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RESEARCH ARTICLE

MUCOEPIDERMOID CARCINOMA OF MINOR SALIVARY GLAND IN BUCCAL MUCOSA - A RARE CASE REPORT

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ABSTRACT

Mucoepidermoid carcinoma is the most common malignant tumor of the salivary glands. It is the most common malignant tumor of the parotid gland and the second most common malignant tumor of the submandibular gland, after adenoid cystic carcinoma. (Brad W. Neville, 2002) Mucoepidermoid carcinoma appears as asymptomatic swellings in minor salivary glands, being the second most common site of occurrence after the parotid gland, most commonly located on palate, followed by retromolar area, floor of mouth, buccal mucosa, lips, and tongue. (Fatih Sengul *et al*., 2013) Only few cases have been reported in literature regarding the MEC's of minor salivary gland tumors in buccal mucosa. (Deepak *et al*., 2014) We report a case of Mucoepidermoid carcinoma of minor salivary gland in a 26yr old female patient. She presented with swelling in the left buccal mucosa, which was noticed 6 months back and had gradually increased to its present size. In children and adolescents, MECs have a female predilection and occur most commonly on the hard and soft palate or both and rare in buccal mucosa. The surgical excision of the swelling was successful with no recurrence reported. The evaluation, diagnosis and treatment of a mass occupying this territory of minor salivary glands represent intellectually stimulating diciplines because of the relative paucity of theses lesions in these anatomic sites.

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INTRODUCTION

The mucoepidermoidcarcinomais one of the most common salivary gland malignancies. Because of its highly variable biologic potential, it was originally called mucoepidermoid tumor (Brad, 2002). In 1945, Stewart *et al* introduced the term Mucoepidermoid to defined it as salivary gland tumor characterized by a mixed pattern of two main cell types: Epidermoid and mucus producing cells. However, third cell type, intermediate cell, which is not mucous or fully epidermoid, is often present. Subsequent metastases of few of the previously benign tumors have led to all Mucoepidermoidtumors being considered carcinoma (Jeetendra Purohit, 2002). MEC is thought to arise from pluripotent reserve cells of the excretory ducts of salivary gland that have the potential to differentiate into squamous, columnar, mucous cells, clear cells, epidermoid cellsand also reveal conspicuous cystic development (Dr. Kandukuri Mahesh Kumar, 2014). Mucoepidermoid carcinoma displays 29% with 34% of malignant tumors arising in both a minor &major salivary glands (Omar, 2016). Although no specific etiologic factors have been identified, exposure to ionizing radiation has been reported in some cases (Mahesh Kumar Ranganath, 2011).

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The tumor usually forms as a painless, fixed, slowly growing swelling of widely varying duration that sometimes goes through a phase of accelerated growth immediately before the clinical presentation. The gross appearance varies with the grade of the tumor. Pain and tenderness along with rapid enlargement may be seen with highgrade lesions (Dr. Kandukuri Mahesh Kumar, 2014).

Case Report

A 26 year old female patient reported to the department of oral medicine and radiology, Meenakshi Ammal dental college Chennai with a chief complaint of a painless swelling in left side of cheek since 6 months. On eliciting the history she was apparently normal 6 months back and she noticed a small swelling which had developed spontaneously in the left buccal mucosa and which had gradually increased to the present size. There was no history of discharge from the swelling and she gave a history of difficulty on consumption of hot substances. The past medical history and past surgical history were not contributory. She was moderately nourished and vitals were within normal limits (Fig. 1). On extra oral examination, there was a mild diffuse swelling evident in the left lower one-third of face below the level of occlusal plane behind the left

commissure of lip. The skin over the swelling was pinchable, normal color as adjacent region, smooth and the swelling was soft in consistency and non- tender. No palpable cervical lymph nodes (Fig. 1).

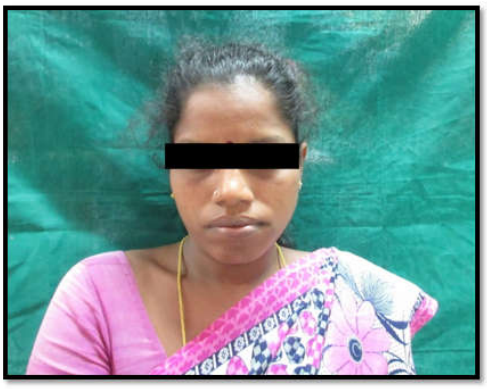


Fig.1. Profile

On intra oral examination, well defined solitary sessile swelling evident in the left buccal mucosa, at the level of occlusal plane measuring 3x2.5cm in its greatest dimension, extending Anteriorly 1cm away from the commissure of lip; Posteriorly adjacent to the distal aspect of 35 region; Superiorly at the level of occlusal plane of 35and36region; Inferiorly 1cm above the lower vestibular sulcus. The surface over the swelling was mildly pale, lobulated and smooth with no visible pulsations. (Fig no: 2, 3) Presence of a single flat well circumscribed greyish black macule 0.3x0.2cm in dimension approximately evident in left buccal mucosa adjacent to buccal aspect of 36 region. (Fig no: 4)On palpation, the margins of the swelling were well defined, lobulated (3 lobules), soft to firm in consistency, mobile and not fixed to the underlying mucosa. The swelling was compressible, not reducible, slip sign was positive. Diascopy being negative. She denied any symptoms attributed to the mass. Based on the history and clinical examination a provisional diagnosis of benign soft tissue tumor of left buccal mucosa was made and differential diagnosis of lipoma, mucocele and salivary gland neoplasm were considered. Guided fine needle aspiration cytology was performed and a yellow viscous fluid was obtained but the results were inconclusive. Routine Hematological investigations were within normal limits. (Fig no 5)

Fig. 2. Right buccal mucosa

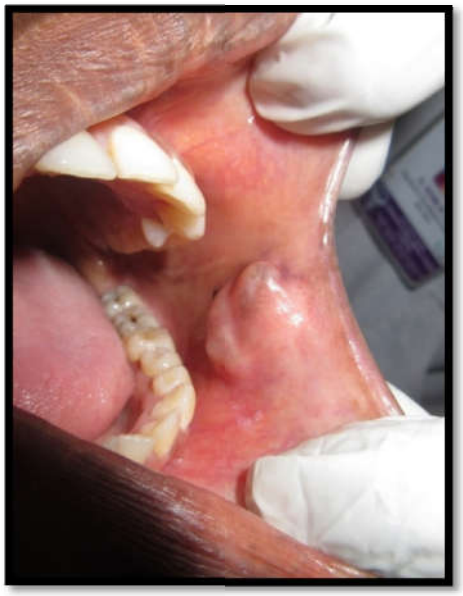


Fig. 3. Left buccal mucosa

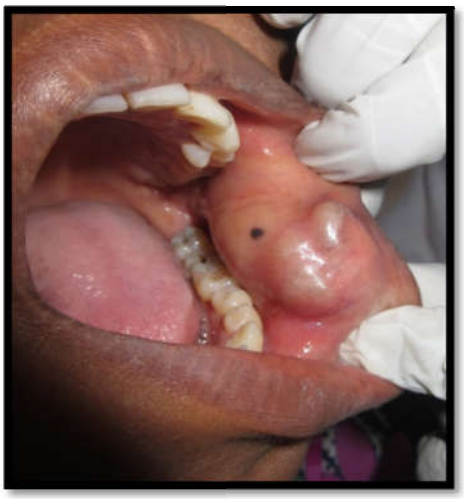


Fig. 4. Nevi and Swelling

Fig. 5. Aspiration

High resolution ultrasound of left buccal mucosa revealed, a well-defined hypoechoic mass with a hyperechoic focus measuring 1.7x0.7cm just behind the left commissure of lip, (Fig no 6) with no evidence of calcifications seen within, and a small amount of fluid collection seen around the periphery.(Fig no 7,8) Internal vascularity was seen within the mass. (Fig no 9, 10) Above features were suggestive of benign minor salivary gland tumor of left buccal mucosa. Since the clinical and ultrasonic examination appeared more towards a benign entity, surgical excision with considerable wide margins was performed and the obtained specimen was subjected to histopathological examination. (Fig no 11) Histopathological examination, revealed large irregular cystic spaces, lined by varying thickness of epithelium which are cuboidal, basaloid

cells with hyperchromatic nuclei, resembling intermediate cells, mucous cells, with foamy cytoplasm along with microcystic spaces.

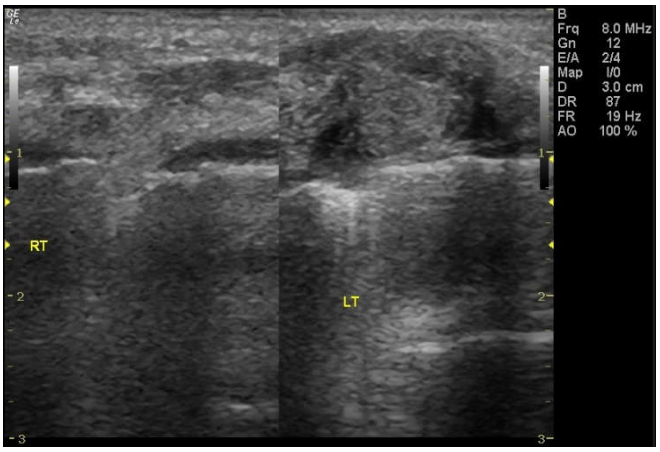


Fig. 6. USG Image: right and left comparison

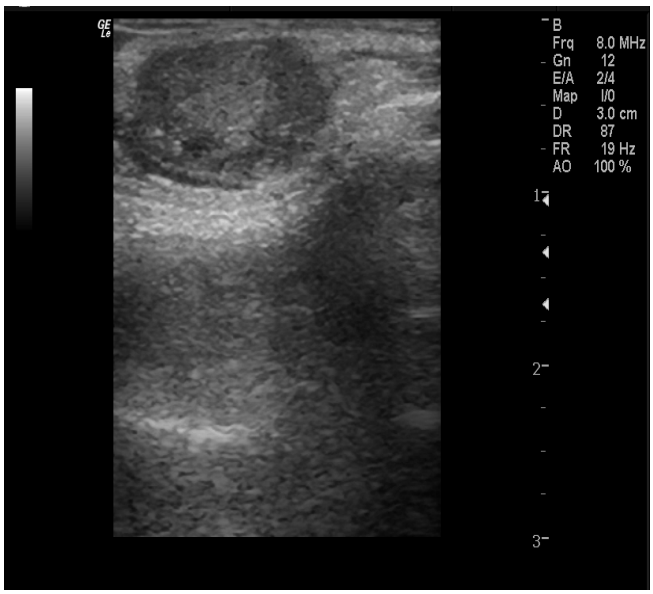


Fig. 7. USG image- left side

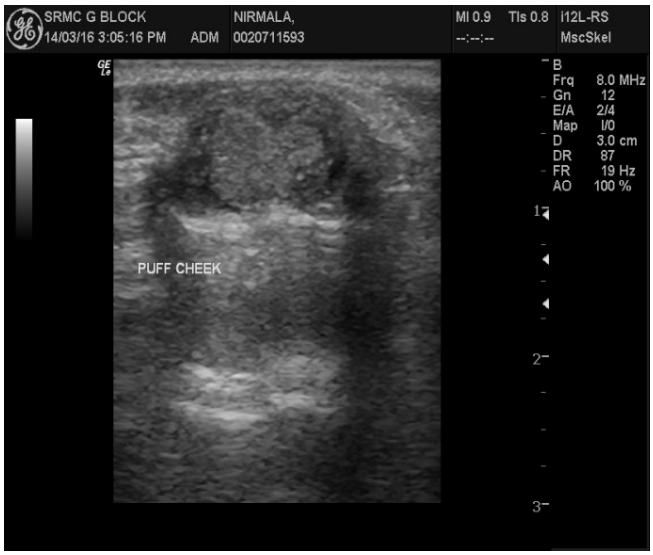


Fig. 8. Puff cheek – To deleniate the borders

Sheets of intermediate cells, few epidermoid cells with vesicular nuclei are also seen along with eosinophilic material within the cystic spaces. Few areas of salivary acini and surface epithelium are also seen.

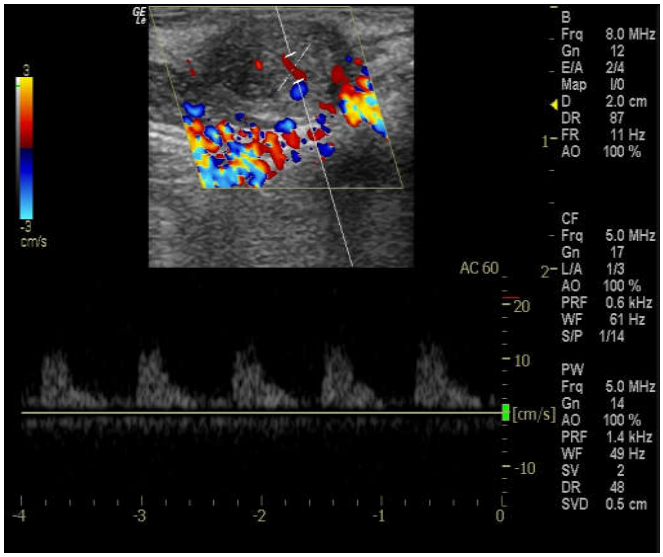


Fig. 9. Color dopler

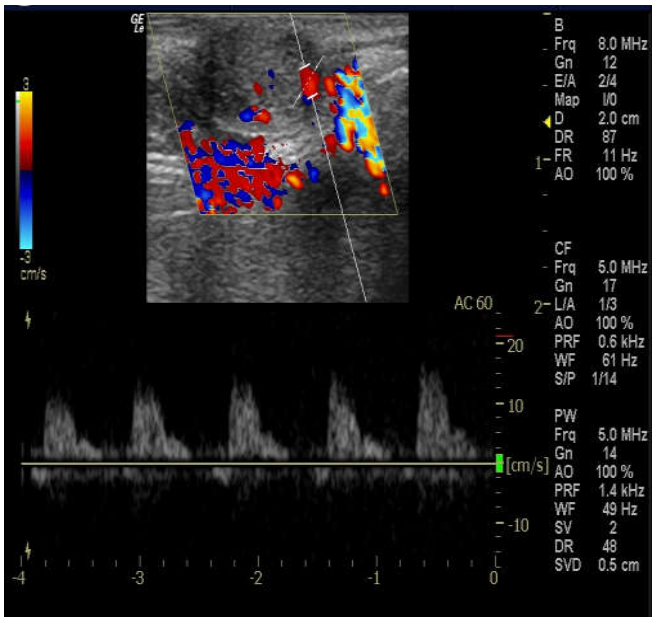


Fig. 10. COLOR DOPLER

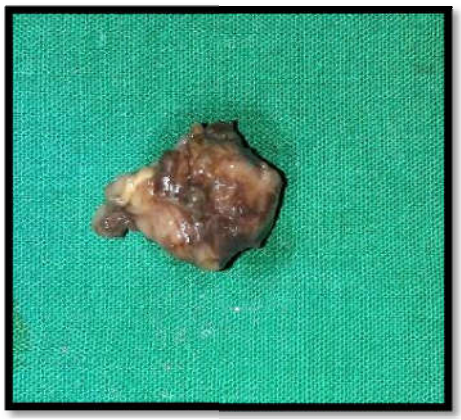


Fig. 11. Specimen obtained after surgical excision

Features were suggestive of Mucoepidermoid carcinoma-intermediate grade. (Fig no 12, 13) Hence a final diagnosis of Mucoepidermoid carcinoma -intermediate grade of left buccal mucosa was made.

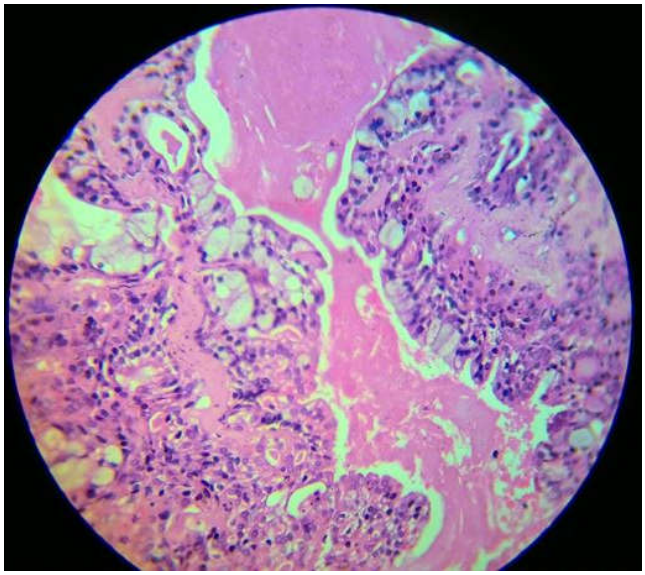
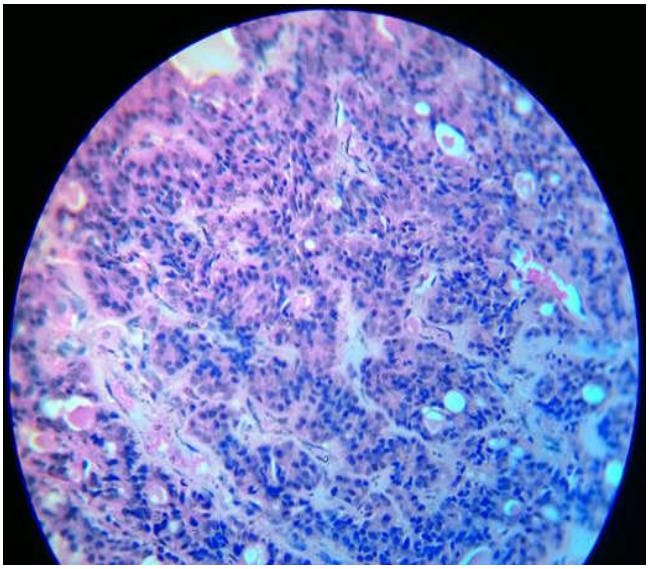
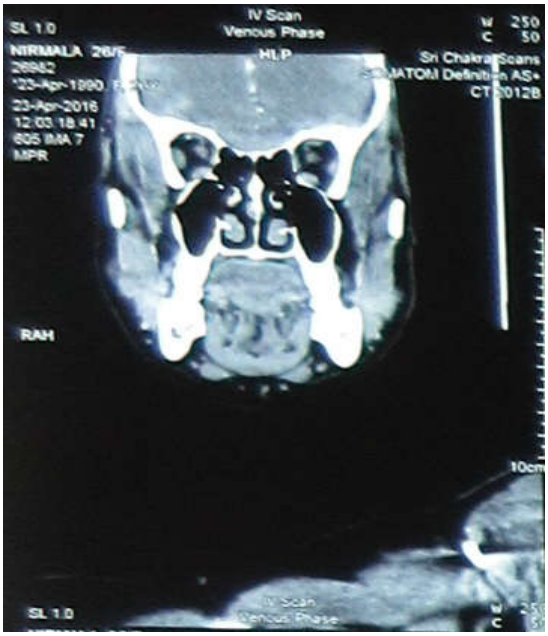



Fig. 12. Histopathological image 40x Fig.13. Histopathological image 10x



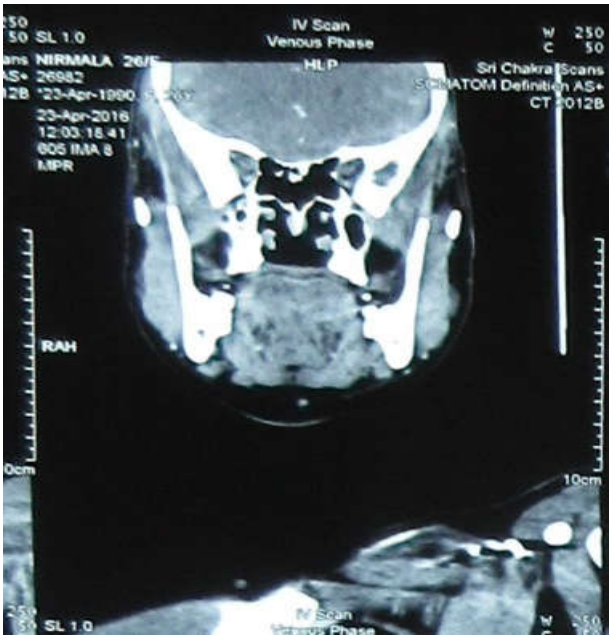
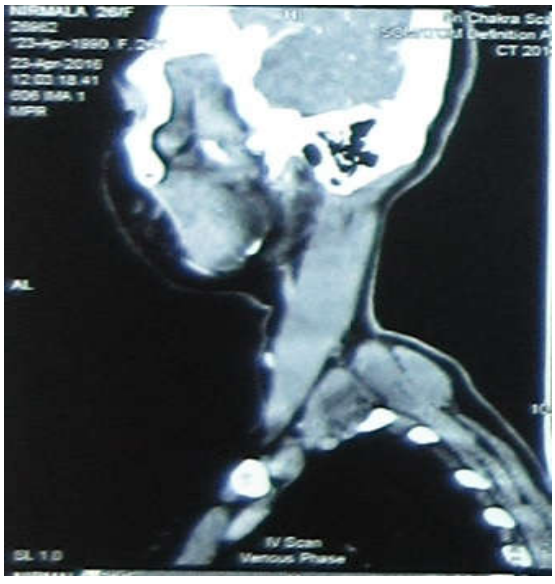


Fig. 14, 15. CT Contrast – head and neck (Coronal Section)



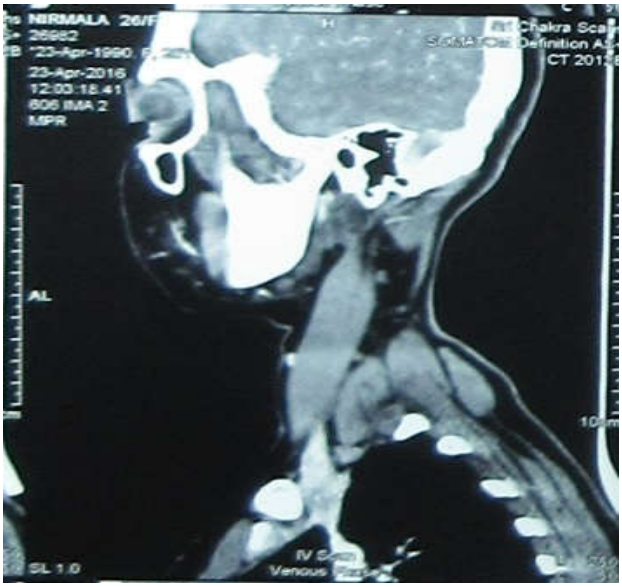


Fig. 16, 17. CT contrast – head and neck (Sagittal Section)

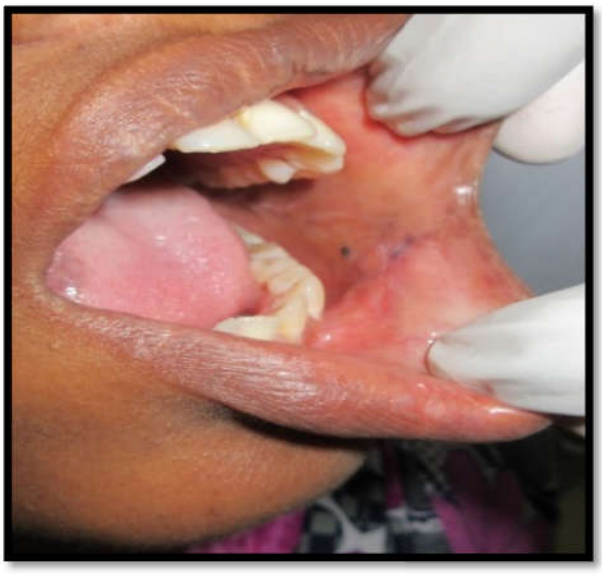


Fig. 18. Follow up 3months

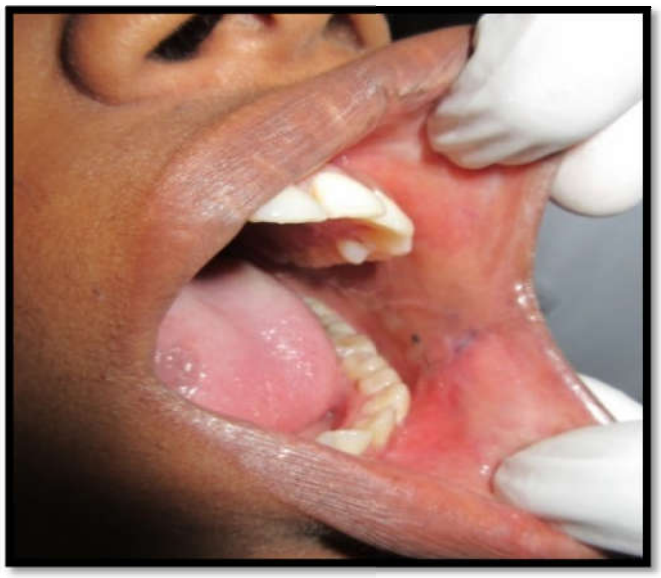


Fig.19. 6 Months follow up

On follow up the patient was subjected to contrast computed tomography of head and neck which revealed, no residual lesion with no evidence of nodal metastasis. (Fig no 14, 15, 16, 17) Patient is under follow up for past one year with no recurrence reported (Fig no 18, 19).

DISCUSSION

Mucoepidermoid carcinoma (MEC) was first described by Volkmann in 1895, which was further elaborated upon by Stewart in 1945 as a Mucoepidermoid tumor. Foot and Frazell (1953), named the tumor as MEC. The MEC can involve with major salivary glands, minor salivary glands, and can also present as an intraosseous tumor frequently called as central MEC (Brandwein, 2011). Mucoepidermoid carcinoma (MEC) is the most common malignant tumor of the salivary glands (12–29%), while for many authors it also represents the most common type of malignancy for minor oral salivary glands (Spiro, 1978 and Brookstone, 1992). MEC is thought to arise from pluripotent reserve cells of the excretory ducts of salivary gland that have the potential to differentiate into squamous, columnar, mucous cells, clear cells, and epidermoid cells (Wedell, 1997). When MEC arises in minor salivary glands it can be located on the palate, in the retromolar area, the floor of the mouth, the buccal mucosa, the lips and the tongue (Noda, 1998; Jansisyamont, 2002 and Chaudry, 1984).

Minor salivary gland carcinomas are a heterogeneous group of malignancies. The etiology remains unknown. Unlike major salivary glands (parotid and submandibular) where only a minority (20-30 per cent) of tumors are malignant, most tumors arising from the minor salivary glands are carcinomas (50-60 per cent) (Parsons, 1996; DM Hyam, 2004 and Castro, 1972). Minor salivary gland tumors (benign and malignant) are a rare clinical entity. Despite this they retain importance as a potential diagnosis for many lesions in the oral cavity, especially lesions arising from the buccal mucosa. Salivary gland carcinomas (major and minor) represent around 3 per cent of all head and neck malignancies, with minor salivary glands accounting for 14-22 per cent of all salivary gland carcinomas. Unlike parotid and submandibular salivary gland tumors the majority of tumors arising from the minor salivary glands are malignant (Seifert, 1986).

The greatest incidence occurs between the third and sixth decade of life, but it may occur at any age. It is the most common malignant salivary gland tumor to arise in children and adolescents of <20 years of age and it has a slight predilection for women (Castro, 1972; Seifert, 1986 and Brandwein *et al*., 2001). The first classification of salivary glands tumors, developed by the World Health Organization WHO in 1972 was revised under the supervision of Prof. Seifert in 1991 (DM Hyam, 2004). The proportion of malignant tumors of the minor salivary glands is very high (50%) – the preferential locations being the floor of the mouth (90%), the retromolar trigone (90%), the tongue (85%) and the lower lip (60%). In contrast, neoplasms of the upper lip are usually benign tumors (75%). The etiopathogenesis of MSGTs remains unclear (Brad W. Neville, 2002). In this context, it has not been possible to correlate smoking to salivary gland cancer, and exposure to ionizing radiation to date has been the only confirmed risk factor for tumors of the salivary glands (Olivia Pons Vicente, 2008). In our review, the preferential location of MSGTs was the posterior third of the hard palate (33.2%), followed by the soft palate (16.7%), the upper lip mucosa (16.7%), cheek mucosa (11.1%), and retromolar trigone (11.1%). A single case was located in the lower lip mucosa (5.6%), with another case in the tuberosity of the upper maxilla (5.6%). Thus, 49.9% of the MSGTs were located in the palate, and 94.1% of the total palatal MSGTs were benign (Olivia Pons Vicente, 2008).

The clinical course of minor salivary gland carcinomas is variable and often characterized by late relapse many years after treatment (DM Hyam, 2004). The MEC in minor salivary glands are generally slowly developing lesions which are asymptomatic with a history lasting from 1½ to 10 years (Parsons, 1996). The most frequent clinical presentation of benign MSGT is in the form of a well defined, smooth and uniform nodular tumor with a normal overlying surface color. The lesion is typically asymptomatic and displaceable, usually single, and without adherence to either superficial or deep layers (Olivia Pons Vicente, 2008). Often lesions have been present for many months, or even years, with a history of asymptomatic slow growth prior to diagnosis. Lesions may present submucosally as well as being overtly ulcerative. The clinical data most suggestive of malignancy are pain, adherence to deep or superficial layers, epidermal involvement and/or

ulceration, and the presence of neck adenopathies (Olivia Pons Vicente, 2008). Some of the MEC present as bluish or red-purple, fluctuant, smooth surfaced mass, which appear very similar to mucocele (Dr. Kandukuri Mahesh Kumar, 2014). The majority of patients with early stage diseases are usually cured although local recurrence and distant metastases are well documented to occur in patients with advanced diseases. (Hyam *et al*., 2004) The diagnosis of MSGTs is based on the clinical history and physical exploration, supported by complementary techniques such as magnetic resonance imaging (MRI), computed tomography (CT) alone or combined with sialography and fine needle aspiration biopsy (FNAC). The combination of some of these techniques is able to offer a tentative diagnosis that posteriorly must be confirmed by the corresponding intraoperative histopathological study (Olivia Pons Vicente, 2008). A cytological study based on FNAC of salivary gland lesions reported histopathological correlation in 40% of the benign neoplasms and in 80% of the malignant lesions, while Chan *et al* reported a diagnostic accuracy of 77% (Olivia Pons Vicente, 2008 and Chan, 1992). But in our case the results were inconclusive. The 46% of MEC's occurring intraorallyin the minor salivary glands arise in a variety of location including ectopic salivary gland tissue (Olivia Pons Vicente, 2008). In the literature the histopathological grading criteria of MEC remain controversial (Triantafillidou, 2006). M.S Brandwein *et al* (2001) classified into low, intermediate or highmalignancy grade based on five parameters: proportionof cystic and solid elements, neural invasion presence,necrosis, anaplasia and mitotic rate (Brandwein, 2001 and Triantafillidou, 2006), Low-grade tumors commonly develop a nesting pattern with multiple well-circumscribed squamous nests containing numerous clear cells. Many low-grade tumors, especially in the minor salivary glands, contain a prominent mucin-secreting component composed of columnar cells lining cystic spaces (Waldron, 1988 and Brandwein, 2000). Intermediate-grade tumors are less cystic and show a greater tendency to form large, more irregular nests or sheets of squamous cells and often have a more prominent intermediate cell population. High-grade tumors are predominantly solid, with greater degrees of atypia, similar to squamous cell carcinoma (Brandwein, 2001 and Triantafillidou, 2006). MECs are histologically graded as low (mucous cells-cystic pattern), intermediate (mucous and intermediate cells) or high (squamous cells-solid pattern). Our case histopathologically diagnosed as intermediate grade.

Other suggested grading criteria had included the degree of maturation of various cellular components, mitotic rates, presence or absence necrosis, neural invasion and bony invasion as they are proposed by WHO (Seifert, 1991). Auclair *et al* (1992) studied the grading criteria of MECs presenting 143 cases of MECs of minor salivary glands. The clinical features suggesting aggressive behavior were short duration presence of clinical symptoms and location of tumor in the tongue and the floor of the mouth (Triantafillidou, 2006). Routine neck dissection is rarely warranted as the incidence of nodal metastases is low (Hyam, 2004). Radical surgery is the treatment of choice for all highgrade MECs of low/ intermediate-grade that are large and involve the bone (Caccamese, 2002). Adjuvant radiotherapy to the excision site is often recommended in the setting of positive or close margins, high-grade carcinomas or local invasion into bone. Radiation therapy is used with surgery although this carcinoma seems to be radio resistant. Radiation therapy should be added in high-grade tumors and for patients with unclear surgical margins or for patients with positive lymph nodes (Brandwein, 2001). Radiotherapy aims to reduce the risk of local recurrence (DM Hyam, 2004). In addition, immunohistochemical studies have demonstrated Ki-67 expression in immunoreactivity between low- and high-grade MECs (Triantafillidou, 2006).

However cure rates of 100% were reported in adults with low- and intermediate-grade MECs utilizing local and wide local excision respectively, with bone removal only when erosion was present. It is believed that radical surgery is contraindicated in small, localized tumors with low- to intermediate-grade histological appearance (Triantafillidou, 2006 and Eversole, 1970). Disease specific survival at 5 years is reported at around 60-90 per cent in patients treated with this malignancy (DM Hyam, 2004 and Le, 1992). The heterogeneity of tumor characteristics and treatment approaches explains much of the variation in outcome (DM Hyam, 2004). We believe, and agree with many authors, that MECs of minor salivary glands with low to intermediate grade should be treated with wide local excision intraorally, if it can be achieved, with clear surgical and histological margins. Radical surgery with resection of bone (maxillectomy or marginal mandibular resection) is indicated when tumor invadesinto the bone and for all high-grade tumors (Triantafillidou, 2006).

Prognosis of MECs is a function of the histological grade, adequacy of excision and clinical staging. Lowgrade tumors have a 5-year survival rate of 90–100%, Intermediate- and high-grade tumors have a greater tendency to infiltrate, recur and metastasize with reported 5, 10 and 15 year cure rates of 49, 42 and 33%, respectively (Brandwein *et al*., 2001 and Triantafillidou, 2006). Plambeck *et al*. (1996) reported 5- and 10-year survival rates of 91.6 and 89.5%, respectively, regardless of tumor grade (Triantafillidou, 2006 and Plambeck, 1996). Most of the high-grade MECs show their malignant behavior within the first 5 years after surgery. A correlation has been found between prognosis and the following parameters: age (better in younger patients), sex (better in females), extra glandular extension, vascular invasion, mitotic rate, cell proliferation (as measured by Ki-67 antigen) (Triantafillidou, 2006; O'Brien, 1986 and Tran *et al*., 1986). Histopathological features that correlated with poor outcome were cystic component <20%, four or more mitotic figures per 10 high-power fields, neural involvement, necrosis and anaplasia (Brandwein *et al*., 2001). According to triantafillidou *et al* the immunohistochemical findings in correlation with prognosis with a common finding is no expression or minimum expression 1% of Ki-67 in low-grade MECs with progressive increase from intermediate-grade 4% to high-grade 10% tumors (Brandwein, 2001; Triantafillidou, 2006 and Hicks *et al*., 1995). Treatment outcome of these tumors is influenced by clinical stage and histological tumor grade. Radical surgery is used for all high-grade MECs or low/ intermediate-grade tumors that are large and involve the bone. In patients with positive surgical margins or for high-grade tumors radiotherapy could be combined with surgery. Proliferative markers (Ki-67) demonstrate the histological grade of MECs and provide additional prognostic information regarding the expected biological behavior, recurrence, metastatic potential and overall survival (Triantafillidou, 2006).

Conclusion

Low- and intermediate-grade MECs of salivary glands tend to have a favorable outcome when compared with high-grade

MECs that have a greater tendency to recur and to metastasize. Minor salivary gland tumors have a wide variation in presentation and dental practitioners should consider them in differential diagnosis when assessing an intra-oral pathology. Although Mucoepidermoid carcinoma and other tumors in this region are exceedingly rare, patients with these kinds of swellings must be considered cautiously for a better clinical outcome.

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