

Mucoepidermoid carcinoma involving hard palate and a rare presentation on maxillary sinus: two case reports with immunohistochemical evaluation.

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ABSTRACT

Background: Mucoepidermoid carcinoma (MEC) is a malignant salivary gland tumour seen more frequently in females and occurs mostly in the fifth decade of life. MEC is composed of mucous cells, intermediate cells and epidermoid cells in different compositions and according to the predominant cells, it is graded as low grade, intermediate grade, and high grade.

Case presentation: In this case series, we present two cases of mucoepidermoid carcinoma involving maxillary sinus and hard palate which were diagnosed as intermediate grade and low grade MEC respectively. The diagnosis was made based on the clinical features of the lesion,

H&E staining, special stains like mucicarmine, immunohistochemistry and radiological features.

Management and prognosis: In the first case the patient was treated by radiotherapy and palliative care as the lesion was widely spread to adjacent structures and spaces. In second case, the patient was treated with surgical excision and regular follow up.

Conclusion: Despite the fact that these patients presented with the same pathology, their clinical presentations were different. Since MEC is malignant in nature, its early detection and proper treatment helps to reduce the morbidity and better prognosis.

Key words: Mucoepidermoid carcinoma, maxillary sinus, low grade, intermediate grade.

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INTRODUCTION

Mucoepidermoid carcinoma is one of the most common salivary gland malignant tumours in adults and children.¹ It is thought to be arising from pluripotent cells of excretory ducts of salivary gland epithelium.² It was first described by Stewart, Foote, and Becker in 1945 after the analysis of 45 cases. It accounts for 12-15% of all salivary gland tumors and 29.3% to 34 % of malignant tumours originating from salivary glands.³ It is most commonly occurring in the parotid gland (45%-56.9 %) followed by minor salivary glands (22.9%-37.1%), with a slight female predilection.⁴ As the name indicates, MEC is characterized by mainly three types of cell groups, mucous, epidermoid, and intermediate cells in various proportions.⁵

Here, we present two cases of mucoepidermoid carcinoma, involving maxillary sinus and hard palate with different clinicopathological features.

CASE REPORT-1

A 47 year old male patient reported to the department with severe pain and swelling on the right side of face since 4 weeks. Extra orally, a solitary and diffuse swelling was noticed extending from the infraorbital region to the right corner of the mouth with mild proptosis of the eye. On palpation, the swelling was firm and tender. Intra orally, a solitary, soft and tender swelling was noted on 17 region extending to the tuberosity of maxilla and palate

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with obliteration of buccal vestibule in relation to 16 and 17 region. Level II lymph nodes were palpable. Based on the above mentioned findings, the differential diagnosis considered were carcinoma of the maxillary sinus, mucoepidermoid carcinoma, adenoid cystic carcinoma and pleomorphic adenoma.

Panoramic radiograph revealed a massive radiolucent lesion extending anteroposteriorly from 16 to maxillary tuberosity, superiorly from the middle third of maxillary sinus to retromolar region (Fig 1). CECT of the maxilla revealed a soft tissue density in

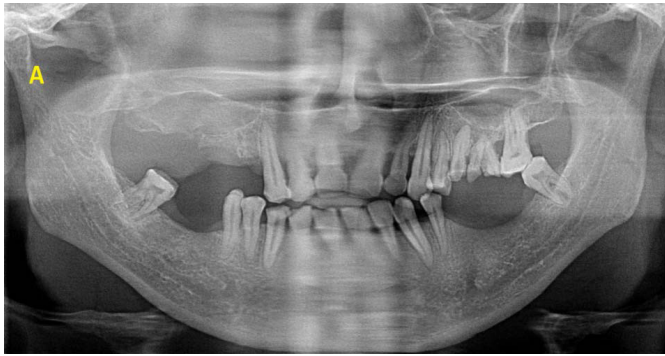


Fig 1 : Panoramic radiograph showing a radioopacity over 16 to 18 region and an ill defined radiolucency in the alveolar region of 16 with erosion of the floor of maxillary sinus.

the right maxillary sinus with an osteolysis of all walls of the maxillary sinus, floor of the right orbit, hard palate and right nasal cavity. Other sinuses like ethmoidal, sphenoidal, and frontal sinuses were also involved (Fig 2 A & B).

Biopsy was performed. H&E-stained sections showed connective tissue infiltrated with tumour islands composed of mucous cells, intermediate cells and epidermoid cells. The predominant cell type was epidermoid cells which showed pleomorphism, hyperchromatism, numerous mitotic figures and multiple prominent nucleoli. At areas, groups of clear cells were also seen (Fig 3 A, B). Cytoplasmic mucin in the tumor cells was demonstrated as cells with magenta-pink colored cytoplasm by mucicarmine stain (Figure 3 C). On immunohistochemistry, the lesion showed positivity for CK7, p63, and negativity for S-100 (Fig 3 D, E, F).

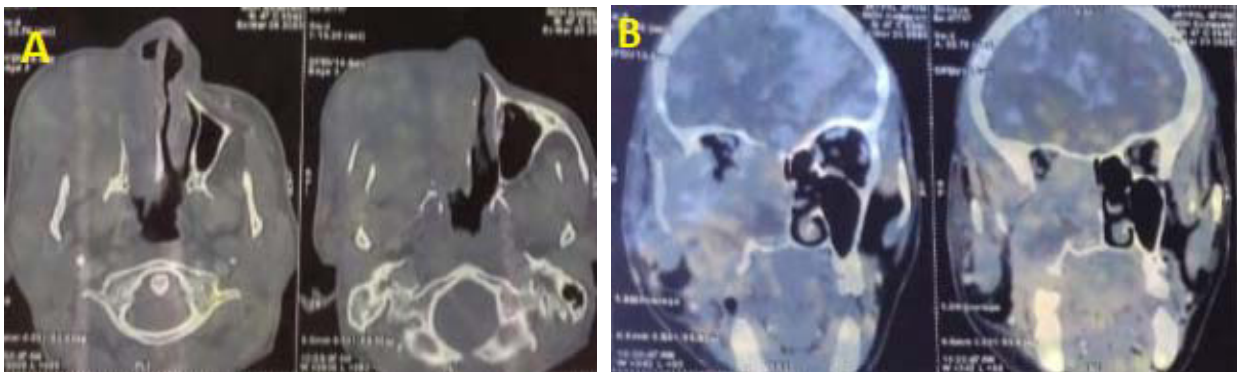


Fig 2: CT scan (axial section) (A) revealing complete obliteration of right maxillary sinus. CT scan (coronal section) (B) showing contrast enhanced lesion involving maxilla, orbital, nasal and palatal region.

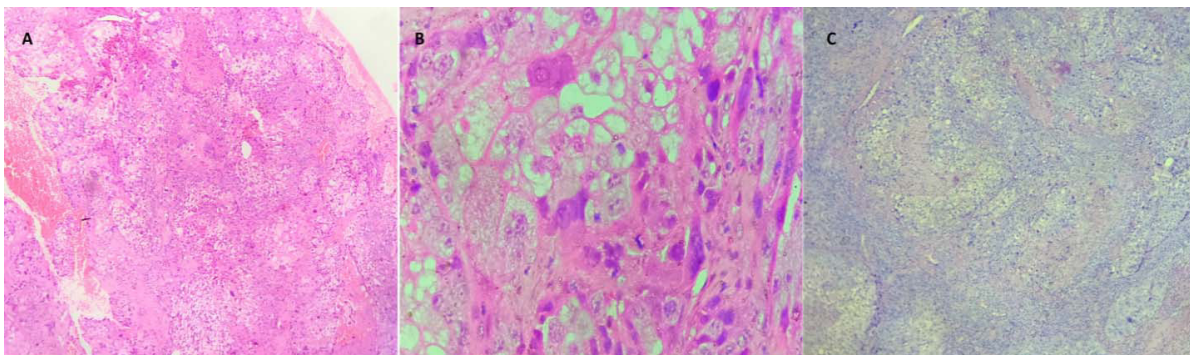


Fig 3 A, B, C: (A) Photomicrograph showing lesion with few cystic spaces and more solid areas predominantly clear and epidermoid cells (H &E, 100x) (B) Extensive degree of cellular atypia (H &E, 400x). (C) Cells stained with mucicarmine stain (mucicarmine stain, 100x)

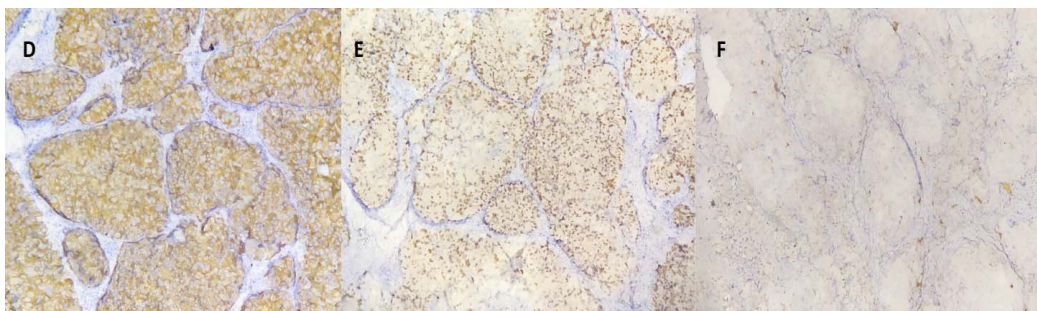


Fig 3 D,E,F: Photomicrograph showing immunohistochemistry staining; (D) diffuse and strong positive immunostaining for CK7 (CK7 stain, 100x). (E) Positivity for p63 (p63 stain, 100x). (F) Negative immunorexpression for S-100 (S100 stain, 100x).



Fig 4: Patient undergoing radiotherapy treatment.

The final diagnosis was suggestive of an intermediate-grade mucoepidermoid carcinoma. The patient was referred to a higher center for further treatment. Since the lesion was highly extensive and locally advanced, radiation therapy and chemotherapy were advised along with palliative care. Figure 4 shows photograph of patient after radiotherapy. Due to covid restrictions, preoperative photographs were not recorded.

CASE REPORT- 2

A 51 year old male patient reported with a complaint of swelling on the palate for 15 years. On examination, a swelling of size 5×4 cm on the palate involving the midpalatine raphe with no surface ulceration was noted. On palpation, the swelling was firm, ten-

der with irregular borders and indurated (Fig 5).

Histopathological examination revealed numerous large and small cystic spaces within the connective tissue stroma. The cystic spaces were lined by mucous cells, epidermoid cells and intermediate cells. Within some of the cystic spaces, an extensive proliferation of these cells was noted. Spilled mucin was seen within many of these cystic spaces. The stroma also showed numerous hyalinized areas (Fig 6&7). Mucicarmine special stain was also done, which highlighted the intracytoplasmic mucin in the tumor cells (Fig 8). On immunohistochemistry, the lesion showed positivity for CK7.

Surgical resection with wide margin and inferior partial maxillectomy was done and the patient was followed up every 15 days for 2 months and later every month for 1 year during which he remained asymptomatic



Fig 5: Photograph showing swelling on the left side of the palate involving midpalatine raphe.

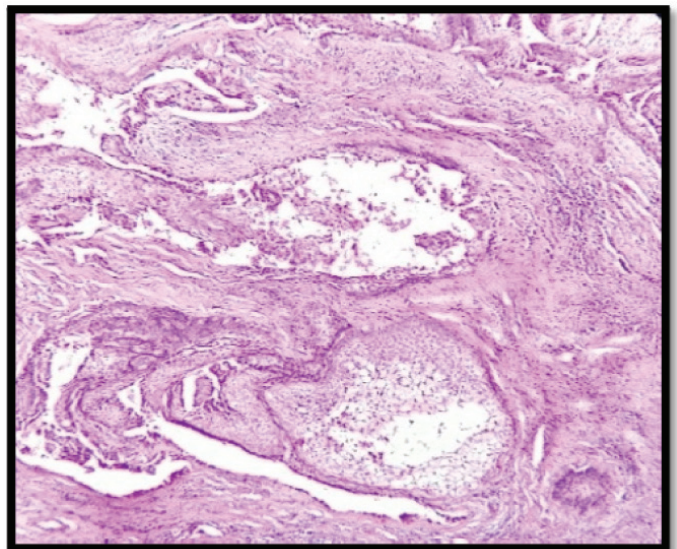


Fig 6: Low grade mucoepidermoid carcinoma composed of several large and small cystic spaces. Spilled mucin is also noted within many of these cystic spaces (H&E stain, 100x).

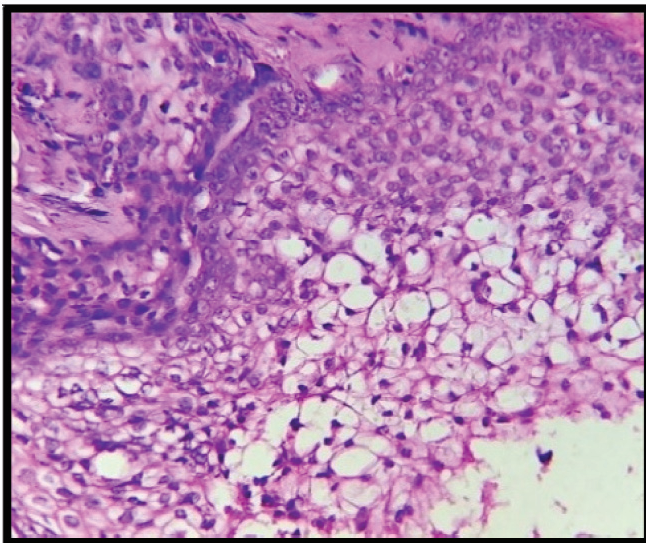


Fig 7: Cystic lumen is lined by mucous cells, epidermoid cells with minimal pleomorphism and occasional intermediate cells (H&E stain, 400x).

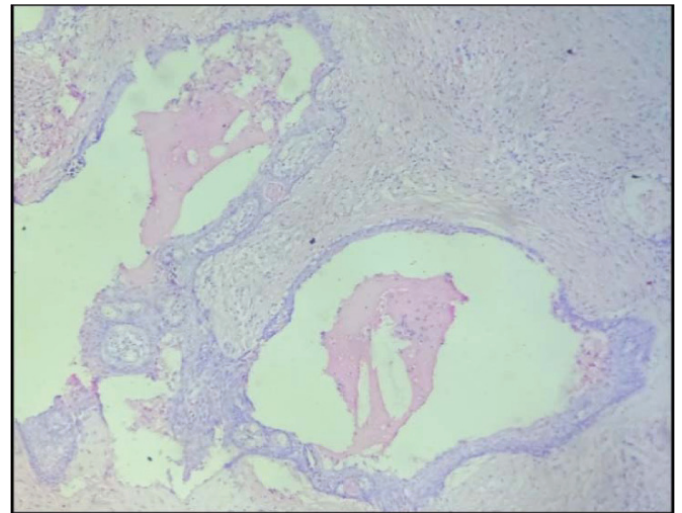


Fig 8: Mucicarmine staining (Mucicarmine stain, 100x)

DISCUSSION

Mucoepidermoid carcinoma (MEC) is a malignant salivary gland neoplasm composed of a mixture of mucous cells and epidermoid cells in varying proportions and in addition to it, intermediate cells are also seen which is believed to be a progenitor cell of both mucous and epidermoid cells.⁶ After several research, its histology and degree of differentiation point towards its malignant behavior and later the WHO classification in 1991 suggested that the term to be changed from "mucoepidermoid tumour" to "mucoepidermoid carcinoma".⁷ Definite etiology of MEC is still unknown. Exposure to therapeutic radiation, presence of foreign materials, genetic predisposition, viral infections, cigarette smoking, cellular phone use etc are considered as causative factors.^{3,8,9}

According to Armed Forces Institute of Pathology (AFIP), the most commonly occurring site of MEC is parotid gland (46.5%); intraorally, palate (17.9%) shows a strong predilection and MEC in maxilla accounts for 0.8%.³ Mucoepidermoid carcinoma arising from mucous glands of maxillary sinus are extremely rare and reports shows that approximately 13% of all malignancies occurring in maxillary sinus.¹⁰ In a review of the National Cancer Database, among the 183 patients with sinonasal-MECs, maxillary sinus (45.7%) was the most common primary site followed by the nasal cavity (41.5%). The majority of patients diagnosed with sinonasal-MEC were white (78.7%) and black patients represented the second most commonly affected race (15.2%).¹¹

MEC occurs over a wide age range from second to seventh decade of life with a slight female predilection.³ Sinonasal malignancies occur twice as often in males as in females and are most often diagnosed in patients 50 to 70 years of age.⁶ Both patients in this case report were males with a mean age of 50 years.

Histopathologically, the mucoepidermoid carcinoma can be categorized as low, intermediate and high grade according to the degree of cytological atypia, amount of cyst formation and relative numbers of mucous, epidermoid and intermediate cells. Even though there is no universally accepted grading system, the most popular ones are: the modified Healy grading, the AFIP grading (recommended by the World Health Organization for grading all salivary gland MEC) and the Brandwein grading system.¹²

Low-grade MEC presents as a slow-growing swelling and shows predominance of mucous-secreting cells with numerous mucin filled cystic spaces.¹¹ In the present study (case 2) MEC was presented as a slow growing swelling of 15 years duration and the histologic picture was suggestive of low grade MEC.

Intermediate grade MEC contains a large number of intermediate cells often with scattered mucous cells and zones of epidermoid cells forming solid islands of the tumor with few cystic elements. Clinically, they are presented as solid and/or ulcerated mass. Compared to low-grade tumors they are fast growing and show some infiltrative behavior.¹² In the first case of the present study, MEC was histologically presented as a solid tumour with numerous tumour islands composed of mucous cells, intermediate cells, and epidermoid cells. The predominant cell type was the epidermoid cell which showed many dysplastic features.

The high-grade tumours have a high ratio of epidermoid cells with very few mucinous cells. These tumours demonstrate high cellular atypia and pleomorphism with a rapid growing behavior and

local tissue invasion even in the early stages. Distant metastasis is also observed in some cases with an unfavorable prognosis.¹³

Mucoepidermoid carcinoma shows immunopositivity for p63, EMA, carcinoembryonic antigen (CEA), and cytokeratin like CK5, CK6, CK7, CK8, CK14, CK18, and CK19. It is negative for CK20, SMA, muscle-specific actin (MSA) and S100. Ralph N. Sams et al reported 100% p63 staining in all 24 cases of MEC. The extensive p63 immunostaining helps in differentiation of MEC from acinic cell carcinoma and oncocytic carcinoma. Epidermoid and intermediate cells in MEC express p63. CK7 expression helps to distinct mucoepidermoid carcinoma from squamous cell carcinoma. Mucoepidermoid carcinomas also express a variety of membrane-bound mucins like MUC1, MUC4, MUC5AC, and MUC5B. Strong positivity for MUC5AC helps to differentiate high-grade mucoepidermoid carcinoma from squamous cell carcinoma.^{14,15,1} In the immunohistochemical analysis of first case, diffuse and strong positive immunostaining for CK7 and positivity for p63 was seen.

Mucicarmine stain, a special stain helps in the diagnosis of MEC, highlights cytoplasmic mucin in the tumour cells. The epidermoid cells of MEC are negative to mucicarmine but the mucous cells show positivity and it indicating the presence of sulphated mucins.¹⁶

Most of the previous reports showing mucoepidermoid carcinomas are best treated by surgery. For low-grade tumours, surgical excision or local resection is the treatment option but intermediate grade and high-grade tumours require wide surgical resection with proper follow-up. Radiotherapy will be done in selective cases or in cases where the surgical option is not possible.³ The patient of the case 1 diagnosed with intermediate grade of MEC was treated with radiation therapy and chemotherapy as the lesion was highly extensive and locally advanced. So that surgical excision was not suggested.

The prognosis of the lesion is determined by clinical stages and histological grades of the tumour. Studies reported that the 5-year survival rate for low-grade lesions is up to 95% and in high or intermediate-grade tumours the ratio is lower than 50%. It has been reported that the recurrence rate is 10% for low-grade tumours and 74 % for high-grade tumours.^{3,19}

Malignant tumours in the maxillary sinus are very difficult to treat and have been associated with poor prognosis. The main reason for this poor prognosis is the close anatomic proximity to vital structures as the skull base, brain, orbit and carotid artery. This complex location makes the complete resection of the tumour a challenging and impossible task. Another reason is mucoepidermoid carcinoma of maxillary sinus may present to be asymptomatic at the early stage and shows symptoms more frequently at later stages once the local invasion has occurred.⁶ Overall, 5-year survival rate of maxillary sinus mucoepidermoid carcinoma is approximately 36% and the early diagnosis is critical for better prognosis of this tumour.¹⁰

CONCLUSION

Although mucoepidermoid carcinoma is one of the most common malignant salivary gland tumours and palate is the most common site for minor salivary gland involvement, its presentation involving maxillary sinus is very rare. Atypical sites, different clinicopathological presentations of the same lesion can mislead the clinicians. In such cases a detailed knowledge about histopathological

features of mucoepidermoid carcinoma is helpful in its early detection and appropriate timely treatment for better prognosis.

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