UNUSUALLY DELAYED RECURRENCE OF A LOW GRADE MUCOEPIDERMOID CARCINOMA OF THE MAXILLARY SINUS

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ABSTRACT:
Mucoepidermoid carcinoma (MEC) is a malignant epithelial neoplasm composed of both mucus secreting cells and epidermoid-type cells. Mucoepidermoid carcinoma arising from mucous glands of maxillary sinus is extremely rare and accounts for 13% of all malignancies occurring in maxillary sinus. While the high-grade MEC is a highly aggressive tumor, its low-grade counterpart usually demonstrates a more benign nature. However, both local recurrence and an aggressive clinical course have been reported to occur even with low-grade tumors.

We report a case of low grade mucoepidermoid carcinoma of the maxillary sinus who presented to us with a recurrence 20 years after undergoing a total maxillectomy and post-operative adjuvant radiotherapy. The patient was successfully managed with wide excision of the tumor.

KEYWORDS- Maxillary sinus, Low grade, Mucoepidermoid carcinoma

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INTRODUCTION:
Mucoepidermoid carcinoma (MEC) is a malignant epithelial neoplasm, believed to arise from the reserve cells of excretory ducts. Mucoepidermoid carcinoma arising from mucous glands of maxillary sinus is extremely rare and accounts for 13% of all malignancies occurring in maxillary sinus. 1 Mucoepidermoid carcinoma displays a spectrum of biological behaviors; while
the high-grade MEC is a highly aggressive tumor, its low-grade counterpart usually demonstrates a more benign nature. However, both local recurrence and an aggressive clinical course have been reported to occur even with low-grade tumors. The prognosis of patients with MEC depends on the adequacy of treatment, the clinical stage, and the tumor grade and location.\textsuperscript{2-6}

We report an unusual case of low grade muco-epidermoid carcinoma of the maxillary sinus who presented with a delayed recurrence 20 years after a total maxillectomy and post-operative adjuvant radiotherapy. The patient was successfully managed by a wide excision of the tumor.

**CASE REPORT:**

A 42 year old female patient presented to our outpatient department with a progressively increasing left cheek and intra-oral swelling since 3 months. It was not associated with pain, nasal obstruction, and epistaxis or reduced vision. 20 years back, this lady had developed same sided cheek swelling in addition to a palatal swelling for which she had undergone total maxillectomy at an outside centre. Records indicated that the post-operative histopathology was suggestive of mucoepidermoid carcinoma subsequent to which she had received adjuvant radiotherapy. Detailed pre-operative or intra-operative records were not available to us and neither were the details of radiation dose or fields. Physical examination revealed a 5 cm X 4 cm swelling over her left cheek extending between the zygomatic arch laterally, naso-maxillary groove medially, oral commissure inferiorly and the lower lid superiorly. On palpation, the swelling was non-tender with a variegate consistency with both firm and cystic areas. A healed scar of Weber-Ferguson incision was evident along with ectropion of the medial part of lower eyelid. Left ala was pulled inwards causing narrowing of the left nostril (Figure 1). Intra-oral examination revealed a 4 cm X 3 cm mucosa-covered swelling in the region of maxillectomy defect extending medially upto the midline and posteriorly upto the anterior margin of the soft palate. There was a 2 cm X 0.5 cm fistula just adjacent to the medial margin of swelling (Figure 2).
Figure 1: Maxillary swelling left side with ectropion (black arrow)

Figure 2: Intraoral swelling left side with oro-nasal fistula (black arrow)

A contrast-enhanced CT scan of the nose and paranasal sinuses revealed the post-maxillectomy status. It showed a well-defined hypodense soft tissue lesion measuring 3 X 2.2 X 2.8 cm in the operated left maxillary region, anterolateral to the intact pterygoid plate. It appeared to project into the oral cavity and also showed a rim of peripheral post contrast enhancement. There was a soft tissue lesion of similar characteristics in the left infraorbital region, measuring 3.2 X 5.2 X 2.5 cm. Overlying skin and subcutaneous tissue appeared to be uninvolved. (Figure 3-6)
In view of the suspected recurrence, a PET-CT scan was done. It revealed a low-grade FDG uptake of SUV Max 2.0 and 1.23 in the two lesions respectively. There was no evidence of cervical adenopathy or distant metastasis (Figure 7). The patient was taken up for a revision surgery by an external approach. A Weber-Ferguson incision over the previous scar was made and the cheek flap elevated. En-bloc wide local excision of both the lesions was performed including the overlying oral mucosa (Figure 8). The same incision was used to correct ectropion of lower lid. Oro-nasal separation was achieved with an obturator.
Histopathological examination of the resected specimen revealed a multiloculated cyst filled with inspissated mucus and lined by cells resembling squamous epithelial cells, cells with moderated to abundant cytoplasm having irregular, eccentric nuclei resembling clear cells, and a few intermediate cells. There was no evidence of atypia/necrosis/mitosis. A pathological diagnosis of low grade mucoepidermoid carcinoma was made with all the resected margins free of tumor. Post-operatively, the patient achieved a normal oral feeding and good voice. No recurrence has been observed at 6 months and the patient has been advised a long term regular follow-up.

**DISCUSSION:**

Mucoepidermoid carcinoma is a malignant epithelial neoplasm composed of both mucus secreting cells and epidermoid-type cells in varying proportions. It was first studied and described as a separate entity by Stewart et al. in 1945. After a systematic review of its histology and degree of differentiation, the WHO classification in 1991 recommended that, the term “mucoepidermoid tumor” be changed to “mucoepidermoid carcinoma”. Mucoepidermoid carcinoma is the most common malignant neoplasm observed in the major and minor salivary glands among children and adults. Spiro et al in his study of 367 mucoepidermoid carcinomas found an incidence of 2 % for nasal cavity and 3% for maxillary antrum.

Malignant tumors of the paranasal sinus are uncommon, constituting less than 1% of all malignancies and 3% of all head and neck cancers. The majority of these tumors are in the maxillary sinus, and squamous cell carcinoma is the commonest histological type. As a subset of maxillary sinus malignancies, non-squamous cell cancers of the maxillary sinus are rare entities. Kraus et al. in a study of 49 patients with nonsquamous tumors of maxillary sinus reported sarcomas, adenoid cystic carcinomas, lymphoma, and adenocarcinoma accounting for most of
their cases. In contrast Bhattacharya in his series of 188 cases had adenoid cystic carcinoma (34%) as the predominant histological type followed by sarcomas (24%). Mucoepidermoid carcinoma arising from mucous glands of maxillary sinus is extremely rare and accounts for 13% of all malignancies occurring in maxillary sinus.

MEC arising in maxillofacial region can have its origin from the maxillary sinus lining or central MEC arising from within the bone or from the minor salivary gland. In the absence of pre-operative imaging from the first surgery, it is difficult to determine the origin of tumor in our patient. The prognosis of patients with MEC depends on the adequacy of treatment, the clinical stage, and the tumor grade and location.

Maxillary sinus malignancies are traditionally considered to be difficult tumors to treat and consequently have been associated with a poor prognosis. Close proximity of these tumors to vital structures such as the skull base, brain, orbit, and carotid artery often makes complete surgical resection a challenging task. Moreover, these tumors, including the MEC of maxillary sinus tend to be asymptomatic at early stages, appearing more frequently at late stages once extensive local invasion has occurred. This unfortunate combination of complex anatomy, vital surrounding structures and advanced stage at presentation leads to the frequent local recurrence and subsequent poor outcome associated with sinonasal malignancies.

The 3-level grading approach to classifying tumors has found general acceptance among pathologists, and differences in biologic behaviour can be demonstrated, even though clinical stage became a better prognosticator. Suggested grading criteria for MEC have included, either singly or in combination, the relative proportion of cell types, degree of invasion, pattern of invasion, mitotic rate, proportion of tumor composed of cystic spaces relative to the solid growth degree of maturation, and neural and vascular invasion. Various histological grading systems are in use among the pathologists. In our patient, the presence of macrocysts lined by differentiated epidermoid and clear cells, few intermediate cells, and extravasated mucin with absent mitoses and pleomorphism led to a diagnosis of low grade mucoepidermoid carcinoma according to Batsakis and Luna’s modification of Healey’s system. Even with the Auclair and Goode’s grading system, or by its Brandwein’s modification, the tumor in our patient would be classified as low grade with a score of 0, considering the presence of > 20% cystic component, absence of necrosis, mitoses, perineural spread and atypia. Survival is closely related to histologic grade.

Although staging and grading are related, they seem to function independently of each other. Low-grade lesions behave less aggressively than do high-grade lesions, regardless of stage; conversely, stage I and II tumors have a better prognosis than do stage III or IV tumors, regardless of grade. Patients are more likely to experience a recurrence if the margins of resection are positive, regardless of grade. Healey et al reported that 0 of 33 low-grade and intermediate-grade lesions recurred when the margins were free of carcinoma, but 6 of 12 of the same grade recurred when the margins were positive.
Ozawa et al experienced two patients with low-grade MEC who were diagnosed as stage IV and had multiple neck metastases at first medical examination and died as a result of distant metastasis. Moreover, when a discrepancy existed between the grade and stage of a tumor (high-grade, stage I or low grade, stage III), the outcome was influenced more by the clinical stage than the histologic grade.

Although, mucoepidermoid carcinoma has been considered a radioresistant tumor, postoperative radiation is thought to be effective. Postoperative radiotherapy for MEC patients with positive surgical margin has been reported to decrease local failure. Although, most of the mucoepidermoid carcinomas that recur do so within 1 year of therapy, delayed recurrences have been reported. Varghese reported a case of mucoepidermoid carcinoma of the base of tongue which recurred loco-regionally after 20 years. In Chen’s study of recurrences in salivary gland cancer, three recurrences occurred after a period of 15 years, the maximum being 23.1 years but they did not correlate the time to recurrence with specific tumor type. To our knowledge, our patient seems to be the first case reported in literature, of a low grade mucoepidermoid carcinoma of the maxillary sinus to recur after an unusually long period of 20 years.

Thus, it is important to remember that patients with low grade MECs are neither “immune” to local recurrences, nor to distant metastasis. The local recurrence in our patient occurred after a long period of around 20 years and the patient had received adjuvant radiotherapy after her first surgery. In the absence of a detailed histopathological report of the first surgery, we can only speculate on the cause of recurrence. It could probably be the result of an inadequate resection done at the first instance with the subsequent indolent growth of the low-grade tumor. Thus, it is important to ensure a wide excision with negative margins even in cases of low grade MECs. Thus, post-operative local recurrence is likely to occur when the resection is inadequate (or margins are positive) irrespective of tumor grade. Adjuvant radiotherapy may not be able to compensate for an incomplete excision, as demonstrated in our case. Considering that the final histopathology was consistent with a low grade tumor and all the resected margins were free, we decided not to re-irradiate the patient. She has been recurrence-free so far and has been advised a long term follow-up.

In view of the delayed recurrence as seen in this case, we advise a long term follow-up of all patients with low grade muco-epidermoid carcinomas.

CONCLUSION:

Mucoepidermoid carcinoma of the maxillary sinus is a rare entity. Through this case report, we wish to emphasize that although, low grade MECs are biologically less aggressive tumors, they are not immune to loco-regional recurrences. It is imperative to ensure an en-bloc excision of these tumors with negative margins to avoid recurrences. Long term follow-up for all patients is recommended as delayed recurrences may occur.
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