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Benign Look, Malignant Outcome: Unexpected Nodal Spread in Upper Lip Mec

Dr. Kotra Soumya Kumari[1], Dr. M. Rajini Kanth[2], Dr. Pavani Vidhyadhari[3], Dr. K.S Vidya[4], Dr. G. Spandana[5], Dr. K. Sowmya[6]

[1]M.D.S, Oral And Maxillofacial Pathology, G.Pulla Reddy Dental College And Hospital
[2]Profeesor & H.O.D, Oral And Maxillofacial Pathology, G.Pulla Reddy Dental College And Hospital
[3,4,5,6]Reader, Oral And Maxillofacial Pathology, G.Pulla Reddy Dental College And Hospital

Abstract

Background: Tumors of the salivary glands are uncommon neoplasms, representing approximately 3-6 % of all head and neck tumors, with minor salivary gland tumors (MiSGTs) accounting for about 10–15% of all salivary gland neoplasms. Among minor salivary gland malignancies, mucoepidermoid carcinoma (MEC) is an important subtype that commonly arises in sites such as the palate and retromolar region; its occurrence in the upper lip is extremely rare. MEC shows variable biological behavior, tumor grading, staging, and correlation with prognosis and risk of recurrence or metastasis.

Case Presentation: A 22 year old male presented with a firm, non-tender swelling in the right upper lip without functional impairment since 1 month. Clinical examination revealed a benign lesion, and excisional biopsy was performed. Histopathological analysis revealed an encapsulated lesion composed of sheets and islands of predominantly intermediate- cells, along with mucous cells and focal capsular invasion, leading to a diagnosis of intermediate- grade MEC. Within 45 days of the procedure, a submental swelling developed. Histology of the excised lymph node demonstrated microcystic spaces with mucin material, mucinophages, signet ring–type mucinous cells, and sheets of intermediate cells, confirming nodal metastasis. Given the intermediate grade and nodal involvement, the patient underwent combined chemoradiotherapy, receiving a total of 50 Gy and two cycles of cisplatin and 5 fluorouracil.

Conclusion: This case highlights the rare presentation of MEC in the upper lip with early regional lymph node metastasis, emphasizing the need for careful histopathological evaluation and grading to guide treatment. Although uncommon in this anatomic location, MEC can demonstrate aggressive behavior, even in intermediate -grade forms, necessitating multimodal treatment and long-term follow-up to detect recurrence or further spread.

INTRODUCTION:

Salivary gland tumors are uncommon neoplasms, accounting for 3-6 % all of head and neck tumors. Minor salivary gland tumors (MiSGTs) are a rare subtype of salivary tumors, constituting 10–15% of all salivary

gland neoplasms. The palate is the most commonly affected area, and these tumors also have a comparatively higher chance of being malignant than those of major salivary glands[1]
Mucoepidermoid carcinoma (MEC) is the most common malignant salivary gland tumor. The World Health Organization (WHO) defines it as a malignant epithelial neoplasm composed of mucous-producing, epidermoid, and intermediate cells, exhibiting a spectrum of cystic and solid growth patterns.[2] Epidemiologically, MEC represents approximately 10–15% of all salivary gland tumors and accounts for approximately 30% of malignant salivary neoplasms.[3]
Tumor stage and histological grade are significant predictors of outcome, both clinically and prognostically, with high-grade tumors exhibiting aggressive behaviour and low-grade tumors associated with a better prognosis. The Armed Forces Institute of Pathology (AFIP) grading system is widely used and categorizes MEC into low, intermediate, and high-grade based on histopathological features such as solid growth pattern, mitotic activity, necrosis, and perineural invasion.[3]
Among intraoral minor salivary gland tumors, MEC is an important and common malignant type, with pooled data showing that it represents approximately 16.5% of all cases.[4] However, MEC in minor salivary glands most frequently arises in the palate,buccal mucosa,tongue, and retromolar area. In contrast, MEC occurring in the upper lip is exceptionally uncommon, with only a few cases reported in the literature. Reports of upper lip MEC emphasize the need for a careful evaluation.[4] This article focuses on the current evidence on MEC's epidemiology, clinical features, histopathology, grading systems, and treatment approaches, with special focus on its rare presentation in the upper lip.

CASE REPORT:

A 22-year-old male presented to the outpatient department with a chief complaint of a swelling in the upper lip since one month . The patient did not report any associated pain, sensory disturbances, or functional impairment. Intraoral examination revealed a small nodular swelling on the right side of the upper lip, detectable only on palpation. The lesion was firm, rubbery in consistency, and non-compressible, with an intact overlying mucosa and no evidence of ulceration or extraoral involvement.
Clinically, the lesion was asymptomatic and nontender, and there were no associated systemic symptoms. Based on the clinical findings alone, a provisional diagnosis of neurofibroma was considered, and an excisional biopsy was performed for definitive histopathological evaluation.
On gross examination, the excised lesion appeared grayish-white and measured approximately 1.5 × 1.2 cm. The specimen was subjected to routine tissue processing and stained with hematoxylin and eosin (H&E). The H&E examination showed an encapsulated lesion. Connective tissue showed cells arranged in the form of sheets and islands, predominantly round cells with hyperchromatic nuclei resembling intermediate cells. Few cells were pale with homogeneous eosinophilic cytoplasm and eccentrically placed nuclei resembling mucous cells. Bundles of collagen fibers, chronic inflammatory cell infiltrate predominantly consisting of lymphocytes, and endothelial-lined blood capillaries with extravasated red blood cells were observed. The focal areas showed capsular invasion. Muscle, adipose tissue, and salivary gland acini were also evident. Based on these findings, a final diagnosis of intermediate-grade mucoepidermoid carcinoma was given.
Within 45 days, the patient developed a solitary swelling in the submental region of the mandible, for which an excisional biopsy was performed. The received specimen consisted of a single nodular grayish-brown

tissue measuring approximately 3.5 × 3 cm. On cut sections, grayish-white areas were observed. Routine processing and H&E staining were performed. The H&E examination revealed a lymph node with microcystic spaces containing mucin-like material, clusters of mucinophages, and a few signet ring–type mucinous cells. Sheets of intermediate-type squamous cells with vesicular nuclei were also observed. In view of these histopathological features, a final diagnosis of metastatic deposit of mucoepidermoid carcinoma was made.

After obtaining informed consent, the patient was treated with chemoradiotherapy. A total radiation dose of 50 Gy was administered. Chemotherapy was administered in two cycles at a 4-week interval, consisting of cisplatin at a dose of 80 mg/m² on day 1 and 5-fluorouracil at a dose of 800 mg/m² per day from days 1 to 5.

FIG 1: GROSS SPECIMEN –greyish white- measuring around 1.5× 1.2 cm

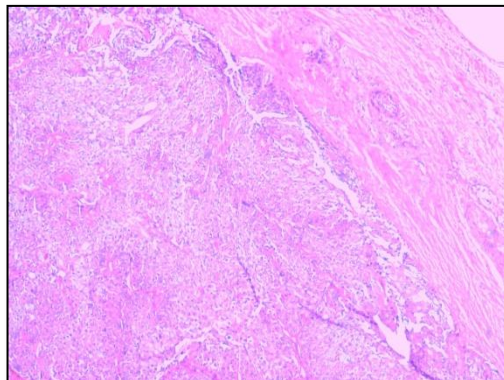

FIG 2: Capsular Invasion

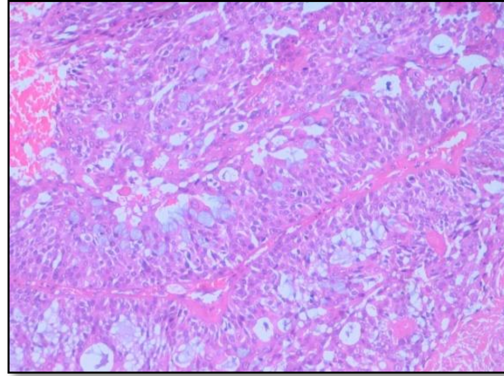

FIG 3: Sheets of intermediate cells along with mucous cells

DISCUSSION:

Mucoepidermoid carcinoma (MEC) is the most common malignant salivary gland neoplasm, demonstrating a wide spectrum of clinical and histopathological behaviors. MEC accounts for a significant proportion of both major and minor salivary gland malignancies, with the parotid gland being the most frequently affected site, followed by the minor salivary glands of the palate, buccal mucosa, floor of the mouth, and retromolar areas[5]. While MEC is common in the parotid and palate sites, its occurrence in the upper lip is relatively uncommon, and the presence of early regional lymph node metastasis, as seen in the present case, further highlights its aggressive potential.

Histologically, MEC is composed of varying proportions of mucous, epidermoid, and intermediate cells arranged in cystic, solid, or mixed growth patterns, as described by the WHO and multiple clinicopathologic studies. Tumor grading plays a crucial role in predicting biological behavior and clinical outcomes. In this case, we considered grading based on three histological criteria:

1. Amount of cyst formation
2. Degree of cytological atypia
3. Relative amounts of mucous,epidermoid, and intermediate cells[6].

Other classification criteria are the AFIP and Brandwein et al. criteria, of which the AFIP is the most followed.

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Criteria	AFIP	Brandwein
Cystic component	(<20%) + 2	(<25%) + 2
Perineural invasion	+2	+3
Necrosis	+3	+3
≥4 mitoses per 10 hpf	+3	+3
Anaplasia	+4	+2
Lymphovascular invasion	-	+3
Aggressive pattern of invasion	-	+2
Bony invasion	-	+3
Grade	Low Grade – 0–4 Intermediate – 5–6 High grade – 7–14	Low Grade – 0 Intermediate – 2, 3 High grade – ≥ 4

[7]

In the present case, the tumor showed a predominance of intermediate cells, focal capsular invasion, and limited cystic areas, supporting a diagnosis of intermediate grade MEC based on the above mentioned criteria. Studies comparing grading systems have shown that the Brandwein grading system tends to categorize more tumors as high-grade, while the AFIP grading system tends to classify more tumors as low-grade; however, both systems correlate with clinical behavior. [8]

Regional lymph node metastasis is uncommon in low-grade MEC but is more frequently observed in intermediate- and high-grade tumors. In a large cohort of MECs by Bradwein et al., lymph node positivity was significantly associated with higher grade and poorer outcomes, reinforcing the importance of histologic assessment and appropriate staging.[9] The early development of submental lymph node involvement within 45 days in the present case correlates with these published cases.

Diwakar et al. reported a rare case of mucoepidermoid carcinoma of the parotid gland with mandibular metastasis, emphasizing that MEC can metastasize to unusual sites, particularly in high- grade tumors with adverse histopathologic features.[10]Their findings reinforce the concept that MEC possesses metastatic potential beyond typical regional lymph nodes.

Common Histologic Variants Include:

- **Classical MEC:** Balanced proportions of mucous, intermediate, and squamous/epidermoid cells.
- **Clear cell variant:** The predominance of clear cells may complicate the diagnosis and mimic other clear cell tumors of the salivary glands
- **Oncocytic (Warthin-) variant:** Characterized by abundant oxyphilic cytoplasm and can resemble Warthin tumors
- **Spindle cell variant:** Predominance of spindle shape tumor cells.
- **Sclerosing variant:** Significant stromal fibrosis
- **Trabecular variant:** Exhibits a dominant trabecular/nested pattern distinct from classical MEC architecture, as confirmed in molecular studies.
- **Intraosseous variant:** A rare central MEC that originates within jaw bone and may be associated with MAML2 fusions — requiring integration of clinical, radiologic, and histologic data for diagnosis.[10]

The management of MEC primarily involves wide surgical excision with clear margins. However, the presence of intermediate grade, capsular invasion, and lymph node metastasis necessitates adjuvant therapy, such as radiotherapy or chemoradiotherapy, particularly when aggressive features are observed. Multimodal treatment approaches and long-term follow-up are emphasized due to the risk of recurrence and distant spread. In the present case, combined chemoradiotherapy was administered due to the intermediate grade and nodal metastasis.

Surgery alone	Surgery and radiotherapy	Additional neck dissection	Systemic chemotherapy
Negative margins	Close (<2 mm) or positive margins	All cN+	Metastatic or unresectable disease
		cN0 but high grade histology	
Low grade histology	High grade histology	cN0 but high risk (angioinvasive) histologic subtype	
Low risk (non angioinvasive, non infiltrative) histologic subtype	High risk (highly infiltrative) histologic subtype	cN0 but high T stage (T3 or T4)	
Low T stage (T1 or T2)	High T stage (T3 or T4)		
	pN+		
	Perineural invasion[a]		

T = tumor stage in TNM classification, cN+ = clinically node positive, cN0 = clinically node negative,pN+ = pathologically node positive [a]Somewhat controversial depending on tumor type The reported overall 5 year survival for MEC ranges from 92 to 100% for low-grade tumors, 62–92% for intermediate-grade tumors, and 0–43% for high-grade tumors.

Conclusion:

This case highlights the importance of meticulous histopathological evaluation and grading of MEC, particularly in lesions arising from minor salivary glands with a clinically benign presentation. Even intermediate tumors may demonstrate aggressive behavior with early metastatic spread, emphasizing the need for early diagnosis, appropriate grading, treatment planning, and long-term follow-up.

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