous pink material (Figures 3A & 3B). Specimen was then subjected to immunohistochemical stains, which were positive for ACTH (Figure 4a), Synaptophysin (Figure 4b), Chromogranin A (Figure 4c), and focally positive for S-100 supporting the diagnosis of esthesioneuroblastoma.

Patient subsequently underwent endoscopic endonasal excision of left intranasal mass with creation of pericranial flap for repair of CSF leak. Endoscopic endonasal excision of the nasal mass was carried out by ENT service while repair of CSF leak was simultaneously done by Neurosurgery service (Figure 5a). A bicoronal Soutar incision was done and carried down to the



A **B**

Figure 3. A case of a patient with Cushing's syndrome secondary to esthesioneuroblasoma. A) gross appearance of tumor B) microsection of tumor on high power field.

Figure 4. A) ACTH positive B) Synaptophysin positive C) Chromogranin A positive

pericranium followed by creation of a vascularized pericranial flap (Figure 5b). Nasionectomy using a pneumatic drill was done (Figure 5c) to create a communication with the nasal cavity through which the pericranial flap was passed after successful excision of the intra-nasal mass. The pericranial flap was then placed over (Figure 5e) the exposed bony defect (Figure 5d) denuded of mucosa and fixed using BioGlue® surgical adhesive. Patient tolerated the procedure well with no post-operative complications.

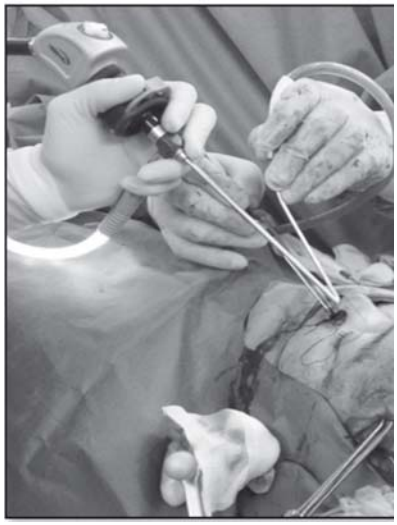


Figure 5a. Endoscopic endonasal excision of mass with simultaneous creation of pericranial flap.

Repeat cortisol at 6 and 12 days post-op revealed decreasing levels at 824.91 nmol/L and 733.22 nmol/L, respectively. ACTH taken on the 13th post-op day likewise revealed a significant decrease to 35.254 pg/mL. Patient was discharged on the 10th post-op day.

Discussion

The patient presented with typical Cushingoid appearance with elevated cortisol and non-suppressed ACTH/cortisol levels. In patients presenting as such, the question to consider is whether this is an ectopic ACTH syndrome or overproduction of ACTH by a pituitary adenoma (Cushing's disease). This patient, however, had an evident tumor in the nasal cavity with a normal pituitary gland on MRI. Biopsy done by ENT service revealed sheets of fairly uniform round cells with hyperchromatic, round nuclei surrounded by proteinaceous pink material. Given this histology, consideration at this time was esthesioneuroblastoma versus ectopic pituitary adenoma as both could appear as described above. In 2002, Cohen, et al. reported the frequency with which esthesioneuroblastoma was misdiagnosed with other tumors of the paranasal sinuses such as neuroendocrine carcinoma (NEC), pituitary adenoma, melanoma, lymphoma, and sinonasal undifferentiated carcinoma (SNUC).[12] Of the studied cases, 25% were in fact pituitary adenomas on reevaluation. On histopathology,

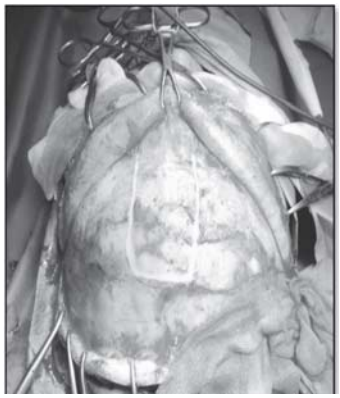


Figure 5b. Creation of a vascularized pericranial flap.

Figure 5c. Nasionectomy using a pneumatic drill.

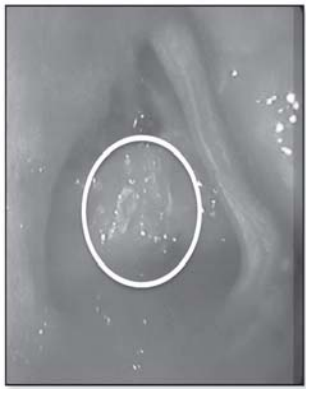


Figure 5d. Bony defect (encircled) .

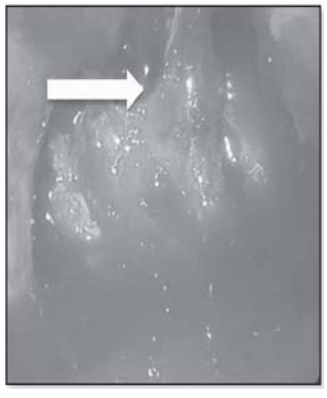


Figure 5e. Overlay of pericranial flap (yellow arrow) over bony defect.

pituitary adenomas are usually cytologically bland tumors in which there are regular round nuclei, delicate chromatin pattern, and rare mitotic figures while esthesioneuroblastoma are also homogeneous but tend to have more mitotic figures. Homer-Wright rosettes are variably seen, but their presence can aid in the diagnosis of esthesioneuroblastoma. Differentiation between the tumors therefore requires immunohistochemical stains and at times, electron microscopy. Cohen et al. summarized the characteristics of immunohistochemical testing of paranasal sinus tumors (Table 1).

Immunohistochemical stains, namely Synaptophysin, chromogranin A, S-100, ACTH, HGH, CK PAN, TTF-1, FSH, LH, TSH, p53, and Ki 67, were therefore requested for this patient to achieve definitive diagnosis. Of these, ACTH, Synaptophysin and chromogranin A were positive while S-100 was focally positive, p53 less than 5% positive, and a weakly positive Ki67 (less than 5%). Diagnosis of ACTH secreting esthesioneuroblastoma was therefore established and patient subsequently underwent endoscopic endonasal excision of left intranasal mass with creation of vascularized pericranial flap for repair of anterior cranial fossa defect to prevent CSF leak.

For decades, the pericranial flap has been the mainstay of anterior cranial base reconstruction.[13] Two types of reconstruction are currently in use. The free graft wherein a tissue from another site is cut and transplanted to patch the defect and the pedicle flap, which is a tissue left attached to its donor site and transposed to patch the defect (Figure 6). The decision to use one or the other depends on the size of the defect and rate of CSF leak. For small defects (<1cm) with low-flow CSF leak, multilayered free grafts are preferred with a reported success rate of >90% while vascularized pedicle flaps are preferred for large defects (>3cm) with high-flow CSF leak with a reported success rate of approximately 95%.[14] Given the patient's defect is approximately 2cm with significant CSF leak rate and a high likelihood of post-operative radiotherapy; a pedicle flap was deemed prudent. It was also anticipated that a septal mucosal flap would not be feasible for reconstruction due to tumor involvement of the nasal cavity and so a pericranial flap was used. Possible complications include CSF leak, meningitis, and anesthesia/hypoesthesia of the frontal scalp, none of which occurred in this patient.

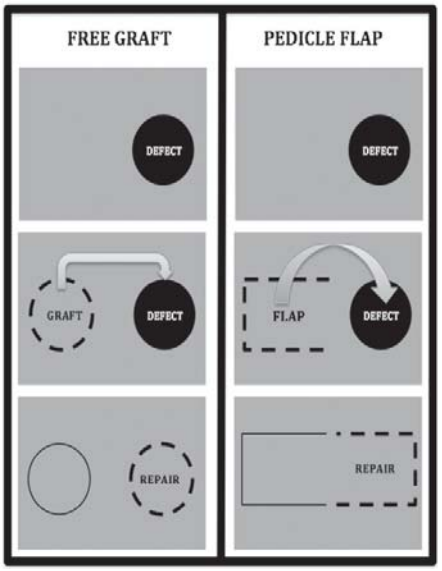


Figure 6. Free graft (left) vs. Pedicle flap (right)

Table 1. Characteristics of immunohistochemical staining of paranasal sinus tumors (Cohen, et al. 2002).

Tumor Type	Nueronal Markers	Keratin	Pituitary Hormones	S-100, HMB-45	CD45 (LCA)
ON	+	–	–	–	–
SNUC	–	+	–	–	–
NEC	+	+	–	–	–
pituitary adenoma	+	+	+/–	–	–
melanoma	–	–	–	+	–
lymphoma	–	–	–	–	+

ON= Olfactory Neuroblastoma, SNUC= sinonasal undifferentiated carcinoma, NEC= neuroendocrine carcinoma.

Conclusion

The authors have described a rare case of an ACTH secreting esthesioneuroblastoma presenting with typical Cushingoid appearance and CSF rhinorrhea along with the repair of the anterior cranial fossa defect by means of a vascularized pericranial flap. Although endoscopic reconstruction of skull base defects has advanced significantly in recent years, the diversity of lesions continue to make skull base repair a challenge. Open technique or a hybrid of both therefore remains to be viable option especially for large defects with high flow CSF leak, cases with high likelihood of post-operative radiotherapy, and in cases where septal mucosal flap is deemed unusable due to tumor involvement.

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