Primary Carcinoid Tumor of the Cavernous Sinus

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Key words
- Brain tumor
- Cavernous sinus
- Intracranial carcinoid
- Neuroendocrine tumor

Abbreviations and Acronyms
5-HT: 5-Hydroxytryptamine
CgA: Chromogranin A
IMRT: Intensity-modulated radiation therapy
LOH: Loss of heterozygosity
NET: Neuroendocrine tumor
PET: Positron emission tomography

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BACKGROUND: **Intracranial carcinoid tumors belong to the class of neuroendocrine tumors and their incidence is extremely rare. The pathogenesis and clinical manifestations of carcinoid tumors of the skull base are outlined in this case report.**

CASE DESCRIPTION: **A 61-year-old multimorbid woman presented with transient memory loss. Computed tomographic and magnetic resonance imaging scan of the brain demonstrated a left cavernous sinus mass extending into the infratemporal fossa. The lesion was biopsied using the Caldwell-Luc approach, and histology showed a low-grade neuroendocrine tumor. The tumor was subtotally resected with a neurosurgery/head and neck combined preauricular infratemporal and subtemporal extradural approaches to the cavernous sinus. Further histologic evaluation revealed that the tumor was of carcinoid differentiation with no other primary or metastatic sites detectable.**

CONCLUSION: **Primary intracranial carcinoid tumors, though rare, should be included in the differential diagnosis of extradural and dural-based lesions.**

INTRODUCTION

Carcinoid tumors are a rare type of neoplasm arising from neuroendocrine cells, representing an estimated annual incidence in the United States of 4.7 per 100,000 (28). Most of these tumors derive primarily from the gastrointestinal tract (55%) and the bronchopulmonary segments (30%) (11) but are capable of arising throughout the body. The incidence of a primary intracranial carcinoid lesion is exceedingly rare, with only three cases reported in the literature (5, 8, 17). We present here a case of a primary, biopsy-proven neuroendocrine tumor (NET) of the cavernous sinus, which underwent radical subtotal resection.

CASE REPORT

History and Physical

A 61-year-old female presented to her primary care physician for evaluation of significant acute transient memory loss lasting up to 30 minutes that started about 4 months prior to the consultation. The patient had a documented history of multiple medical problems such as diabetes mellitus and history of lacunar infarcts 15 years ago, which manifested as right-sided numbness and unsteady gait. Furthermore, the patient had systemic lupus erythematosus, rheumatoid arthritis, Sjögren syndrome, and hypertension. On neurologic examination, no abnormalities were found, all extraocular movements were intact and visual fields were full. Pupils were equal and reactive bilaterally and corneal reflex was positive in both eyes. Facial sensation and motor function was normal. She underwent computed tomographic scan imaging, which revealed an incidental finding of a left cavernous sinus mass. Subsequent magnetic resonance imaging demonstrated a weakly enhancing mass extending from the posterior aspect of the cavernous sinus to the anterior aspect of the lateral orbital wall, measuring approximately 3.4 × 1.5 cm (**Figure 1A, C**). Additionally, there was abnormal widening of the left pterygopalatine fossa, involvement of V2 and V3, and encircling of the cavernous carotid artery (**Figure 1B, D**).

Bone scan using Tc-99m-MDP with magnetic resonance imaging correlation showed reactive bone changes in the left lateral maxillary wall without soft tissue involvement and ^{18}F fluorodeoxyglucose positron emission tomography (PET) of the brain and torso showed minimal metabolic activity of the cavernous sinus mass without distant metastatic disease. The initial differential diagnosis included schwannoma/neurinoma, adenoid cystic carcinoma, meningioma, lymphoma, and teratoma.

Surgical Treatment

A transoral sublabial Caldwell-Luc approach was used to gain access to the pterygopalatine fossa for biopsy. Immunohistochemical analysis of the tumor showed positivity for synaptophysin, chromogranin, and keratin and was negative for prolactin, growth hormone, adrenocorticotropic hormone, follicle-stimulating hormone, calcitonin, and serotonin (5-hydroxytryptamine [5-HT]). Ki67 proliferation index was low. Therefore, the presumption was a neuroendocrine neoplasm.

Resection was planned with a team approach from neurosurgery and head and neck surgery. A combined preauricular infratemporal and subtemporal approach to the cavernous sinus and pterygopalatine fossa was used to radically resect the lesion in a subtotal

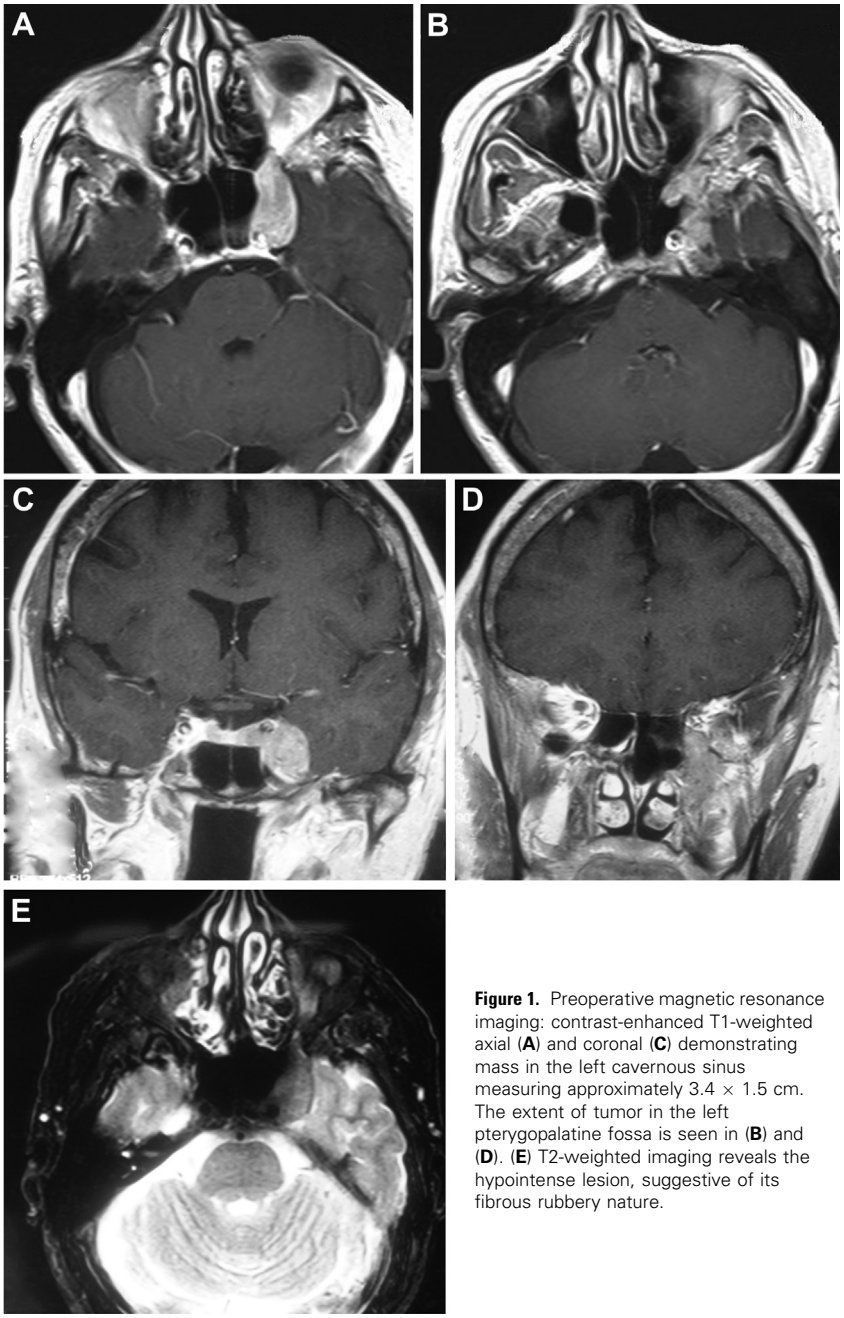

Figure 1. Preoperative magnetic resonance imaging: contrast-enhanced T1-weighted axial (**A**) and coronal (**C**) demonstrating mass in the left cavernous sinus measuring approximately 3.4 × 1.5 cm. The extent of tumor in the left pterygopalatine fossa is seen in (**B**) and (**D**). (**E**) T2-weighted imaging reveals the hypointense lesion, suggestive of its fibrous rubbery nature.

fashion (Figure 2A, B). Upon initial inspection, the tumor appeared like a pituitary adenoma. However upon entering the lesion it had a firm, rubbery consistence. Because the tumor was firm and not easily removable with suction, we shaved the final portion off the cavernous carotid artery, leaving a small crescent of tumor in the wall of the sinus. A modified level II and III neck dissection was also performed with parotidectomy at the same operation and a gross total resection of the pterygopalatine component was carried out. The pathology report indicated a low-grade neuroendocrine carcinoma; the specimen was positive for chromogranin, synaptophysin, and 5-HT (Figure 3A-D).

Postoperative Course and Outcome

Neurologic exam at discharge revealed numbness of the left cheek and mild dilation of the left pupil compared to the right. Extraocular movements and light reflexes were normal and neurologic exam was otherwise normal. Follow-up imaging revealed a small amount of residual tumor in the medial aspect of the cavernous sinus. We initially thought that radiosurgery to the visible residual tumor would be the appropriate adjuvant postoperative therapy, but after consultation with the radiation oncology group and because of the involvement of the infratemporal fossa, the patient received fractionated external beam radiation therapy, which was begun 2 weeks after surgery following removal of sutures. She received intensity-modulated radiation therapy (IMRT) at a dose fraction of 180 cGy for 25 fractions, with an additional boost for 3 fractions. Total treatment dose was 5040 cGy.

The patient was followed periodically and has done well. Fiberoptic nasal endoscopy was performed recently bilaterally and demonstrated a well-healed maxillary open cavity on the left side with a wide antrostomy. Ethmoid cavity and sphenoidotomy are patent, with no purulent drainage seen. The left nasal cavity is otherwise clear. She is now $7^{1}/_{2}$ years postoperation, and the follow-up magnetic resonance imaging shows the same stable enhancing mass in the left cavernous sinus (Figure 4A, B). On physical examination, pupils are equal and reactive to light, with extraocular movements intact. She has decreased sensation on the left in a V1, V2, and V3 distribution and sensorineural hearing loss on the left and shows no new complaints and no indication of recurrent disease. Follow-up imaging is performed every 2 years.

DISCUSSION

Carcinoid tumors are well-differentiated, low- to intermediate-grade NETs arising from enterochromaffin cells that underwent neoplastic transformation. These enterochromaffin cells, also known as Kulchitsky cells, are concentrated in the submucosa of the intestinal lumen and bronchopulmonary tract (22). It is also recognized that epithelial cells or their progenitors in virtually every organ have