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RESEARCH ARTICLE

Malignant Myoepithelial Carcinoma Expleomorphic Adenoma of the Hard Palate: An Aggressive Tumor with Diagnostic Dilemma

[1]Ashok M Shenoy, [2]Rajshekar Halkud, [3]Akshay Shivappa, [4]Purshottam Chavan, [5]KC Sunil, [6]Jagdish Sarvadyna
[7]M Samskruthi, [8]KT Siddappa, [9]Siddharth Biswas, [10]Sudhir M Naik

ABSTRACT

Background/Objectives: Myoepithelial carcinomas are uncommon neoplasms that account for about 10% of all myoepitheliomas. The invasiveness varies from a locally aggressive to highly metastatic tumor which may arise *de novo* or in a pleomorphic adenoma. Myoepitheliomas arise from myoepithelial cells lacking ductal differentiation which exhibit both epithelial and smooth muscle cell elements.

Case report: We report a case of palatal swelling excised 4 years back, as pleomorphic adenoma, which later recurred as malignant myoepithelial carcinoma expleomorphic adenoma of the palate. CECT of the paranasal air sinuses did not show any bony invasion of the hard palate. So he was given radical radiotherapy with concurrent chemotherapy but after 3 years developed recurrence and metastasis to the skin and the lungs. The patient was referred to oral chemotherapy on a palliative basis.

Conclusion: Malignant myoepithelial carcinoma expleomorphic adenoma of the hard palate is a highly aggressive rare tumor of the hard palate. Radical management with surgery and adjuvant chemoradiotherapy improves survival in these patients. Follow-up with metastatic workup should be accurate as the tumor is highly aggressive with poor prognosis.

Keywords: Myoepithelial carcinoma, Carcinoma expleomorphic adenoma, Minor salivary glands, Recurrence.

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INTRODUCTION

Myoepithelial carcinomas are uncommon neoplasms that account for about 10% of all myoepitheliomas.[1] The invasiveness varies from a locally aggressive to highly metastatic tumor which may arise *de novo* or in a pleomorphic adenoma (malignant myoepithelioma ex pleomorphic adenoma CXPA).[1] Myoepitheliomas arise from myoepithelial cells lacking ductal differentiation which exhibit both epithelial and smooth muscle cell elements.[2] Myoepithelial carcinomas the malignant counterparts are seen in the major salivary glands, the parotid, nasopharynx, paranasal sinus, nasal cavity rarely in the palate and breast tissue while the benign forms are seen in the extremities and the head and neck region.[3,4]

Carcinoma ex-pleomorphic adenoma (CXPA) is a rare, aggressive tumor arising in a primary or recurrent pleomorphic adenoma (PA).[5] The pathogenesis is poorly understood and it forms 3.6% of all salivary neoplasms, 11.7% of salivary malignancies and nearly 7% of the cases occur in the palatal minor salivary glands.[6,7] Primary myoepithelial carcinoma rarely occurs in the palate and the incidences of the tumor arising from CXPA is also very rare.[8] Histopathology and immunohistochemistry are crucial in diagnosis of myoepithelial carcinoma due to its differentiation limited to myoepithelium.[1,2] A solid, reticular and trabecular arrangement histopathologically composed of round, epithelioid or spindle cells, frequently infiltrated by clear or plasmacytoid cells are usually seen.[1,2] Immunohistochemistry is positive for both epithelial and myogenic markers in myoepithelial carcinoma cells.[1,2]

Carcinoma expleomorphic adenoma contains elements of benign PA as well as frankly malignant epithelial components amounting to 2 to 5% of the PA.[9,10] Carcinoma arising in CXPA is most commonly adenocarcinoma, undifferentiated carcinoma and rarely squamous cell carcinoma.[11,12] Misdiagnosis are bound to occur as the carcinoma represent various subtypes in the residual PA on histopathology while the imaging modality plays no role.[13,14] Here, we report a rare case of malignant myoepithelial carcinoma expleomorphic adenoma of the hard palate and its management.

CASE REPORT

We report an interesting case of hard palatal swelling being excised 4 years back transorally in a 42-year-old man. It was a nontender, smooth mucosal lined 3 × 3 cm swelling in the

[1]Professor and Head, [2,4]Associate Professor, [3,5-7,10]Fellow
[8]Assistant Professor, [9]Professor

[1-5,7,8,10]Department of Head and Neck Oncosurgery, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

[6]Department of Oral Oncosurgery, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

[9]Department of Pathology, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India

Corresponding Author: Sudhir M Naik, Fellow, Department of Head and Neck Oncosurgery, Kidwai Memorial Institute of Oncology, Bengaluru, Karnataka, India, Phone: 09916807109 e-mail: sud223@gmail.com

left half of the hard palate with no signs of inflammation and discharge and with 1 year duration with gradual increased in size. The mass was immobile with uniform firm consistency with FNAC showing pleomorphic adenoma. The tumor was excised with a centimeter margin all around.

The tumor recurred in a matter of 8 months and the biopsy was taken which had features of myoepithelial carcinoma arising from a pre-existing pleomorphic adenoma, so a diagnosis of myoepithelial carcinoma expleomorphic adenoma was made (Fig. 1) immune markers study demonstrated positive myoepithelial markers, cytokeratin, EMA and S-100. Contrast enhanced CT scan of the paranasal sinuses showed mucosal irregularity in the region of the hard palate on the left side with no bony invasion. Maxillary sinuses, nasal cavity, nasopharynx with no lymph nodes enlargements. Orbits, orbital contents and both the parotid and other salivary glands were normal.

As the bony infiltration was not seen, and the patient was not willing for surgery thus avoiding the morbidity of subtotal maxillectomy, the patient was referred to radical radiotherapy. No other medical comorbidity existed in the patient. The patient was given 70 grays of external beam radiotherapy as he could not afford Intensity modulated radiotherapy (Fig. 2). The patient was followed up every 3 months with accurate examination of the primary site as well as the neck. After 3 and half years the patient on follow-up presented with firm nodules on the anterior abdominal wall and the left forehead region (Fig. 3). The fine needle biopsy of the lesions on the left forehead, anterior abdominal wall and on the chest wall revealed metastatic salivary tissue in the form of myoepithelial lesions.

Chest X-rays showed multiple round to oval well-defined opacities in both the lung fields showing multiple pulmonary metastasis. Contrast enhanced CT scan of the thorax revealed multiple pleural and pulmonary metastasis (Fig. 4). No mediastinal or other cervical and thoracic lymph nodes were enlarged. Rest of the abdomen and the pelvis was normal. ^{99m}Tc-MDP whole body none scan showed both axial and appendicular skeleton with normal tracer distribution, with both kidneys visualized. No skeletal metastasis was evident on bone scan (Fig. 5).

The patient was referred to chemotherapy with the regimen of palliative intent given. The patient is alive with the disease for the past 7 months with appearance of new lesions on the chest wall but no compromise of the KPS scale.

DISCUSSION

Myoepithelial carcinomas are tumors arising from myoepithelial cells located between the epithelial cells and the basal lamina of acini and ducts of salivary glands, breast and sweat glands of the skin.[15] WHO classifies myoepithelial carcinoma as tumor composed almost exclusively of tumor cells with myoepithelial differentiation without luminal differentiation.[16,17] Currently, benign and malignant myoepitheliomas are differentiated by mitotic count, nuclear atypia, presence of invasive growth, cellular polymorphism, tumor necrosis, or their combination.[18] Myoepithelial carcinoma shows aggressiveness and recurrence even after adequate therapy, and is disproportionately common in pediatric age group having an aggressive clinical course.[18]

These tumors have a multinodular pattern with solid sheet-like growths of tumor cells, with myxoid or collagenous, hyaline background appearing in 4 different benign histological types epithelioid, spindle cell, plasmacytoid and clear cell.[19,20] Myoepithelial carcinoma has a multilobulated architecture without duct formation and myoepithelial

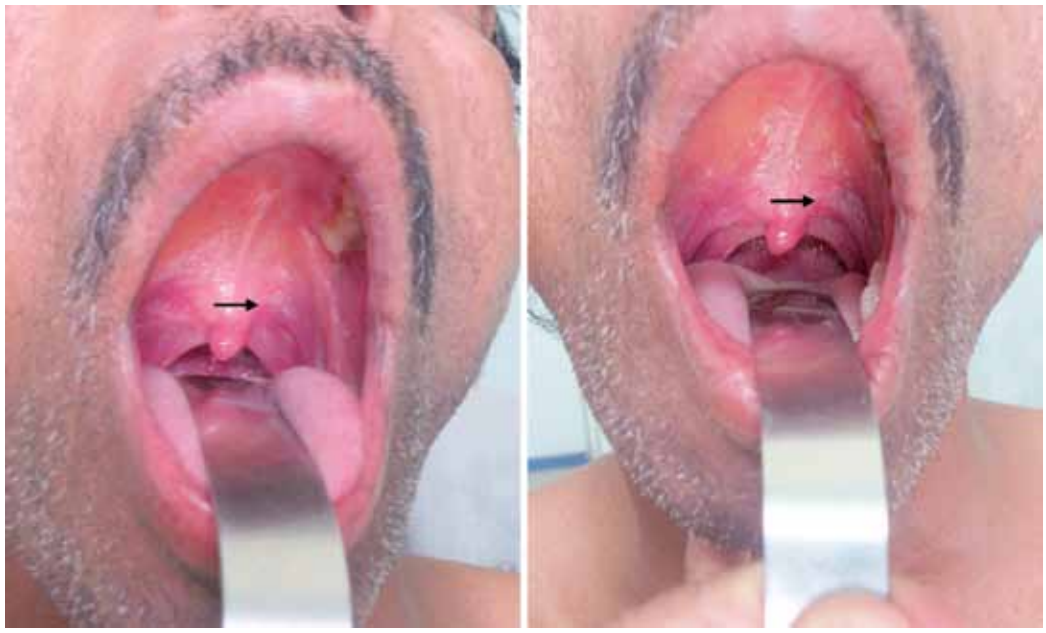

Fig. 1: Primary site at the hard palate area after excision of recurrence

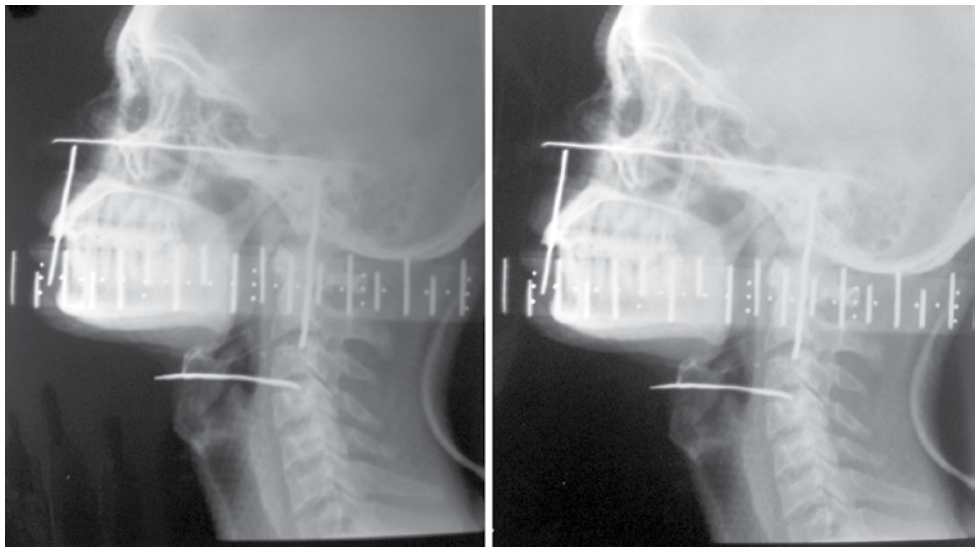

Fig. 2: External beam radiotherapy portals

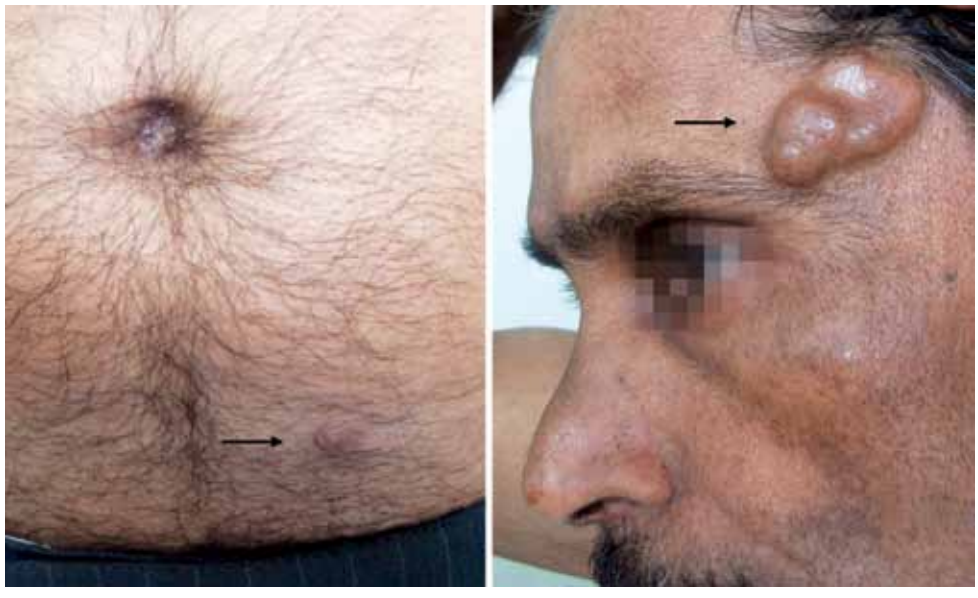

Fig. 3: Skin metastasis lesions at the anterior abdominal wall and forehead

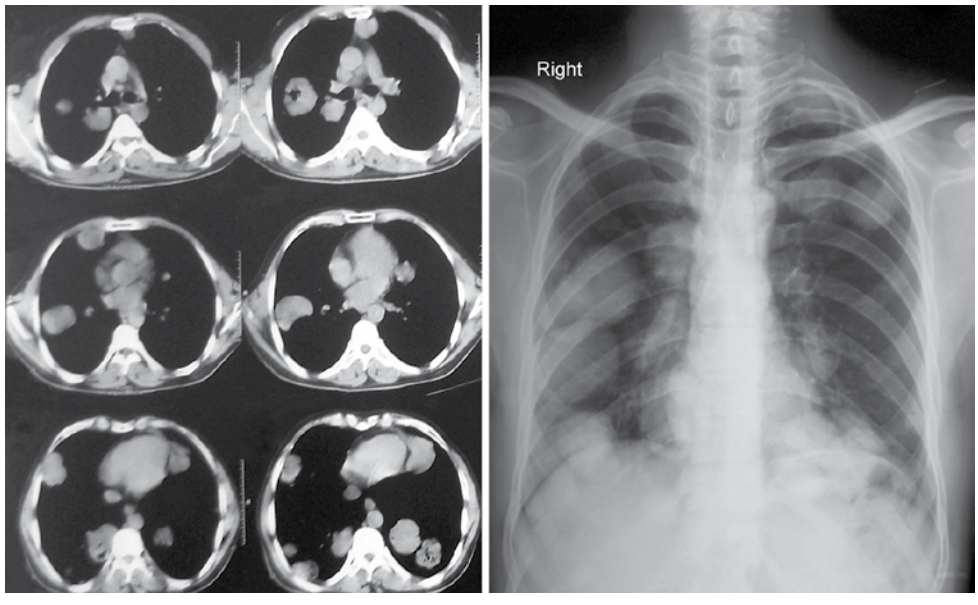

Fig. 4: Pulmonary metastasis on X-ray chest and CT chest

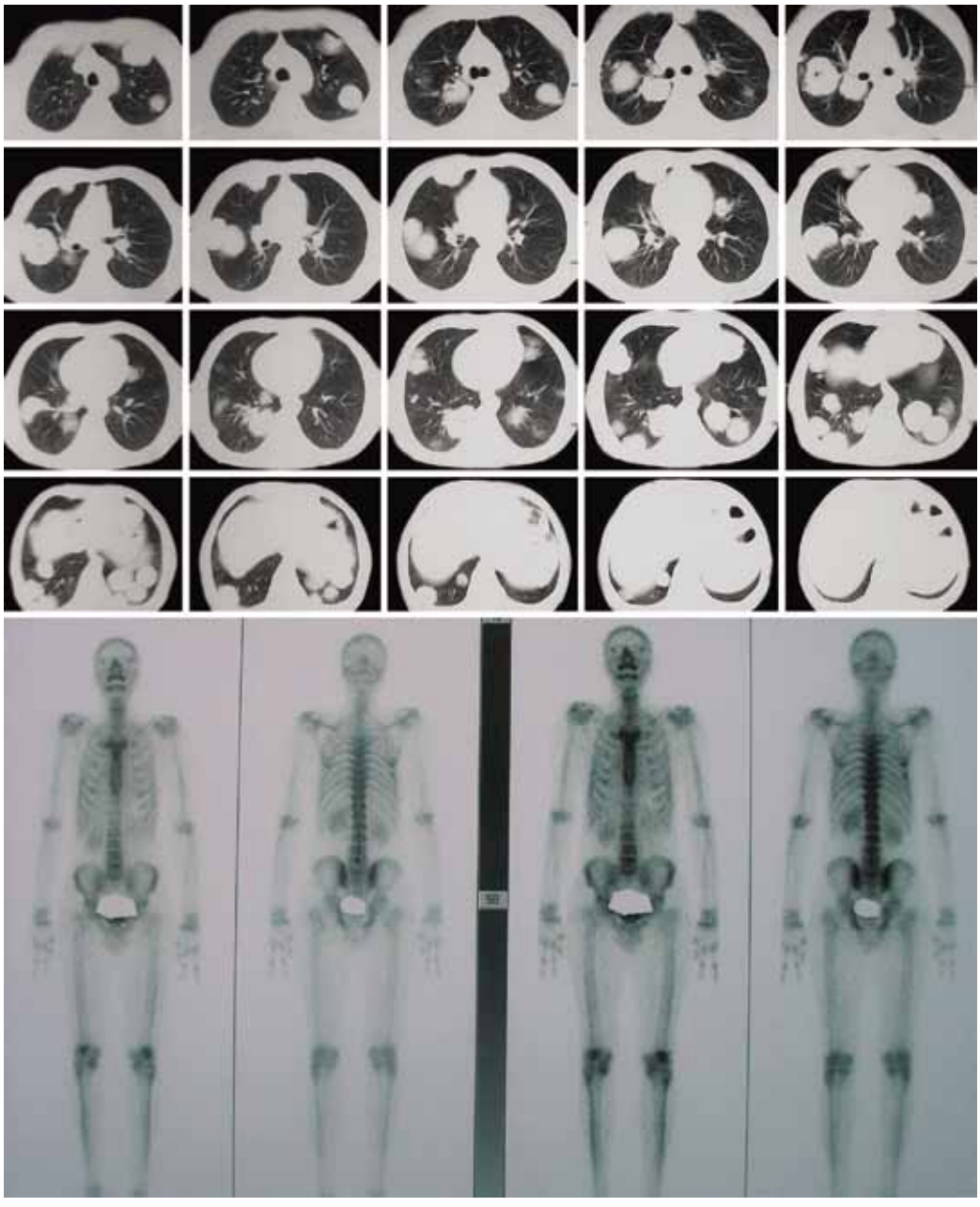

Fig. 5: Pulmonary metastasis on contrast chest CT but no skeletal metastasis

differentiation with the tumor cells being spindle shaped, stellate, epithelioid, plasmacytoid (hyaline), and occasionally vacuolated with a signet-ring-like appearance.[21]

Savera et al proposed the malignant criteria include the presence of seven or more mitoses per high-power field, tumor necrosis, perineural-angiolymphatic invasion and tumor infiltration of adjacent tissues.[22] Nagao et al claimed more than 7 mitoses/10 HPFs and a Ki67 index greater than 10% are generally malignant as some tumors will be invasive, yet show little evidence of cellular pleomorphism or mitotic activity.[1]

Pleomorphic has characteristic ducts and chondromyxoid stroma while myoepitheliomas are exclusively composed of myoepithelial cells while PA show 8q12 and 12q13- q15 alterations cytogenetically.[23,24] Myoepitheliomas have high expression of epithelial markers such as cytokeratin (CK), epithelial membrane antigen (EMA), S-100 protein, and smooth muscle markers as smooth muscle actin and calponin.[23,24] Confirmation is by double positivity for both cytokeratins (pan CK or preferentially basal type CK) and one or more myoepithelial markers (S-100, calponin, p63, GFAP, maspin, actins).[23,24]

Myoepithelial carcinomas displayed slightly more chromosomal events than benign counterparts with recurrent gains of large genomic regions distinguish it from benign.[25] The most frequent gains of chromosomes in the benign tumors were at 22q11.1-q13.33 (40%) and 11q23.3 (38%).[25] Both benign and malignant myoepithelial tumors show deregulated expression in p16INK4a and p53 pathway members with malignant ones expressing p53 and EZH2 at

a higher level.[26] This indicates additional inactivation of p53 is needed in neoplastic transformation and aggressive tumor growth of myoepithelial carcinomas.[26]

Complete wide excision and observation is sufficient for myoepithelioma while the malignant counterpart needs complete wide excision with tumor free margin with post-operative concurrent chemoradiotherapy.[22] The benign tumor hardly show recurrence while overall prognosis of myoepithelial carcinoma is poor with average metastatic rate being 47% and the mortality rate being 29% after a mean of 32 months.[18,27] Recurrence and metastasis are more common in children than in adult even with a negative excision margin and adjuvant therapy making them high-grade malignancies.[18,27] A review of 70 myoepithelial carcinomas reported the mean age was 50 to 60 years (14-86 years) with a male to female ratio of 1:1 to 1:2 with 64% in parotid, 13% in submandibular gland and 23% in minor salivary glands.[18,27] Size ranged from 2.0 to 20.0 cm with a mean size of 3.5 to 5.0 cm.[18,27] The patients were followed up with 22 to 67% having local recurrence, 23 to 47% had metastases (lung, liver, bone, lymph nodes) and that 29 to 47% died of their tumor.[18,27]

WHO classifies the malignant changes in PA into 3 types CXPA, carcinosarcoma, and metastasizing PA while CXPA being the commonest (11.7% of salivary malignancies).[6,13] Malignant changes occur commonly in the parotid, rare un the minor salivary glands (7%).[7,9] They appear in longstanding parotid PA, with 30% presenting with pain, facial nerve palsy, enlarged lymph nodes, skin ulceration and dysphasia.[14,28] Usually present in the 6 to 8th decade of life and onset of malignant changes in PA varies from I month to 52 years.[6]

Malignant changes in PA cannot be specifically identified by imaging and histopathology is needed for confirmation.[13] As CXPA is an highly malignant tumor, incidence of positive margins, perineural invasion, facial nerve involvement, and lymph node metastasis are higher than any salivary gland malignancies.[28-30] Postoperative adjuvant radiation eradicate residual deposits of microscopic disease but frequent recurrence and metastasis regional lymph nodes, lung and bones are common.[28-30] Currently, radical surgery and post-operative adjuvant radiation therapy improves locoregional control and increased survival.[29,31] The 5-year survival rate of CXPA ranges from approximately 25 to 65%.[30]

PA is the most commonest tumor arising in the minor salivary gland of the palate.[8] In malignant palatal tumors, mucoepidermoid carcinoma and adenoid cystic carcinoma are common while CXPA is rare. Waldron et al reported 4 CXPA out of the 181 palatal tumors, Guangyan et al, reported 19 out of the 160 cases but Ragezi et al did not see any CXPA in 109 cases of palatal tumors.[8,31] Sudhir et al reported CXPA with foci of high grade mucoepidermoid carcinoma arising from the left submandibular gland.[32]

Here we report a rare case of malignant myoepithelial carcinoma expleomorphic adenoma of the hard palate with recurrence. As this is a highly aggressive tumor radical surgery with adjuvant radiotherapy and chemotherapy is indicated with regular follow-up.

CONCLUSION

Malignant myoepithelial carcinoma expleomorphic adenoma of the hard palate is a highly aggressive rare tumor of the hard palate. Radical management with surgery and adjuvant chemoradiotherapy improves survival in these patients. Follow-up with metastatic workup should be accurate as the tumor is highly aggressive with poor prognosis.

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