Case study

Sclerosing Central Mucoepidermoid Carcinoma: Rare Case Series and Review

Abstract:

Mucoepidermoid carcinoma (MEC) comprises approximately 30% of all salivary gland malignancies, making it the most common malignant tumour of the salivary glands. Multiple histologic variants with a wide range of differentiation have been described. Sclerosing MEC (SMEC) is a rare subtype that may be misdiagnosed as a benign reactive condition or low-grade non-SMEC malignancy. The sclerosing variant of central or intraosseous MEC is extremely rare and no cases are reported till date. We report 2 cases of Sclerosing central MEC, in which histologic examination demonstrated relatively well-circumscribed, nonencapsulated tumours composed of extensive central sclerosis and scattered epithelial islands of low-grade MEC. In the second case, the tumour showed similar sclerotic stroma; but the epithelial component was of intermediate grade. A Mayer mucicarmine stain and PAS stain were positive in both the cases and revealed abundant intracytoplasmic mucin. A diagnosis of sclerosing central mucoepidermoid carcinoma was made. A complete resection of the tumour was performed on both the cases and remained disease free to date.

Introduction

Mucoepidermoid carcinoma is the commonest exocrine gland malignancy, accounts for about 34% of the malignant epithelial salivary gland tumors which was first described by Volkmann in 1895.[6] Of this, the central mucoepidermoid carcinoma comprises 3-4% of all MECs and presents with an unknown pathogenesis. The multiple subtypes of MEC are reported which includes unicystic, oncocytic, clear cell and sclerosing. Among these, the sclerosing morphologic variant is an extremely rare entity, first identified by Chan and Saw in 1987.[2],[3]The distinctive feature is an extreme sclerotic stroma that is present in the tumor mass which may obscure their typical morphologic features and result in diagnostic difficulties.[6] Until date, no sclerosing variant of central mucoepidermoid carcinoma has been reported within the literature. This case series documents rare cases of sclerosing variant of central mucoepidermoid carcinoma.

Case Report

Case I

The 35-year-old male patient reported to the outpatient department complaining of a painless swelling in the upper right posterior region of the jaw since one and half months. On examination, intraorally, a solitary swelling was noted on buccal and palatal alveolus with respect to the right posterior maxilla. Swelling was irregular in shape, extending from alveolar region of 14 to tuberosity of maxilla, partially obliterating the buccal vestibule. Palatally, a minimal swelling was noticed extending till midline, the associated palatal mucosa was erythematous. On palpation the swelling was nontender, firm, not fluctuant, not mobile, compressible, and not reducible. Orthopantamogram revealed a single well defined multicystic irregular corticated lesion involving upper right 16, 17 ,18 and tuberosity of maxilla of size approximately 6 cm × 5 cm, resulting in the destruction of right maxillary process involving maxillary sinus. Computed Tomography Scan revealed an evidence of expansile lytic lesion involving alveolar process of maxilla on right side with soft tissue component filling right maxillary sinus suggestive of a destructive lesion.

Based on the clinical and radiological examination, provisional diagnosis of salivary gland malignancy, odontogenic tumor or the connective tissue malignancy was considered. After an incisional biopsy, diagnosis of MEC was established and the patient was subjected to surgery with his consent. During the surgery a large cystic lesion was observed, containing large cystic spaces filled with mucoid material. Complete removal of the lesion was performed, and sent to the Department of Oral Pathology for confirmation of diagnosis.

On gross examination, the lesion was a resected specimen retrieved from the right side of the maxilla involving maxillary sinus. The cut surface showed heterogeneity with some well demarcated cystic area filled with mucin and firm areas at places. (Figure 1)

The tissue was subjected to routine tissue processing procedure and stained with haemotoxylin and eosin. The histopathological examination revealed lesional glandular tissue with numerous cystic spaces filled with mucin. The cystic spaces were lined by numerous clear cells and also mucous cells against the sclerotic background stroma. (Figure 2) The connective tissue stroma was also comprising few areas of dispersed nests and groups of intermediate cells and very few epidermoid cells along with dense irregularly arranged dense bundles of collagen fibres exhibiting areas of hyalinization and the presence of reactive bone formation in many areas. The tumor nests cells displayed clear to eosinophillic cytoplasm, well-defined cytoplasmic membranes. The nests were surrounded by extensive hyalinized stromal sclerosis devoid of lymphocytic infiltration. More than 60% stroma of the examined tissue section was hyalinized. No evidence of perineural invasion or necrosis. The mucin filled cystic spaces and mucous cells showed positivity for PAS and mucicarmine (Figure 3 & 4). Thus, on the consolidation of these histological features the reported case was classified as a Sclerosing variant of low grade central Mucoepidermoid carcinoma.

Case II

The 49-year-old female patient reported to the outpatient department complaining of a swelling in the lower right posterior region of the jaw for the past 2 years. On examination, intraorally, a solitary swelling was noted on the buccal alveolus with respect to the right posterior mandible and measured about 3 x 3 cm in diameter. Swelling was irregular in shape, extending from 46 to the ascending part of the ramus. On palpation, the swelling was tender. The submandibular lymph nodes in association with the swelling were soft, mobile and palpable. Orthopantomogram revealed a multilocular radiolucency with ill-defined borders extending anteroposteriorly from 46 to the ascending part of the ramus, and superioinferiorly from the upper border of the mandible till the mandibular canal. (Figure 6) Computed Tomography scan revealed an evidence of buccal and lingual cortical perforation and bone marrow space involvement approximating mandibular canal.

Based on the clinicopathological examination, provisional diagnosis of osteolytic granulomatous lesion or odontogenic cyst was considered. After an incisional biopsy, diagnosis of MEC was established and the patient was subjected to surgery with her consent. During the surgery, a large tumor mass with a few cystic spaces containing mucoid material was observed. Complete removal of the lesion was performed and sent to the Department of Oral Pathology for confirmation of diagnosis.

On gross examination, the lesion was a solid mass which was firm in consistency exhibiting few mucins filled cystic spaces. (Figure 5)

The tissue was subjected to routine tissue processing procedure and stained with haemotoxylin and eosin. Histopathological examination revealed an unencapsulated lesional tissue with few

nests of tumour cells and multiple cystic spaces filled with mucin dispersed sclerotic background stroma. The cystic spaces were lined by numerous clear cells and mucous cells. (Figure 7) Tumor nests comprising of mucous cells, intermediate cells and epidermoid cells with intervening hyalinized area were also observed. Connective tissue was densely collagenous with irregularly arranged bundles of collagen fibers, also exhibiting areas of hyalinization and focal aggregates of chronic inflammatory cells. (Figure 8) The lesional glandular tissue with a few cystic spaces filled with mucin showed positivity for PAS and mucicarmine (Figure 9& 10). Thus, on the consolidation of these histological features the reported case was classified as a Sclerosing variant of low grade central Mucoepidermoid carcinoma.

Discussion

Mucoepidermoid carcinoma comprises of 16% of all salivary gland's tumors and approximately 30% of salivary gland malignancies.[2] It is most commonly seen in women, with the highest incidence in third and sixth decades of life.[6] The lesion usually demonstrates highly variable clinical behavior ranging from slow to indolent to locally aggressive and highly metastatic tumors. Radiographic appearances largely depend on the grade and presents as a radiolucent lesion. Histologically, MEC is characterized by three main cell types: Epidermoid, mucin-producing and intermediate cells originating from the epithelial lining of ducts and is graded into low, intermediate and high grades based on the predominant cell type.[6],[2]

3-5% of mucoepidermoid carcinomas comprised of the central variant and is thus, a rare phenomenon. Lepp in 1939 reported the first case of central mucoepidermoid carcinoma of the mandible.[1] It is seen commonly in the mandible (82%)**,** having a female predilection and unknown pathogenesis. There is no definitive hypothesis about the pathogenesis of central MEC. Several theories have been described, including: (1) mucous metaplasia and neoplastic transformation of the epithelial lining of an odontogenic cyst; (2) entrapment of the submandibular, sublingual, or retromolar mucous glands during embryonic development within the mandible, which subsequently undergo neoplastic transformation; (3) iatrogenic entrapment of minor salivary glands; (4) neoplastic transformation of maxillary sinus epithelium; and (5) remnants of the dental lamina.[4]

The criteria for the diagnosis of central MEC include cortical bone void of perforation by tumor invasion, radiological evidence of bone destruction, and histopathological verification. Radiographic expression of central MEC consistently shows bone destruction with a multilocular or cystic-like radiolucent appearance. Also, this tumor has the potential to form hard tissue and be expressed as a mixed lesion.[7]

Based on the considerable variation existing in the type, distribution, and growth pattern of MEC cells, the histopathologic appearance of MEC will differ and exhibit as: conventional, sclerotic, unicystic, oncocytic, sebaceous, clear cell, spindle, and psammomatous types.[2] Amongst these, the sclerosing type of MEC is an extremely rare entity, more so when in combination with the central variant and in this case series, two sclerosing central mucoepidermoid cases is described at two different sites, the maxilla and mandible.

As its name suggests, SMEC is characterized by an intense central sclerosis that occupies the entirety of an otherwise typical tumor, frequently with an inflammatory infiltrate of plasma cells, eosinophils, and/or lymphocytes at its peripheral regions.[9] The possible pathogenetic mechanisms causing this type of sclerosis are tumour infarction and mucin extravasation.[6] The mucin acts as a foreign material, resulting in fibrosis that forms as an attempt to wall-off the mucin.

The sclerosis associated with these tumors may obscure their typical morphologic features and result in diagnostic difficulties. Some major salivary gland lesions show similar sclerotic stroma, and these lesions include sclerosing polycystic adenosis, hyaline clear cell carcinoma, malignant mixed tumor, sclerosing sialadenitis and polymorphous low-grade adenocarcinoma. [5] Of all the histological features observed in SMEC, a central keloid-like sclerosis rimmed by peripheral lymphoid infiltration is unique enough to distinguish SMEC from the other sclerotic salivary lesions. [5] In our case series, the coupling of such a sclerosing pattern in a central variant was an unusual phenomenon that was observed. Neck dissection is recommended in all cases except in those of low-grade small tumours. [8] Prognosis is dependent on grade with low grade tumours having 90-98% survival and low recurrence rate, compared to 30-54% surviving and a very high local recurrence rate for high grade tumours.

Conclusion:

SMEC is a rare variant of MEC that may mimic benign conditions. Although most cases are low grade tumors, histologic grading should always be attempted for prognostic purposes and possible adjuvant therapy. Central mucoepidermoid carcinoma of the mandible occurs rarely and can be misdiagnosed radiographically.
Late recurrences and metastases are common; hence, prolong follow-up is required. In our study, both cases have not reported with any recurrences till date and are under follow up.

Reference:

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CASE 1

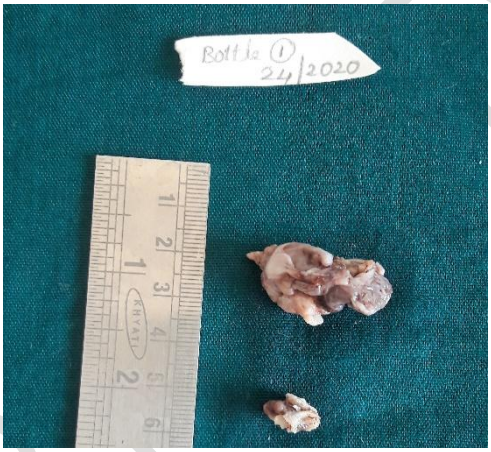


FIGURE 1: On gross examination, the lesion was a solid mass which was firm in consistency.

FIGURE 2: Hematoxylin and eosin-stained section revealed lesional glandular tissue with numerous cystic spaces filled with mucin. The cystic spaces were lined by numerous clear cells and also mucous cells against the sclerotic background stroma (10x magnification)

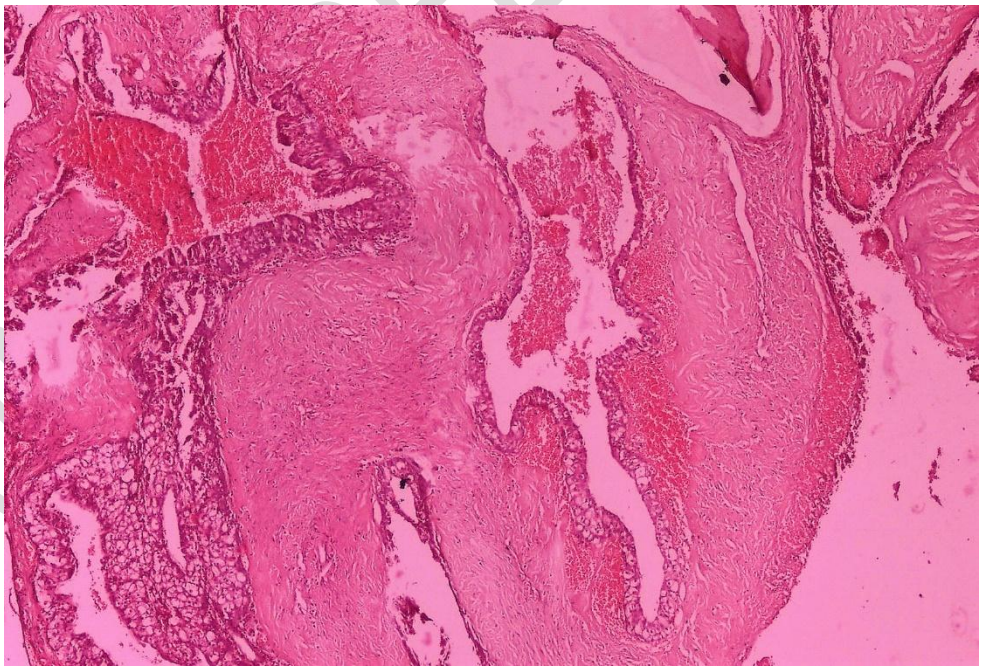
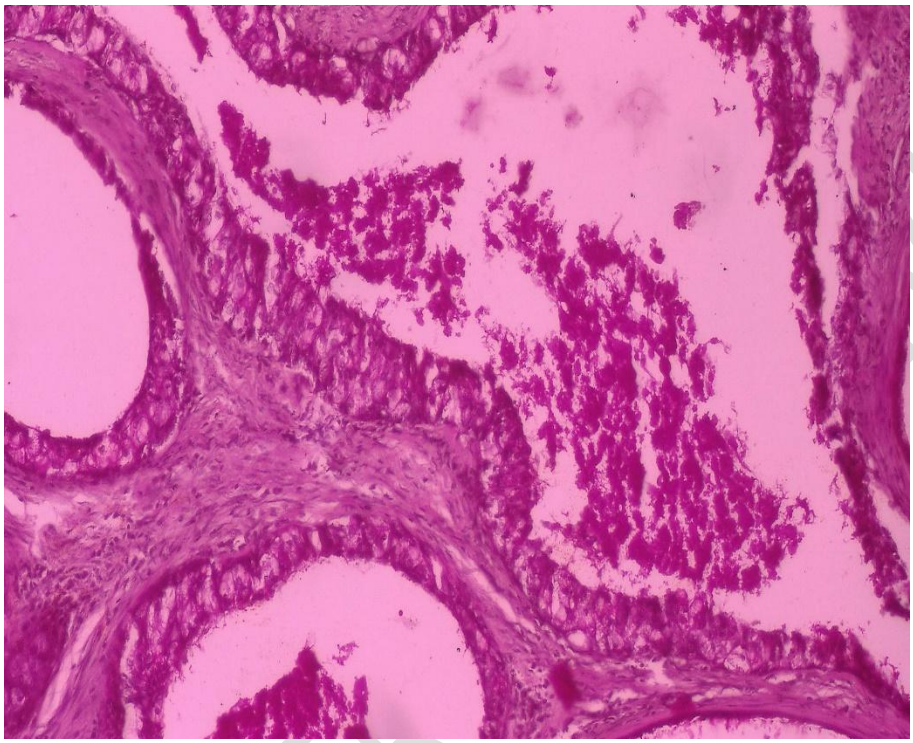


FIGURE 3: The mucin filled cystic spaces and mucous cells showed positivity for PAS (40x magnification)



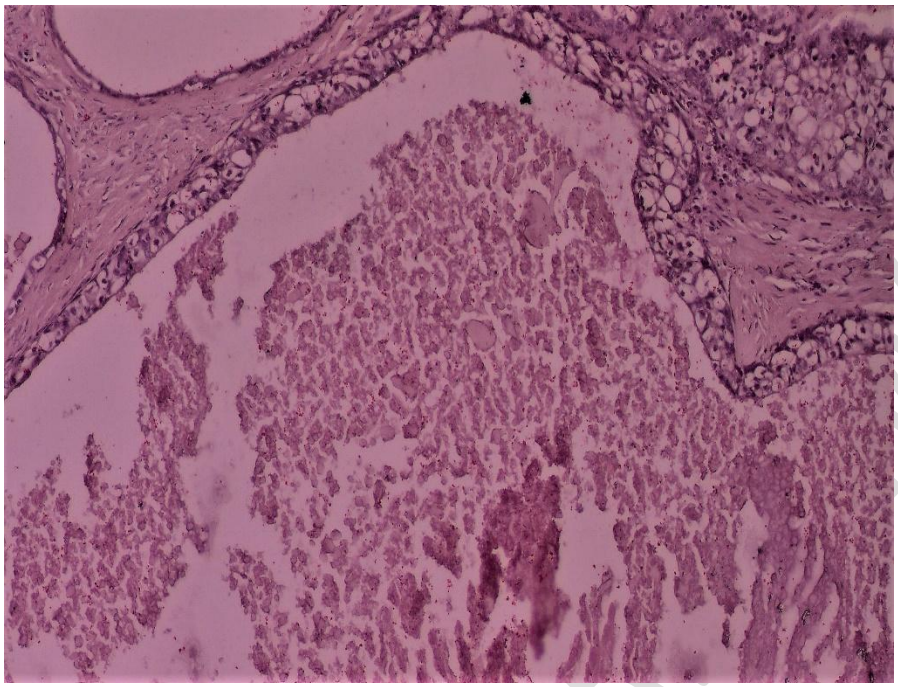


FIGURE 4: The mucin filled cystic spaces and mucous cells showed positivity for mucicarmine (20X magnification)

CASE 2

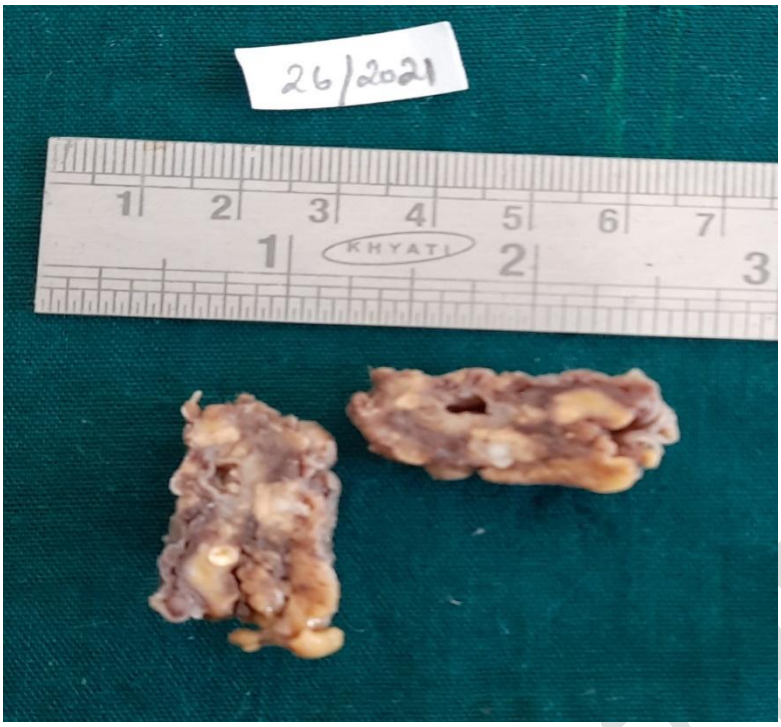


FIGURE 5: On gross examination, the lesion was a solid mass which was firm in consistency with cut surface showing cystic spaces.

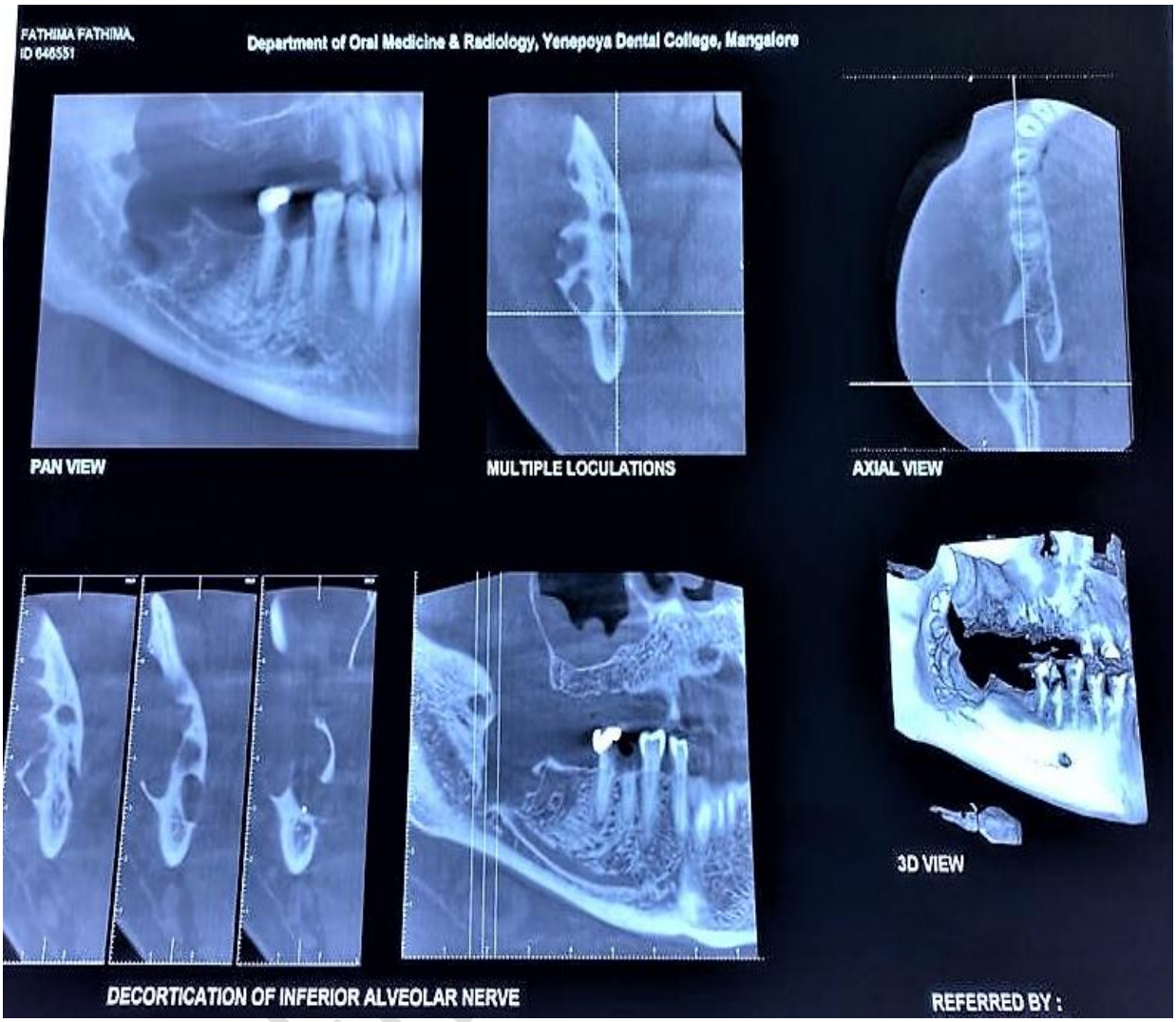


FIGURE 6: Orthopantomogram revealed a multilocular radiolucency with ill-defined borders extending anteroposteriorly from 46 to the ascending part of the ramus, and superioinferiorly from the upper border of the mandible till the mandibular canal. Computed Tomography scan revealed an evidence of buccal and lingual cortical perforation and bone marrow space involvement approximating mandibular canal.

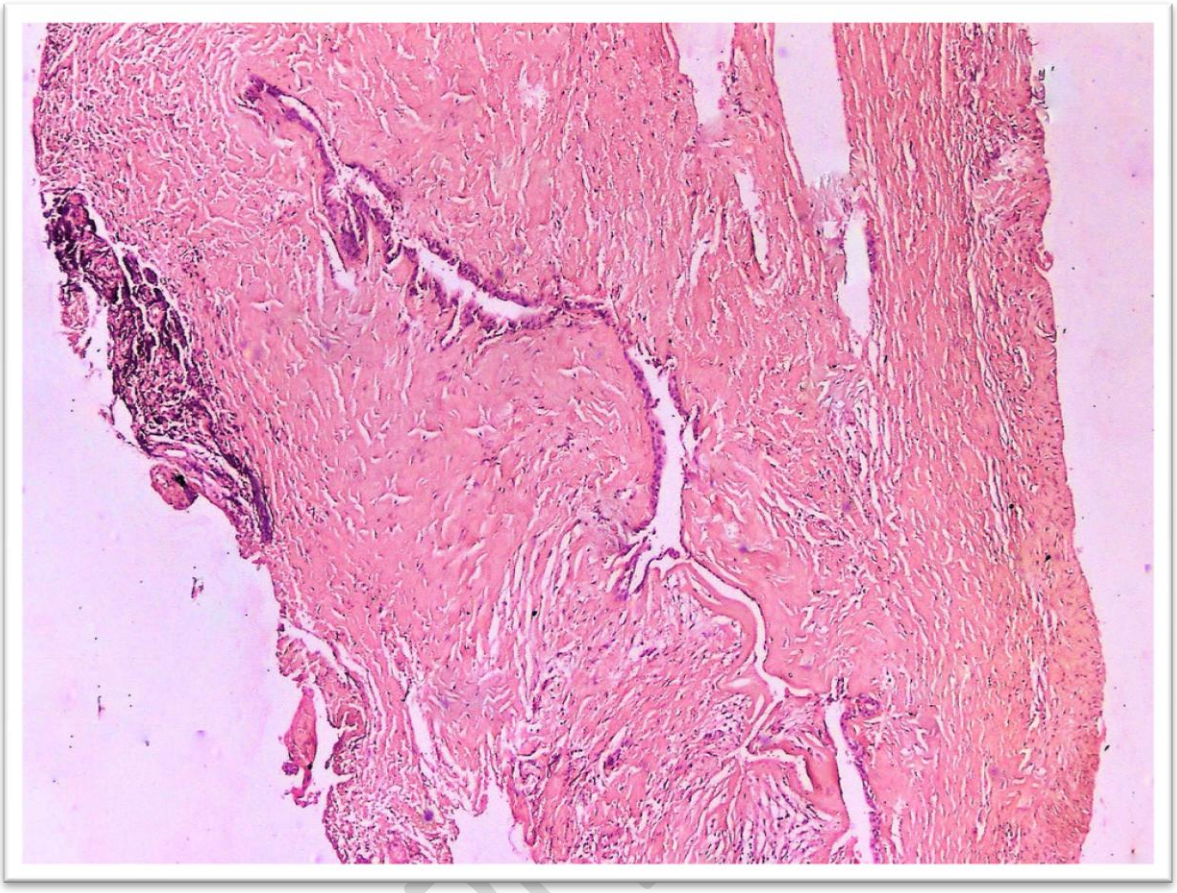


FIGURE 7: Hematoxylin and eosin-stained section revealed unencapsulated lesional tissue with few nests of tumour cells and multiple cystic spaces filled with mucin dispersed sclerotic background stroma. (10x magnification)

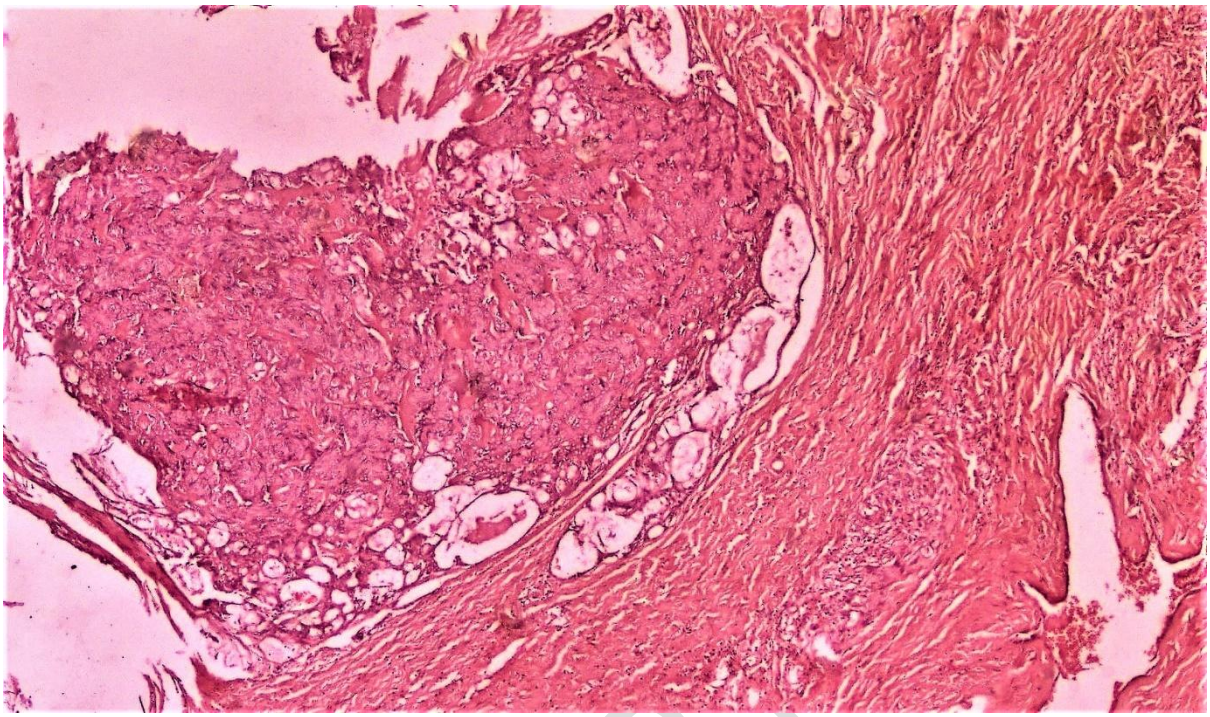


FIGURE 8: Hematoxylin and eosin-stained section revealed tumor nests comprising of mucous cells, intermediate cells and epidermoid cells with intervening hyalinized area were also observed. Connective tissue was densely collagenous with irregularly arranged bundles of collagen fibres, also exhibiting areas of hyalinization and focal aggregates of chronic inflammatory cells

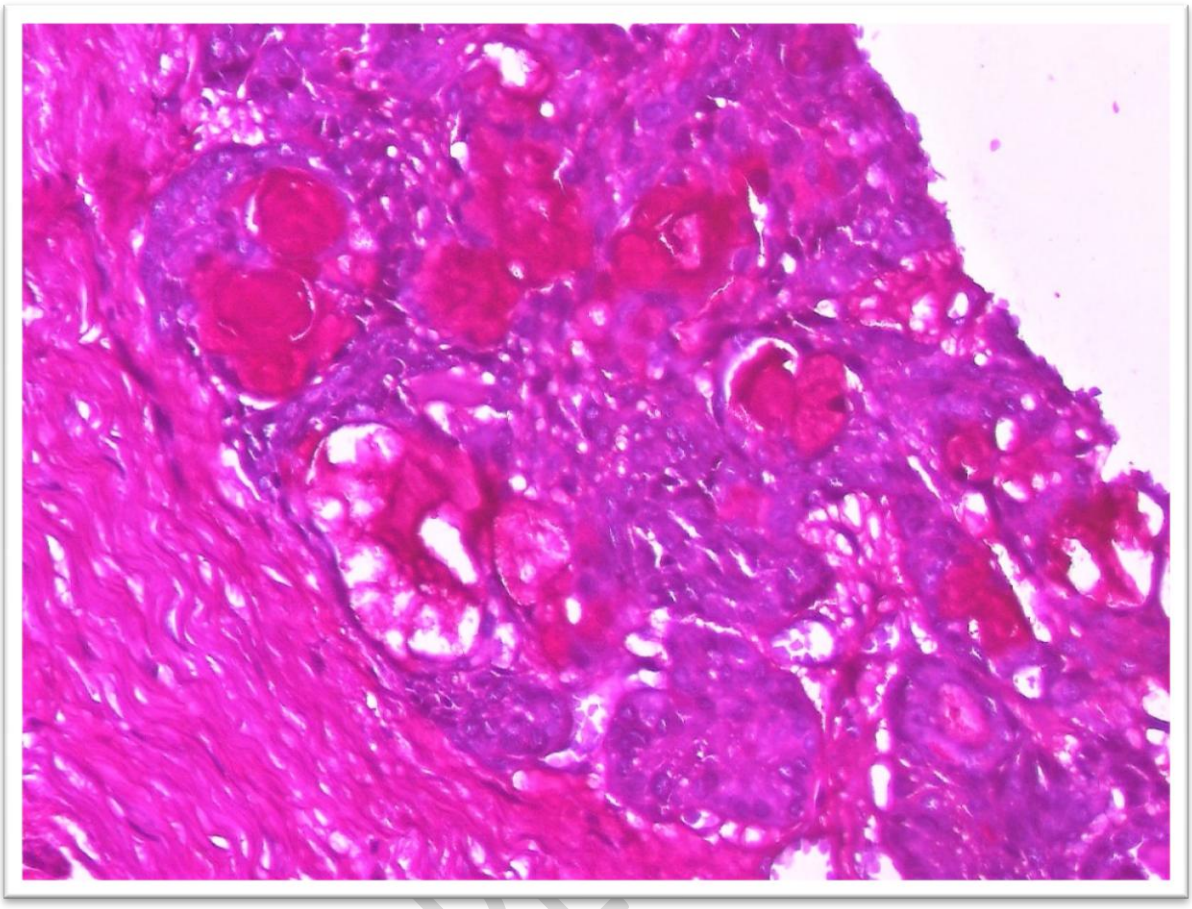


FIGURE 9: The mucin filled cystic spaces and mucous cells showed positivity for PAS (40x magnification)

FIGURE 10: The mucin filled cystic spaces and mucous cells showed positivity for mucicarmine (40x magnification)