CASE REPORT

Concurrent occurrence of adenoid cystic carcinoma of the salivary glands with small cell carcinoma of the liver: A rare case report

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ABSTRACT

Adenoid cystic carcinoma (ACC) is a clinically deceptive and histologically specific malignancy of salivary gland origin. It is the most common minor salivary gland malignancy. Small cell carcinoma (SCC) is a type of undifferentiated malignant neuroendocrine tumor reported rarely in the liver. Though there are many reported cases of SCC involving liver and ACC of minor salivary glands, the review of literature does not show any reports of concomitant occurrence of these two tumors. We describe a rare case of ACC of the oral cavity and its coexistence with a SCC involving liver, identified and confirmed by histological, and immunohistochemical observations. To our knowledge, this is the first reported case of an ACC of the oral cavity and SCC of liver occurring concomitantly in the same patient.

Key words: Adenoid cystic carcinoma, concurrent occurrence, small cell carcinoma

INTRODUCTION

Small cell carcinoma (SCC) is defined as a neuroendocrine tumor originating from multipotential stem cells with the capability of divergent differentiation.[1] The most common site of SCC is the lung. It has rarely been found at extrapulmonary sites such as the trachea, larynx, thymus, esophagus, stomach, small intestine, colon, prostate, gallbladder, skin, breast, and uterine cervix.[2] SCC, involving primarily the liver, is extremely rare; and only 11 cases have been reported in the literature.[3]

Adenoid cystic carcinoma (ACC) is relatively uncommon but highly malignant neoplasm with a remarkable capacity for recurrence. It is a slow growing malignant tumor, characterized by wide local infiltration, perineural spread with a propensity for local recurrence, and late distant metastases.[4]

It is a rare tumor which forms about 1% of all malignant tumors of the oral and maxillofacial region and constitutes about 21.9% of all salivary gland malignancies. Fifty percent of cases of ACC[4] have been found in minor salivary glands, but are also reported in other areas such as nose, sinuses, upper airway, lacrimal glands, and breast.[5] Three histopathologic patterns namely tubular, cribriform, and a solid pattern are seen. Solid pattern is associated with increased local recurrence, high metastatic rate, and higher mortality.[4]

So far, there has been only one case presented as coexisting ACC of breast with SCC of the same region.[6] We describe a case which is similar to the above mentioned rare entity, but in different anatomical locations (ACC of salivary glands coexisting with SCC of the liver) in a 28-year-old female patient, in relevance with pathological and immunohistochemical findings.

CASE REPORT

A 28-year-old female was referred from the surgical department of our college with a swelling in the cheek for the duration of 1 month.

Her medical history revealed that she was diagnosed of SCC of liver confirmed by radiographic, histopathologic, and immunohistochemical investigations; 3 months earlier.

Patient presented a diffuse swelling of about 2 cm in the left cheek region extraorally below the zygomatic area [Figure 1].

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Website: www.jomfp.in

DOI: 10.4103/0973-029X.119774

Extraoral clinical examination showed that the swelling had indistinct limits and there were no surface alterations of the skin over the growth. Palpation of the left side of the cheek identified a firm, nontender mass that was subcutaneously mobile; but partly attached to the underlying structures. The skin covering the tumor was normal. Intraoral examination showed normal mucosa without any surface changes. The mass was palpable from intraoral aspect and was not attached to the mucosa. Initial clinical diagnosis of metastatic tumor in the oral cavity was made. Subsequently, biopsy was performed in the cheek region.

Microscopic findings

Oral biopsy specimen showed islands with basaloid, medium cells with oval hyperchromatic nuclei, distinct nucleoli, and scanty eosinophilic cytoplasm. Atypia was mild to moderate. The subsequent deeper section showed evidence of few cribriform islands with eosinophilic coagulum. The lumina of the islands are surrounded by cells with eosinophilic cytoplasm. Moreover, rare small cysts and pseudo glandular structures filled with mucous material were seen. In addition to cribriform pattern [Figure 2], there were also islands of basaloid, hyperchromatic cells were evident in tissue sections.

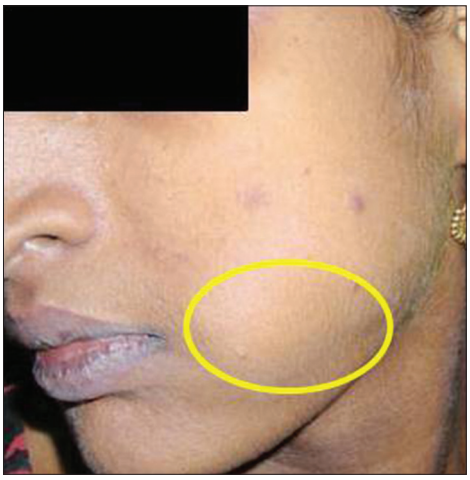

Figure 1: Extraoral photograph shows a diffuse swelling (encircled yellow area) below the zygomatic area in the left cheek region

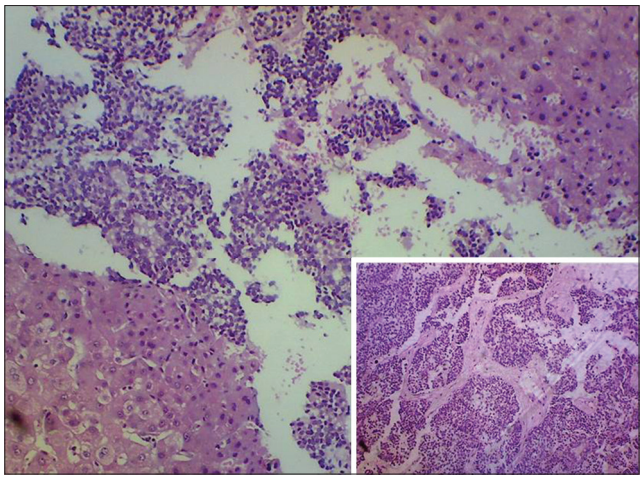

Figure 3: Hematoxylin and eosin stained section shows liver tumor consisting of sheets of small uniform cells with eosinophilic cytoplasm representing hepatocytes and the inset shows hyperchromatic small round cells separated by fibrous septa (×100 magnification)

The histopathology of liver biopsy was in favor of SCC [Figure 3 and 4]. Since the oral biopsy showed areas of ACC, to confirm the diagnosis, the tissue sections were subjected to immunohistochemistry. The markers used were cytokeratin (CK)-5-6, high molecular weight CK anitbody (HMWA), vimentin, S-100, smooth muscle actin (SMA), Bcl2, neuron specific enolase (NSE), synaptophysin, and c-KIT (CD 117) and CD 10 to differentiate ACC from SCC and other salivary gland tumors. Immunohistochemically, tissue section from the cheek region reacted strongly with anticytokeratin antibodies such as CK5-6 [Figure 5], including high molecular weight antibody (HMWA), vimentin, S100 [Figure 6], Bcl2, c-KIT, CD 10 and Anti SMA whereas neuroendocrine markers such as synaptophysin, and NSE did not show positivity.

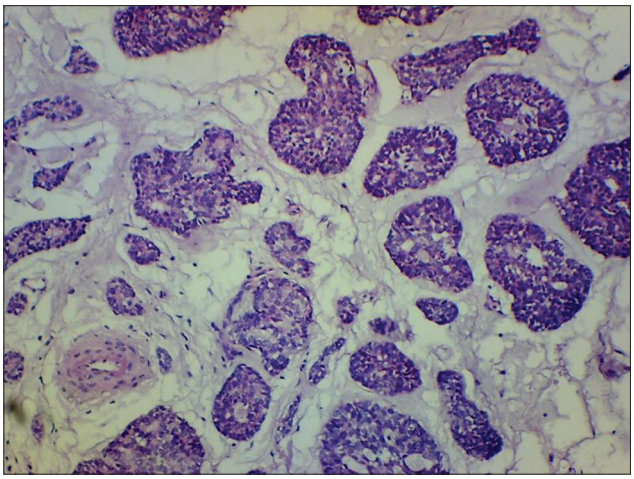

Figure 2: Hematoxylin and eosin stained section shows variable sized cribriform spaces formed by small deeply basophilic cells. Cribriform spaces contain faintly eosinophilic material (×100 magnification)

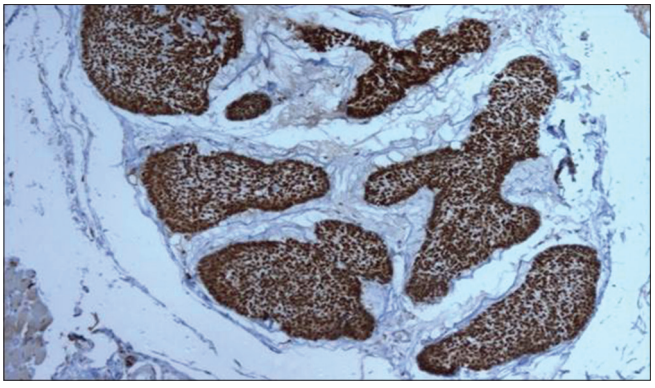

Figure 4: Immunohistochemical staining of adenoid cystic carcinoma shows positive expression for cytokeratin (CK) 5-6 (×100 magnification)

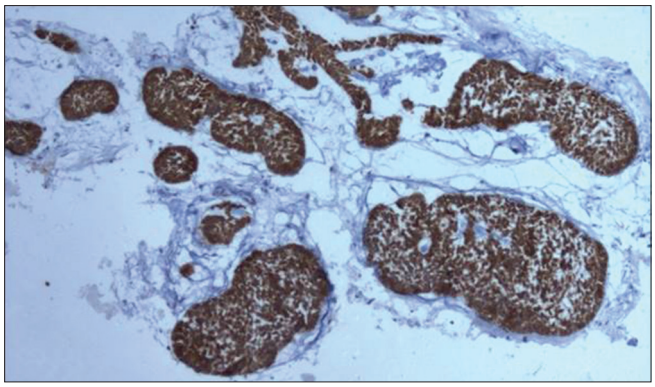

Figure 5: Photomicrograph of adenoid cystic carcinoma immunostained with Bcl2 marker shows positive expression (×100 magnification)

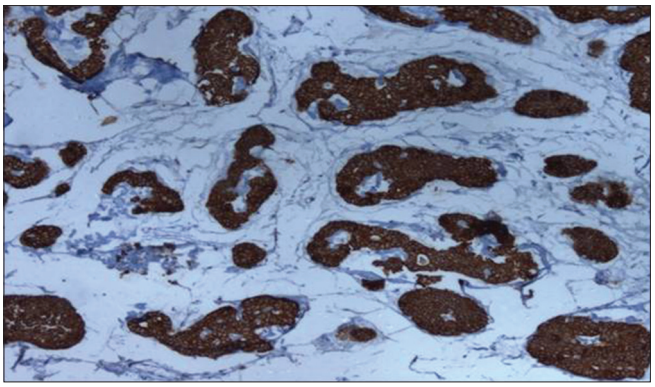

Figure 6: S-100 marker positivity is seen with immunohistochemical staining of tumor cells of salivary gland origin (x100)

DISCUSSION

ACC exhibits a unique malignant profile characterized by slow growth and high propensity to systemic metastases including liver.[7] Extrapulmonary SCC has been reported to occur in 0.1-0.4% of all malignancies. It shows neuroendocrine differentiation, and has propensity to metastasize to distant organs.[2] Both ACC and SCC are prognostically different and therapeutic requirements of these two vary widely. Hence, distinction between these two malignancies is essential.

Coexistence of ACC with other tumors has not been frequently reported except for one case by Cabibi *et al*.,[6] described an ACC coexisting with a SCC in the same tumor. In our case, concurrent occurrence of two malignancies in different anatomical locations is evident which is to be reported first in the medical literature. The differential diagnosis between SCC and ACC is often difficult. Histologically, the absence of glandular structures and of periodic acid Schiff-positive globules are the more striking differences, suggesting a diagnosis of SCC over solid ACC.[6] Immunohistochemically, the two neoplasias show positive expression for markers such as CK5-6, vimentin, and S100.

From the study of nine cases of ACC with basaloid features, Shin and Rosen[8] stated that, the immunohistochemical differential diagnosis between ACC and SCC is based only on neuroendocrine markers (NSE, synaptophysin, and chromogranin), and their positivity suggests a diagnosis of SCC over ACC.

In our case, there were areas with hyperchromatic basaloid islands, resembling SCC. On the contrary, in addition to solid pattern, cribriform islands were evident in deeper sections, conferring to the morphological features of ACC. Both the solid and cribriform islands were negative for neuroendocrine markers; whereas those areas showed positivity for markers such as anti-SMA, HMWA, c-KIT, and Bcl2.

In recent studies, the two markers Bcl2 and CD117 (c-KIT) have been observed in both types.[9] The c-KIT gene encodes a transmembrane tyrosine kinase receptor and signaling by c-KIT plays a central role in cellular transformation and differentiation. Uniform expression of c-KIT in solid variant of ACC was observed by Penner *et al*.,[10] suggesting a loss of cellular heterogeneity in the cells of solid ACC. Therefore, aberrant activation of c-KIT leads to the development[11] and progression of several human malignancies.[12,13]

High grade neuroendocrine carcinomas are more likely to coexpress c-KIT and Bcl2. In our case, there has been coexpression of c-KIT and Bcl2. High frequency of coexpression of these two molecules in high grade neuroendocrine carcinomas suggest that they may be involved in the carcinogenic pathway, contributing to their important roles in carcinogenesis. Therapeutic targeting on both c-KIT and Bcl2 molecules may be beneficial in the management of patients with high grade neuroendocrine carcinomas of the liver.[14]

Other studies have reported that HMWA and SMA are also useful, because they are positive in solid ACC and are completely lacking in SCC.[11] Our case also showed the similar findings. Histopathology of tumor from the liver showed features of SCC, entirely devoid of ductular or pseudoglandular structures. On the contrary, both cribriform and solid patterns of ACC were observed in the sections from oral mucosa, conferring to the neoplasia a morphological aspect compatible with ACC. Both ACC and SCC of liver were indifferently positive for CK5-6, vimentin, S100, Bcl2, CD-10, and c-KIT (CD117).

By contrast, malignant cells from SCC of liver were positive for neuroendocrine markers such as NSE and synaptophysin, and were negative for HMWA and SMA; whereas tumor cells from ACC were negative for NSE and synaptophysin, and positive for HMWA and SMA.

To investigate the histogenesis of these two different neoplastic patterns in different regions, we assessed CD10, markers of myoepithelial cells which has been proved by Cabibi *et al*.[6] The presence of morphological and immunohistochemical

observations and CD 10 positivity of the two tumors justifies an identical myoepithelial origin. Dedifferentiation takes place along neuroendocrine phenotype lines occurring in a multipotential neoplastic stem line which led to the formation of SCC in the liver and along the myoepithelial phenotype leading to ACC in the oral cavity. There had been reports by Shin and Rosen[8] where the dedifferentiation had taken place with different tumors in the same region. But our case will go by an exception that it has occurred at two different sites. The concomitant presence of both the tumors probably attributes to the dedifferentiation along the neuroendocrine phenotype lines leading to SCC in liver and salivary gland.

In conclusion, our immunohistochemical findings were thus in keeping with most of the above mentioned criteria for a differential diagnosis between SCC and ACC, supporting the morphological observation of two different malignancies coexisting in the same patient.

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How to cite this article: Premkumar J, Karthik S, Sathyakumar M, Martin Y. Concurrent occurrence of adenoid cystic carcinoma of the salivary glands with small cell carcinoma of the liver: A rare case report. J Oral Maxillofac Pathol 2013;17:288-91.

Source of Support: Nil. **Conflict of Interest:** None declared.