

# Clear cell myoepithelioma of palate with emphasis on clinical and histological differential diagnosis

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## Abstract

Myoepitheliomas account for less than 1% of all salivary gland tumors and mostly occur in the parotid gland and palate. A 58-year old male patient reported to the Outpatient Department of PMS College of Dental Science and Research (Kerala, India) with a slow growing painless swelling on the palate for 4 years. Pleomorphic adenoma, basal cell adenoma, myoepithelioma, cyst adenoma, lipoma, neurofibroma, neurilemmoma and leiomyoma were considered. Histopathology revealed a thinly encapsulated tumor composed mainly of sheets of clear cells mixed with cells having eosinophilic cytoplasm. Histopathological differential diagnosis included pleomorphic adenoma, oncocytoma, oncocytic hyperplasia, sebaceous adenoma, malignant salivary gland neoplasms and metastatic lesions from kidney and thyroid. Myoepitheliomas mostly occur in the parotid gland and palatal region and various histological types of myoepithelioma are described. Myoepitheliomas of the palate are rare with clear cell variant even rarer.

## Introduction

Salivary gland neoplasms account for approximately 3-5% of all maxillofacial neoplasms.<sup>1</sup> Minor salivary gland tumors include a heterogeneous group of neoplasms with varied histology accounting for 10-15% of all salivary gland neoplasms, most of which are located in the palate.<sup>1,2</sup>

Myoepitheliomas arise from proliferation of myoepithelial cells. It was first described by Sheldon *et al.* in 1943 and was considered a variant of pleomorphic adenoma.<sup>3</sup> In 1991, the World Health Organization classified myoepithelioma as a distinct entity.<sup>4</sup> Myoepitheliomas are uncommon and account for less than 1% of all salivary gland tumors.<sup>5</sup> This

tumor frequently affects the parotid gland and palate, less commonly it can occur on the skin and soft tissue.<sup>6</sup> No sex predilection is noted and usually it occurs as a slow growing painless mass. Various histological types of myoepithelioma described include spindle, plasmacytoid or hyaline, epithelioid, clear and oncocytic (a variant of spindle type). Most tumors are composed of single cell type but combinations may occur. Myoepithelioma of parotid occur in older people and are composed more often of spindle and epithelia cells whereas those of minor glands occur in slightly younger individuals and are composed of plasmacytoid cells.<sup>7-10</sup> Recently, Hakeem *et al.* who reviewed 20 reported cases of myoepithelioma came across only two clear cell variants occurring in the palate, making this lesion extremely rare.<sup>11</sup> Here we discuss a case of clear cell myoepithelioma of palate with emphasis on the clinical and histological differential diagnosis.

## Case Report

A 58-year old male patient reported to the Department of Oral Medicine and Radiology of PMS College of Dental Science and Research (Kerala, India) with a slow growing painless swelling on the palate that had been present for almost 4 years. The patient was a well-controlled diabetic with no other medical problems. Extra oral examination revealed no abnormalities. On intraoral examination, a smooth surfaced sessile swelling was seen at the junction of hard and soft palate, 2 cm from the midline and 1 cm away from the crest of the edentulous alveolar ridge near to the left maxillary tuberosity region. The lesion was slightly yellowish, well circumscribed, and non-tender with a soft consistency. It measured approximately 1x1.5 cm. There was no evidence of superficial vascularity as the lesion did not blanch on palpation. The swelling appeared to slip under the mucosal surface on palpation (Figure 1). Radiographic evaluation did not reveal any bone involvement. The patient was largely edentulous except for the three standing teeth (upper right maxillary central and lateral incisors and maxillary right upper canine). Routine hematological and urine analysis and chest X-ray was normal. ELISA for HIV was non reactive.

## Clinical differential diagnosis

The clinical differential diagnosis of a slow growing, soft, non tender, non ulcerated smooth surfaced sessile mass at the junction of hard and soft palate includes a list of lesions comprising of commonly occurring palatal abscess, cysts both odontogenic and non-odontogenic; soft tissue neoplasms like fibroma, lipoma, neurofibroma, schwannoma, leiomy-

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Key words: myoepithelioma, soft tissue neoplasms, salivary gland, palate.

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oma and also minor salivary gland neoplasms.<sup>12</sup> Palatal abscess was eliminated from the list due to lack of infectious foci. Reactive lesions like pyogenic granuloma was not considered in the differential diagnosis as there was no recognizable irritant like dentures, dental plaque etc.<sup>13</sup> Soft and slippery consistency of the lesion helped in eliminating hard tissue tumors; hard tissue and vascular malformations; and lesions like fibroma, irritation fibroma and ossifying fibroma.<sup>14</sup> While preparing the diagnostic list, several soft tissue tumors of connective tissue (muscle, neural, adipocytic), and salivary gland origin had to be considered, as they have similar clinical features especially when occurring in the palate.<sup>15</sup> The lesion being a slow growing one, high-grade malignancies were not considered in the differential diagnosis. Benign muscle tumor like leiomyoma was considered in the differential diagnosis taking into account the age of the patient and the location, but granular cell myoblastoma was not considered as it was more common in the tongue than in the

palate.<sup>15</sup> Benign nerve tissue tumors like neurofibroma and neurilemmoma had several features similar to this case. Out of the two, neurofibroma was as a more probable option considering its relatively higher frequency on the palate.<sup>14</sup> The color, the size and the feel of the lesion also suggested the possibility of lipoma, in spite of the fact that classical lipomas occur rarely on the palate.<sup>14</sup> Some literature describes sialolipoma, a relatively rare lesion with more incidences in the palate than classical lipoma, to be having certain clinical features similar to this case. Considering the frequency of occurrence in the palate and the softness of the lesion, benign salivary gland tumors had to be strongly considered probably before any of the muscle or nerve tissue tumors in the panel of diagnostic hypothesis.<sup>2</sup> Of the benign salivary gland tumors occurring in the palate, pleomorphic adenoma was the most probable and other tumors like basal cell adenoma, myoepithelioma, and cyst adenoma further down in the differential diagnosis list. The long duration (4 years), the lesion took to grow up to the present size helped in ruling out the possibility of malignant salivary gland neoplasms, however slow growing polymorphous low grade adenocarcinoma and low grade mucoepidermoid carcinoma could be considered. Since palatal involvement of lesions like non-Hodgkin lymphoma is usually associated with human immunodeficiency virus infection,<sup>16</sup> it was not considered as the patient was relatively healthy and free from HIV infection. Even though rare in the palate, possibility of fibrous histiocytoma was kept in mind as the lesion presented as a painless submucosal nodule in an elderly adult.<sup>15</sup>

Thus the clinical differential diagnosis list was formulated considering the clinical features of the patient's tumor, prevalence of previously described lesions, and demographic data. The list of lesions suggested had salivary

gland tumors like pleomorphic adenoma, basal cell adenoma, myoepithelioma, cyst adenoma, low grade mucoepidermoid carcinoma, polymorphous low grade adenocarcinoma occupying the top slots in the list followed by other lesions like lipoma, neurofibroma, neurilemmoma, leiomyoma and benign fibrous histiocytoma. However, the diagnosis of any soft tissue tumor can only be confirmed by histopathological investigation like fine needle aspiration cytology or incisional/excisional biopsy.<sup>12</sup>

The surgical excision of the mass was done and sent for histopathological examination. The postoperative period was uneventful and the patient is asymptomatic till date. The excised tissue was fixed in 10% formaldehyde for 24 h. Routine laboratory procedures were followed by paraffin embedding of the tissue. Five  $\mu$ m thick sections were obtained and stained with hematoxylin and eosin (H&E) for histological analysis (Figures 2-5).

### Histopathology and its differential diagnosis

Microscopically, it was a thinly encapsulated tumor composed mainly of sheets of clear cells mixed with cells having eosinophilic cytoplasm. The cells showed small round to oval, bland nuclei that was eccentrically placed. In between these cells hyalinized fibrous septae were seen. Congested blood vessels and areas of hemorrhage were also noted.

Histopathology revealed the possibility of a clear cell neoplasm. The differential diagnoses of clear cell tumors that can possibly occur in this region include benign and malignant salivary gland neoplasms and metastatic clear cell lesions especially from kidney and thyroid. Malignant primary salivary gland neoplasms include clear cell variant of mucoepidermoid carcinoma, acinic cell carcinoma showing clear cell changes, epithelial myoepithelial carcinoma, clear cell carcinoma, clear cell myoep-

ithelial carcinoma and sebaceous carcinoma. In contrast to carcinomas, myoepitheliomas have a non-infiltrative, well-circumscribed periphery.<sup>17</sup> Malignant primary and metastatic lesions were ruled out as there was no infiltrative growth pattern, cytologic pleomorphism, high mitotic rate, coagulative necrosis or lack of encapsulation.<sup>17</sup>

The benign clear cell tumors of salivary gland include pleomorphic adenoma, myoepithelioma, oncocytoma, oncocytic hyperplasia and sebaceous adenoma. Absence of glandulo-ductal differentiation and chondromyxoid or chondroid foci made us delete pleomorphic adenoma from the differential diagnosis.<sup>18-20</sup> Oncocytoma and oncocytic hyperplasia show the characteristic appearance of oncocytes. In the clear cell variant of oncocytoma, in which the clear cells are a dominant or partial component, the sparse granularity of the typical oncocyte will still be evident. Sebaceous adenoma is composed of irregularly sized and shaped nests of sebaceous cells without cytologic atypia.<sup>17,21</sup>

When pleomorphic adenoma, oncocytoma, oncocytic hyperplasia and sebaceous adenoma were excluded from the histological diagnosis, we came to the conclusion that our case is a clear cell myoepithelioma. Conflicting reports are observed on immunostains of myoepitheliomas. The most consistent was the positive staining for cytokeratin, S100 and SMA whereas vimentin and GFAP expression vary.<sup>20</sup> Among cytokeratins CK7 and CK14 are found usually positive.<sup>17</sup> Pan cytokeratin and myoepithelial markers like calponin, S-100, p63 are also generally positive for myoepitheliomas.<sup>7</sup> In our case, immunohistochemical markers pan cytokeratin, S-100 and SMA was done and most of the tumor cells showed positivity for all the three markers (Figures 6-8).

So a final diagnosis of clear cell myoepithelioma of palate was given.

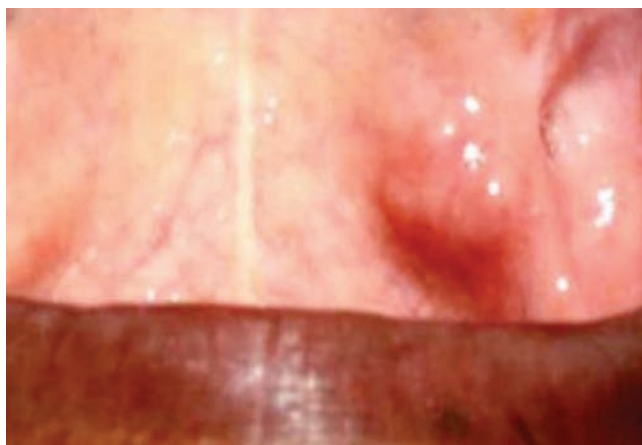


Figure 1. Myoepithelioma presenting as a palatal swelling.

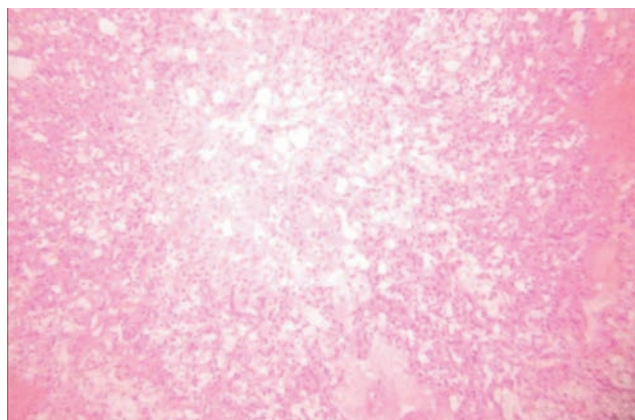


Figure 2. Tumor showing clear cells, eosinophilic cells and hyalinized septae (H&E staining, 100X).

## Discussion

Myoepithelial cells are contractile cells that originate from the ectoderm. Several normal tissues that have secretory function have myoepithelial cells. They are present in major

and minor salivary glands, sweat glands, lacrimal glands, prostate, breast, nasopharynx, lung, retroperitoneal, skin and soft tissue. Though myoepitheliomas can develop in any of these regions, its frequency is much less. Myoepitheliomas develop preferentially in the parotid gland. Minor salivary glands follow in

frequency, especially in hard and soft palate. Submandibular gland, sublingual gland and other minor salivary glands can also be affected. Three-fourths of all cases of myoepitheliomas occur in the parotid gland and palate.<sup>22</sup> Our case was also observed in the palate.

A common stem cell with a bidirectional dif-

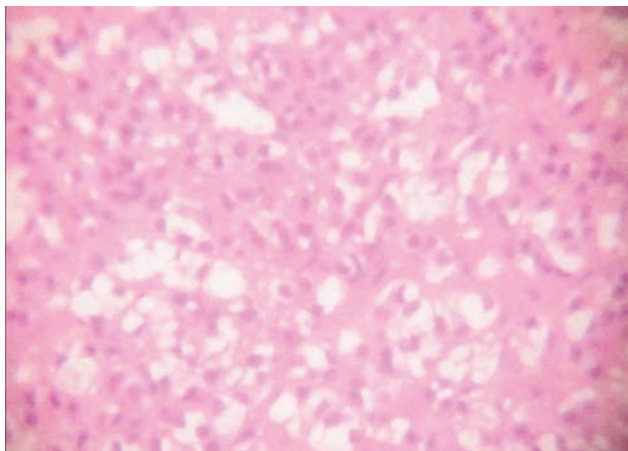


Figure 3. Tumor cells (H&E staining, 400X).

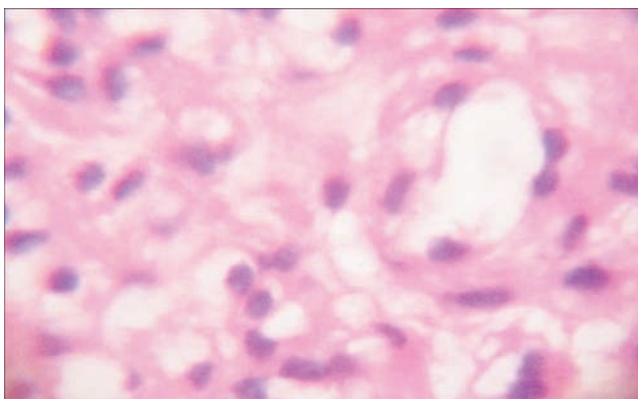


Figure 4. Tumor cells (H&E staining, 1000X).

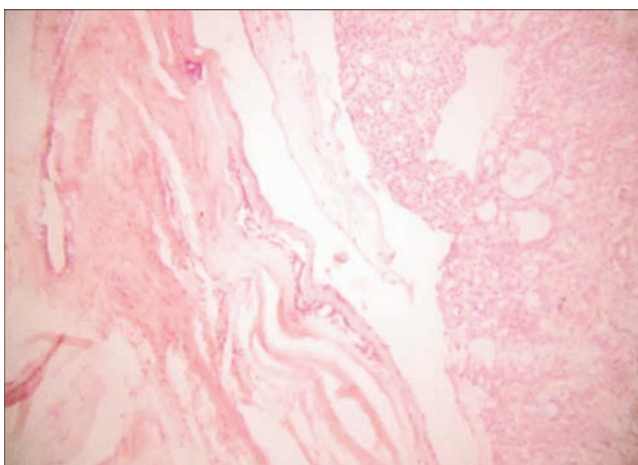


Figure 5. Tumor mass with the capsule (H&E staining, 400X).

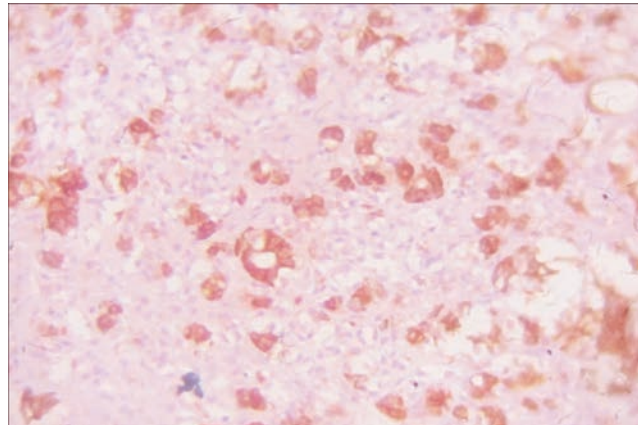


Figure 6. Immunohistochemical stain pan cytokeratin (400X).

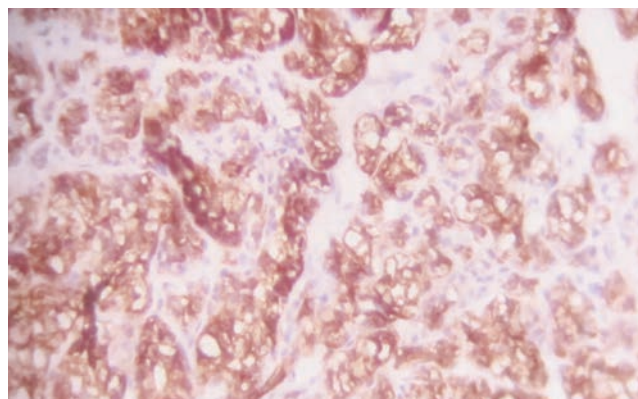


Figure 7. Immunohistochemical stain S100 (400X).

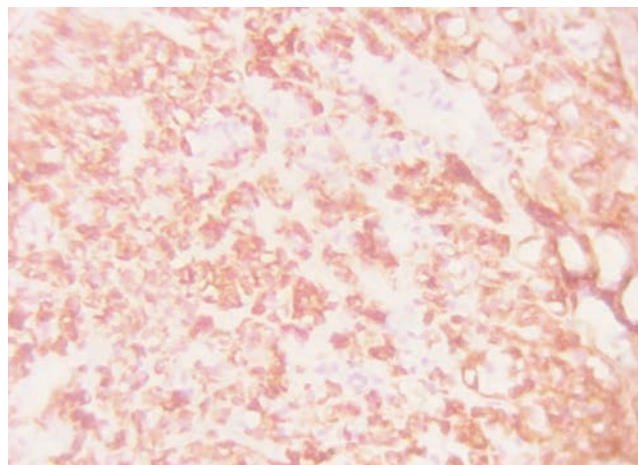


Figure 8. Immunohistochemical stain smooth muscle actin (400X).

differentiation into epithelial or myoepithelial cell is hypothesized to be the cell of origin of this tumor. The varied histological types (spindle, plasmacytoid or hyaline, epitheloid, clear and oncocytic) exhibited by myoepitheliomas can be attributed to the various stages in the differentiation from a cell that has the potential to differentiate into epithelial cells.<sup>23</sup> Though different cell types are recognized in myoepitheliomas, spindle and plasmacytoid variants are most common. In a tumor, either a single cell type predominates or there can be a mixture of different cell types.<sup>7,8</sup> Myoepitheliomas can present several architectural patterns which are non-myxoid (solid), myxoid (pleomorphic adenoma-like), reticular (canalicular-like) and mixed.<sup>19</sup> Our case showed a solid pattern. Most of the cases of myoepitheliomas reported have not specified the architectural pattern. It must be because most of the cases showed a solid, non-myxoid arrangement. Myxoid and reticular variants have been reported suggesting the rarity of these variants.<sup>24,25</sup>

Maiorano *et al.* suggested that clear cell tumors of the salivary glands are almost invariably malignant in nature with rare exceptions in the form of myoepitheliomas and oncocytomas.<sup>10</sup> Both benign and malignant variants of myoepithelioma may contain clear cells with latter being less common. The clear cells of myoepithelioma stain positive for glycogen and negative for mucin and fat. Accumulation of glycogen in the cytoplasm causing cytoplasmic clearing accounts for the pathogenesis of clear cells demonstrated in the myoepitheliomas.<sup>26</sup>

Myoepitheliomas can develop with or without a capsule. Parotid myoepitheliomas are surrounded by a thin fibrous capsule, whereas palatal myoepitheliomas are not.<sup>27</sup> Contrary to this, our palatal myoepithelioma presented with a thin capsule. Our case conforms to the review by Agarwal *et al.* that benign myoepitheliomas present as an asymptomatic mass that slowly enlarges over a period of several months to years. They also added that palatal lesions rarely ulcerate and parotid lesions never produce facial palsy.<sup>28</sup>

A malignant counterpart of myoepithelioma with distinct clinical and histological features has also been reported. They are rarer and comprise less than 2% of all salivary gland carcinomas. Patients with myoepithelial carcinoma are generally aged over 50 years and a majority presents with a painless mass. The parotid gland is the most common primary site, followed by submandibular gland and minor salivary glands. Unusual locations reported earlier include palate, gum, larynx, lateral wall of the nasopharynx, base of the tongue, maxillary sinus and cavernous sinus. It may arise de novo but at least 50% develop in the preexisting pleomorphic adenoma or myoepithe-

lioma.<sup>25,29-32</sup> There are also sporadic reports of malignant myoepithelioma at unusual sites like breast, bone, external auditory canal, skin and vulva.<sup>31</sup> Benign myoepitheliomas can undergo malignant transformation especially in long standing tumors or in tumors with multiple recurrences.<sup>17</sup> It is an intermediate to high grade carcinoma with approximately one-third of patients dying, one-third having multiple recurrences and remaining one third being disease free.<sup>18</sup>

The recommended management of myoepithelioma is surgical excision with a margin of uninvolved tissue around. Recurrence rate of 15-18% is observed. Incomplete resection can result in recurrence.<sup>33</sup> Recurrence of myoepithelioma of parotid gland presenting as a retroauricular cutaneous nodule has also been reported.<sup>23</sup> Our case has been meticulously followed up. Even after six months, no signs of recurrence have been noted.

## Conclusions

Myoepitheliomas of the palate are rare with clear cell variant even rarer.<sup>23</sup> Only two cases of clear cell myoepithelioma of palate have been reported so far. Our case can then be considered as the third. Diagnosis of myoepithelioma is by histological examination and IHC. Electric microscopy in these tumors helps in the identification and characterization of the myoepithelial cells. The rarity of this lesion makes this a diagnostic challenge and while screening all benign clear cell lesions of the palate, diagnosis of myoepithelioma should be kept in mind.

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