

## Low grade primary clear cell carcinoma of the sinonasal tract\*

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### SUMMARY

*Clear cell carcinoma of the salivary glands are rare tumors. Metastatic clear cell carcinoma from a primary in the adrenal glands to the head and neck area have been described in the literature. However, primary clear cell carcinoma of the paranasal sinuses have not been yet alluded to in the literature except in the paper of Newman (1993). We are presenting our experience and long term follow-up in the diagnosis and management of such a lesion in the nose and paranasal sinuses.*

*Key words: clear cell carcinoma, nose, sinus, epistaxis, embolization*

### INTRODUCTION

Clear cell neoplasm of salivary glands have been always a diagnostic dilemma and controversial in their classification. Different nomenclature was used and includes: clear cell carcinoma, glycogen rich tumor, monomorphic clear cell tumor, epithelial myoepithelial carcinoma and others. These tumors are called clear cell carcinoma due to the failure of their cytoplasm to stain with hematoxylin and eosin on light microscopy because of intracellular accumulation of compounds like glycogen, lipids and a rarity of cellular organelles. Clear cell carcinoma arises from different infraclavicular and supraclavicular sites. In the head and neck region primary clear cell carcinoma originate mainly either in the salivary glands or in the thyroid gland.

We had recently the experience with a young woman on whom the diagnosis of primary clear cell carcinoma of the sinonasal tract was established.

### CASE REPORT

The patient is a 22-year old female who presented to our emergency room with sudden severe right epistaxis. She complained of nasal obstruction, but, there was no history of previous epistaxis, no recent trauma, hypertension, bleeding tendency or family history of epistaxis. Anterior rhinoscopy in the emergency unit revealed the presence of profuse bleeding

from the right nostril with no identifiable cause, necessitating anterior and posterior packing for control. The patient was admitted to the hospital for observation and work-up.

Three days later, the packs were removed under general anesthesia. Attempt at endoscopically controlling a potential bleeder failed because of profuse bleeding following packs removal; so the patient was repacked. No definite abnormality was noted endoscopically in the nose and nasopharynx, however examination of the sinonasal tract was limited by the severe bleeding. The packs were kept for 5 days and removed gradually resulting in successful control of bleeding. Five weeks later she presented again with epistaxis and endoscopic exam revealed the presence of a soft fleshy reddish mass located medial to the middle turbinate with a stalk extending superiorly. CT scan revealed an opacity medial to the middle turbinate extending into posterior ethmoidal cells. It reached but did not involve the cribriform plate. There was no intracranial extension (Figure 1). Angiography revealed a tumor blush in the right nasal cavity. The tumor was embolized. Postembolization angiogram showed complete avascularization of the tumor (Figures 3 and 4).

The patient was operated the following day. She bled profusely under general anesthesia immediately after intubation. The nose was packed and a medial maxillectomy and ethmoidectomy with excision of the tumor was performed through a

Weber-Ferguson incision. The excision extended to the cribriform plate superiorly and sphenoid sinus posteriorly. Post-operatively patient did well and was discharged one week after surgery.

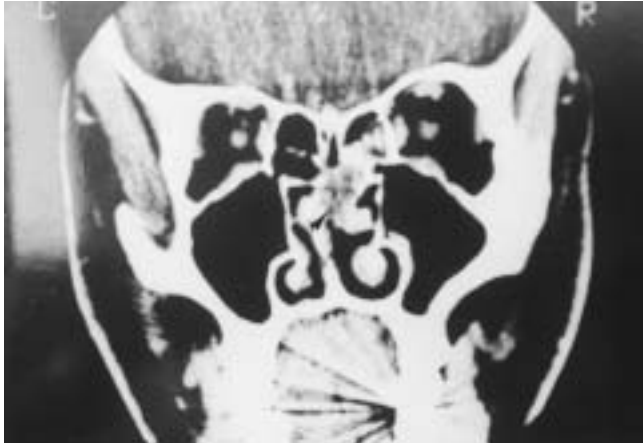


Figure 1. Coronal CT scan of sinuses showing the diffuse well circumscribed opacity (arrow head) medial to the middle turbinate, reaching up to the cribriform plate without violating it.

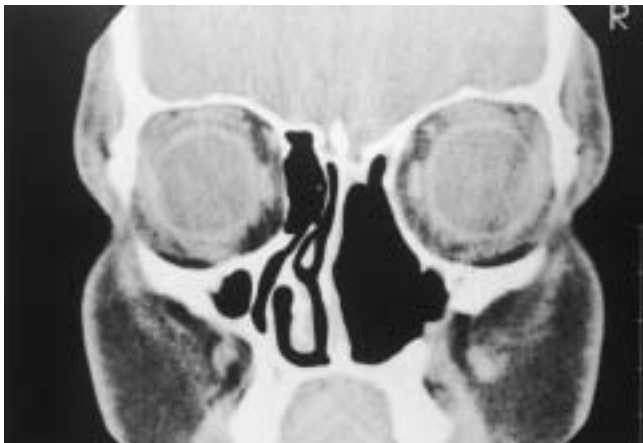


Figure 2. Postoperative CT scan of sinuses at 4 years showing no recurrence of the tumor.

The pathology of the resected tumor consisted of a 2x1.5x1.5cm aggregate of pink fleshy tissue fragments. Microscopic examination revealed a well vascularized low grade epithelial neoplasm composed of well defined acini arranged back to back (Figure 5). The acini were lined by cuboidal epithelial cells with clear cytoplasm and small round bland-looking nuclei (Figure 6). Some acini contained PAS positive and mucin-negative for both stains. There was no detectable mitotic activity and no necrosis. The overall features were those of a clear cell variant of low grade sinonasal adenocarcinoma (Figure 5). With this pathology present, work up for clear cell carcinoma in other head and neck areas (major and minor salivary glands, thyroid) was negative and primary infra-clavicular clear cell carcinoma with metastasis to sinonasal tract was suspected. CT scan of kidneys and adrenals at the time of diagnosis was negative. The patient is well at 4 years of

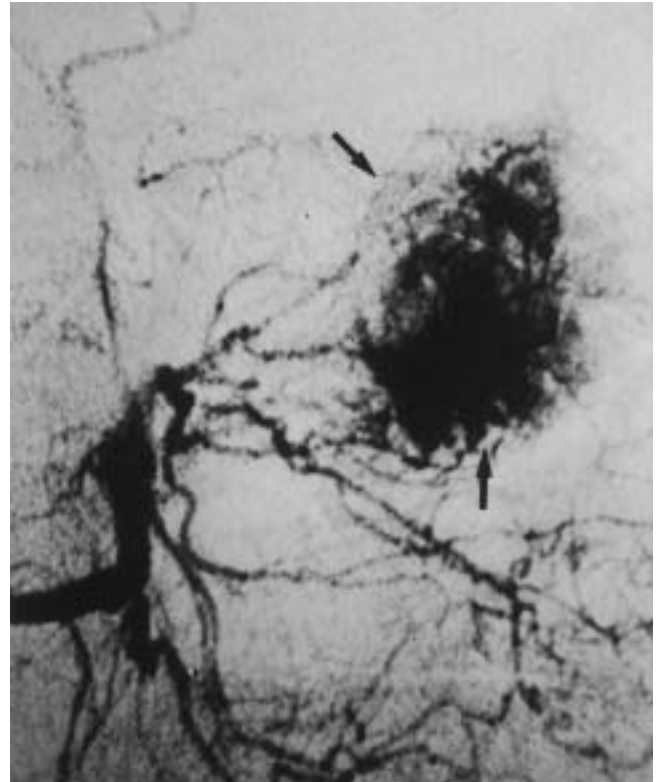


Figure 3. Preoperative angiography revealing the vascularized nature of the tumor (arrows).

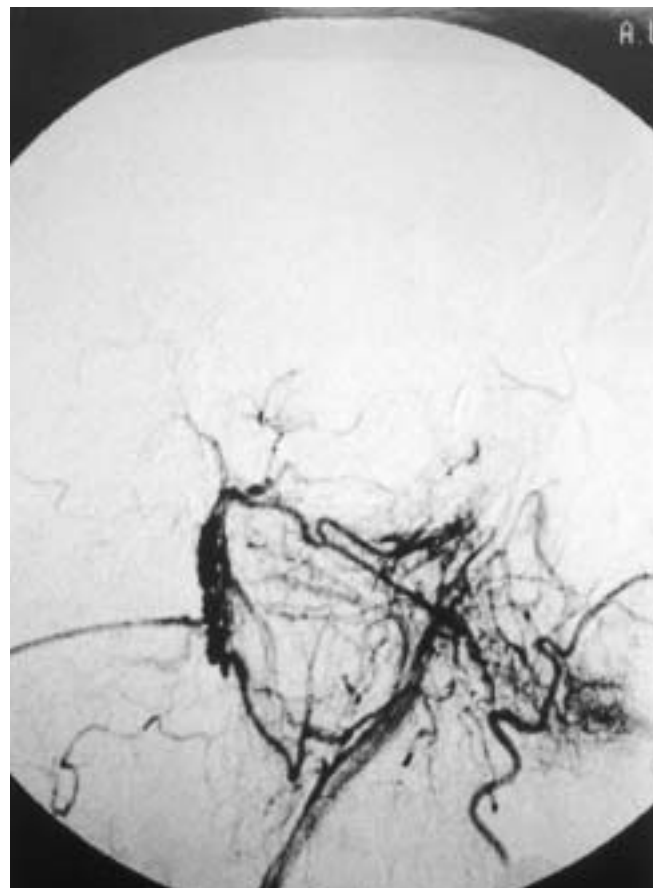


Figure 4. Postoperative angiography revealed complete avascularization of the tumor.

follow-up with no evidence of local recurrence (Figure 2). Repeat CT scan of the abdomen and adrenals at four years did not reveal the emergence of any primary tumor of the adrenal glands.

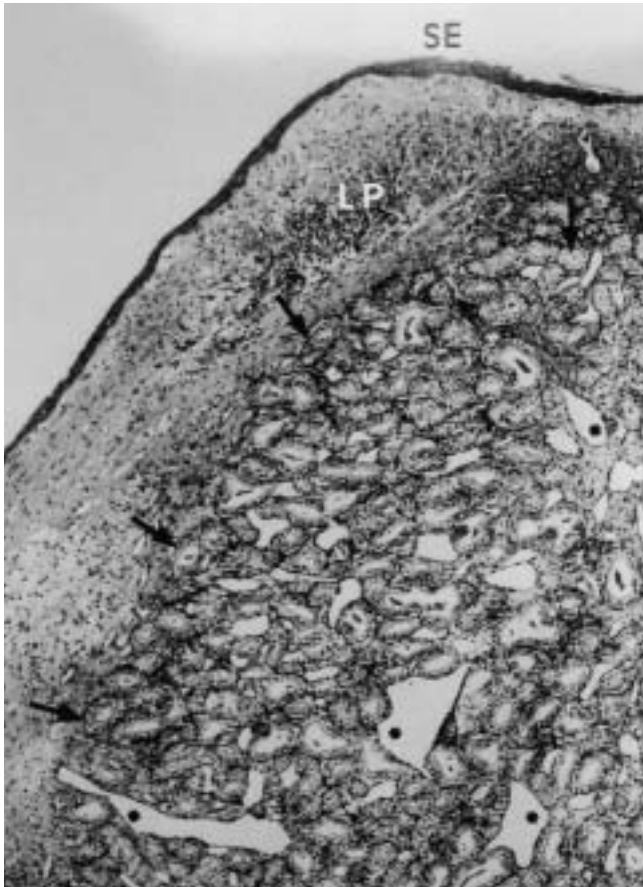


Figure 5. A portion of the tumor (arrows) expanding the lamina propria of the nasal mucosa. Large empty vascular spaces (asterisks) are seen among the crowded small tumor acini. The overlying superficial lamina propria (LP) contains a mild chronic inflammatory cell infiltrate, and the surface epithelium (SE) has undergone squamous metaplasia (H&Ex40).

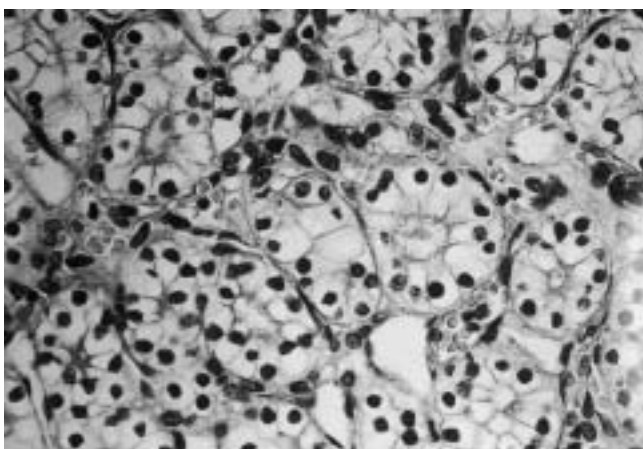


Figure 6. Higher magnification of the tumor showing acini lined by cuboidal epithelial cells with clear cytoplasm and bland-looking nuclei (H&Ex400).

## DISCUSSION

The origin of clear cell carcinoma has been postulated to be the epithelial and myoepithelial cell of the intercalated ducts (Batsakis, 1980). Clear cell carcinoma may originate in different primary tissues like kidneys, salivary glands, lungs, parathyroid, thyroid and female genital tract with each one having its own pathologic and clinical characteristics.

Primary clear cell carcinoma of the head and neck may originate either in the salivary glands or in the thyroid gland (less than 100 cases have been reported). The occurrence of salivary clear cell carcinoma is rare and is estimated to be around 1.5% (Newman et al., 1993; Simpson et al., 1990).

The registry of salivary glands at the Armed Forces Institute Pathology (AFIP) contains 60 cases of clear cell carcinoma of major and minor salivary glands of which 56.6% arise from minor glands at different sites like the palate, the lower lip, tonsillar area, buccal mucosa and floor of mouth. No intranasal clear cell carcinoma was reported (Ellis, 1999). It was not until 1993 when Newman et al, reported the first clear cell carcinoma arising from nasal cavity with no reference to the site of origin of the tumor.

The histology of these tumors is interesting. Most of the clear cell carcinoma tumors are usually not encapsulated with microscopically dominant cell cytoplasm not staining with hematoxyllin & eosin. These cells are round to polygonal, and are rich in glycogen. The nuclei are uniform with little pleomorphism and few or no mitotic figures. The cytoplasmic glycogen stains with PAS and is diastase soluble. Mucicarmine that stains for cytoplasmic mucin is ordinarily negative for clear cell carcinoma (Ellis, 1999).

The differential diagnosis of these tumors includes oncocytomas, mucoepidermoid carcinoma, acinic cell carcinoma, epithelial-mucoepithelial carcinoma and metastatic renal cell carcinoma. It is well known that mucoepidermoid carcinoma and acinic cell carcinoma, like clear cell carcinoma contain significant numbers of clear cells. However, absence of glycogen, presence of epidermoid cells and staining of mucous cells by mucicarmine is nearly always found in mucoepidermoid carcinoma. Moreover, in acinic cell carcinoma the cytoplasm is devoid of glycogen. Furthermore, hemorrhagic nasal and paranasal neoplasms that should be considered in the differential diagnosis include hemangioma, angioendothelioma and angiofibroma (Matsumoto et al., 1980).

Renal cell carcinoma is the most frequent tumor to metastasize to the nasal cavity, paranasal sinuses and nasopharynx (Madison et al., 1988). Metastasis to the head and neck area is infrequent despite rich hematogenic pathways and is around 6% as reported by Folck and Boatman (Folk et al., 1973). Boles and Cerny found that symptoms produced by metastatic deposits in the head and neck were the presenting complaints in 8% of patients with renal tumors (Boles et al., 1971).

Most of these metastases are to bone with secondary soft tissue involvement. Due to the high incidence of renal cell carcinoma metastasis from the kidney: a thorough evaluation of the kidney by CT scan was performed in this case. No primary tumor was identified on presentation and at 4 years of follow-up. Matsumoto et al. (1980) alluded to the occurrence of renal cell carcinoma that presented initially with a nasal mass and profuse epistaxis. However, in their cases, primary renal cell carcinoma became apparent a few months later after management of the nose and paranasal sinus tumor.

The clinical presentation of our patient with severe epistaxis, nasal obstruction, and a nasal mass is typical of metastatic renal cell carcinoma as described by the 2 cases reported by Matsumoto et al. (1980). However, the close follow up and the repeated CT scan evaluation of the kidney in our case failed to identify a primary renal cell carcinoma. This raises the likelihood that the origin of our tumor in the nose and paranasal sinuses, might be from submucosal mucoserous glands (Topozada et al., 1980).

The rarity of primary clear carcinoma of the nose and paranasal sinuses, makes it difficult to draw conclusions about their biological behavior. However, their slow growth rate, infrequent tendency for infiltrative growth, low incidence for lymph node metastasis, and the favorable prognosis for complete local control with relatively low tendency for recurrence, characterizes these tumors as low grade adenocarcinoma (Ellis, 1999).

Surgical resection through a lateral rhinotomy is the recommended route to adequately resect the tumor with wide surgical margins. Perineural invasion and infiltrative growth into surrounding soft tissue has been described. Potential profuse bleeding intraoperatively, might necessitate pre-operative embolization. Potential profuse bleeding intraoperatively, might necessitate preoperative embolization and or intraoperative ligation of the external carotid artery. There are no published studies on the benefit of adjuvant chemotherapy and radiation therapy. In comparison, metastatic renal cell carcinomas to the head and neck area had a poor prognosis and the main treatment consisted of resection of the primary renal tumor as well as that of the metastatic deposit. The role of radiation and chemotherapy remains controversial (Rafla, 1970).

#### CONCLUSION

Our case report is the second to be reported in the literature after an extensive review over the past 30 years. The two cases presented so far do not provide us with enough clinical information as to its mode of presentation, duration of symptoms and natural history of the disease. The presenting symptoms are nasal obstruction and epistaxis. We think that these tumors are highly vascular as evident by the angiography performed in our case.

Primary cell carcinoma of the head and neck seems to have a favorable outcome following surgical resection. However the biological behavior of these tumors is variable and the natural history of primary sinonasal clear cell is hard to predict due to the small number of cases in the literature.

With diversity in biological behavior and with the potential for low grade malignancy of these tumors, we elected to perform a wide local excision with no further adjuvant therapy. Follow up of this patient in the future will dictate further management options.

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