JOURNAL OF ORAL MEDICINE SURGERY PATHOLOGY BIOLOGY

Adenoid Squamous cell carcinoma (Adenoacanthoma of Lever): Differential Diagnosis and Case Report.

Dr.Pinhaj Ahmed Sherashiya, [1] MDS; Dr.Hemavathy S, [2]MDS; Dr.Yogesh T L, [3]MDS; Dr.AkshayShetty, [4] MDS

Keywords: Squamous cell carcinoma; conventional squamous cell carcinoma; adenoid squamous cell carcinoma; adenosquamous carcinoma; angiosarcoma; adenoid cystic carcinoma.

Senior Oral Diagnostic Oncologist, Karnataka Cancer Society.

Professor and Head, Department of Oral Pathology and Microbiology, Sri Rajiv Gandhi College of Dental Sciences & Hospital , Cholanagar, Bangalore 560032.

Professor, Department of Oral Pathology and Microbiology, Sri Rajiv Gandhi College of Dental Sciences & Hospital, Cholanagar, Bangalore 560032

Professor and Head, Department of Oral Maxillofacial Surgery, Sri Rajiv Gandhi College of Dental Sciences & Hospital, Cholanagar, Bangalore 560032.

How to cite this article: Pinhaj Ahmed Sherashiya, Hemavathy S, Yogesh T L andAkshayShetty. Adenoid Squamous cell carcinoma (Adenoacanthoma of Lever): Differential Diagnosis and Case Report. Journal of Oral Medicine Surgery Pathology Biology. Dec- Jul 2016; 1(2): 56-64

Address for correspondence:

Dr.Pinhaj Ahmed Sherashiya, Senior Oral Diagnostic Oncologist

No 1308, 11th B Cross, Vyalikaval, Bengaluru, Karnataka 560003. Bangalore.

E mail id : hi_pinhaz@yahoo.com

Running title: A variant of squamous cell carcinoma

Clinical Significance: A variant of squamous cell carcinoma which is very rare.

ABSTRACT

Adenoid squamous cell carcinoma (ASCC) is a rare but an independently recognized variant of the squamous cell carcinoma of the skin first described by Lever in 1947, and he named it as 'adenoacanthoma 'on the assumption that this tumor arose from the glands and ducts of the eccrine sweat glands. Several years later Lever himself modified the concept and stated that the glandular structures seen in the tumor were the result of acantholysis of squamous cells. Muller and his colleagues later named this tumor as 'Adenoid Squamous Cell Carcinoma.' ASCC has been reported to arise in the sun-exposed area of the head and neck and also in other sites of the body.

INTRODUCTION

The most common cancer in the upper aerodigestive tract is the squamous cell carcinoma (SCC), and almost all of them are the conventional- type SCCs. Subtypes of SCC, which are rare, include the spindle- cell SCC, papillary SCC, verrucous SCC, basaloid SCC, lymphoepithelial carcinoma, adenoid squamous cell carcinoma and adenosquamous carcinoma. They may mimic other neoplasms, resulting in faulty diagnosis and treatment. Adenoid squamous- cell carcinoma (SCC) is a rare histological variant of Squamous cell carcinoma that is characterised by acantholysis of the tumour cells. [1]

DISCUSSION

Squamous cell carcinoma (SCC) is a predominant type of skin cancer. Several subtypes of cancer exist; that have varying clinical behaviors and malignant potential. [1]Acantholytic squamous cell carcinoma is a well-defined variant of squamous cell carcinoma in which significant portions of the neoplastic growth show a tubular or pseudoglandular microscopic pattern. [2]

Pathogenesis of Adenoid squamous cell carcinoma: Acantholysis, which is possibly a result of the changes in adhesion molecule expression by the tumour cells. [1]is said to lead to the formation of pseudolumina; and anastomosing spaces and channels leading to the appearance of glandular areas in the ASCC. [1]The cleft formation is likened to the suprabasilar clefts in actininc keratosis. [3]ASCC is also known as squamous cell carcinoma with gland-like (adenoid) features or adenoid squamous carcinoma, pseudoglandular squamous cell carcinoma, adenoacanthoma, angiosarcoma-like squamous cell carcinoma, pseudoangiosarcomatous carcinoma and pseudovascular adenoid squamous cell carcinoma. It differs from the common conventional squamous cell carcinoma in its histologic features and its destructive behaviour [2] and is also said to have a poor prognosis than conventional SCC.

Clinically: The gross findings are nonspecific. [4]The lesion commonly arises as an ulcer or flesh-colored, red, pink, or brown [5]nodule on the sun-exposed areas of the skin or mucosa [6]especially of thehead and neck areas of the elderly; or it may arise following a previous exposure to ionising radiation. There have been reports of this tumor occurring on the dorsum of the foot, which is a sun-protected area. ASCC occurs most commonly on the lips, [7]especially the vermilion border of the upper and lower lips [6] and rarely does it arise intraorally; although cases of ASCC arising on the lateral surface of the tongue have been reported. [6] The disease has a poor prognosisin the event of lesions, emerging in the sun protected areas as compared to those of the lip and skin [6] and prognosis is worse when it affects the oral cavity as compared to that of the skin. [8]ASCC may also appear as encrustations, scales or areas of ulceration. [5] Oral cavity lesions have been described as ulcerated, indurated, nodular, exophytic, warty, keratotic, or crusted. Tumors often measure several centimeters in diameter and have a tan or tan-white cut surface. [6]Nearly, 2-3% of cases, more than 2 centimeters in size, causes deep invasion and distant metastasis either into the lymph nodes or the visceral organs. [6]The peak incidence of the oral ASCC is observed in the sixth decade of life, and the males are found to be more commonly affected. [7]It has been

included in the WHO Classification of Upper Respiratory Tract tumors, as 'AcantholyticSCC' [6]and though the World Health Organization (WHO) had defined ASCC as an original entity a long time ago, there have been less than 30 cases documented in the international literature so far. [9]

The tumor may also less commonly present as a small, slow-growing lesion similar to an actinic keratosis or more often than not, present as a large, chronic ulcer of many years' duration. The appearance and period of growth are similar to that of a keratoacanthoma. The tumor is a squamous cell carcinoma having distinct adenoid proliferation with dyskeratosis and acantholysis-like cells.[10]

Histologically, the lesion shows strands and islands of atypical epithelial cells that reach subepithelially. Connection to the overlying epidermis is seen in most cases, which may show para and hyperkeratosis. However, this connection may be seen only focally or, in many cases may be absent. [5]The tumor shows cystic degeneration of the neoplastic epithelium, producing a prominent alveolar pattern and loss of cohesion following acantholysis resulting in these pseudoglandular structures to be filled with acantholytic cells.[6] Lobular growth patterns that show tubular and alveolar formations may be present. These may enclose a pseudoglandular space and which is [3]lined by an outer layer of flattened, cuboidal, or ''hobnail'' neoplastic, [4]polygonal basal [5]cells whose nuclei are pleomorphic and often hyperchromatic and whose cytoplasm may be either scanty or prominent and, when present, may be typically eosinophilic. It may also show an occasional giant cell or multinucleated cell. Small, pearl-like aggregates of cohesive, squamous cells may be present within the lumen-like spaces, with larger areas of clear squamous differentiation. Mitotic figures are frequently encountered. [4]Prominent keratin pearl formations may be present. [5]These acantholytic cells may appear incredibly bizarre, large, or multinucleated, [6]dyskeratotic, neoplastic, and "glassy keratinocytic" in nature. Mitotic figures are variably present. [5]

Immunohistochemically, this lesion is positive for pan cytokeratin, high-molecular-weight keratin, cytokeratin (CK) 7/8, CK19, E-cadherin, [11]epithelial membrane antigen (EMA), [6]and p53, but negative for carcinoembryonic antigen (CEA), vimentin, CK20, S-100 protein, [10]CD-34 and Factor VII-related antigen. [6] A gland-like feature of ASCC is associated the loss of cell adhesion at the center of the cancer islands, which can be confirmed by staining with mucin stains; to be neither a conventional squamous cell carcinoma with a ductal involvement or an adenosquamous carcinoma. [11]

Electron microscopic findings have proven the epithelial origin of this lesion by identification of the tonofilaments and desmosomes but have shown no glandular features. [6]

Special stains like PAS stain shows focal positivity whereas mucicarmine and alcian blue appears negative. [12]

Differential Diagnosis

Adenosquamous carcinoma: ASCC is differentiated from adenocarcinomas particularly, adenosquamous carcinomas by absenteeism of actual glandular formations and negativity for [6]intracellular [4]mucin stains. [6]In addition adenosquamous carcinomas show only focal glandular formations, whereas ASCC shows pseudoglandular structures within the lesion.[7]

Mucoepidermoid carcinoma: [13] if the lesions show the presence of a squamous component and glandular architecture, mucoepidermoid carcinoma (MEC) may need to be considered in the differential diagnosis. Low and intermediate grades of MEC show rounded glandular spaces and easily identifiable mucin. Glandular formations are not found in high-grade MEC. [7]

Adenoid cystic carcinoma: ASCC can mimic adenoid cystic carcinomas due to the prevalence of glandular spaces and the fibrin in these areas mimicking mucin. But in ASCC the glandular spaces predominantly have an angular form and mucin stains do not stain positive for epithelial mucins. ASCC is most often than not,

accompanied by foci of conventional SCC thereby helping in verification of the correct diagnosis. [7] The present case is not an adenoid cystic carcinoma since no cribriform patterns were noted.

Angiosarcoma:[13]Although angiosarcomas and ASCC are entirely different tumor entities; their histological features are similar and identified by intratumoral spaces. The presence of the crisscrossing spaces and channels in ASCC closely imitates an angiosarcoma. Interestingly both tumor entities show similar clinical appearances in the oral cavity. The peak incidence of Angiosarcoma occurs in the seventh decade and the ASCC in the sixth decade. [7]Macroscopically both entities located in the oral cavity are eruptive lesions and fast growing, and both have the poor prognosis. [7]Like all oral squamous cell carcinomas, ASCC have a male predilection of 1:3.5 however; sex predilection of oral angiosarcoma is not known. ASCC and angiosarcomas not only share similar clinical features and histopathological patterns in routine histological staining but may show an overlap of expression of vascular differential markers and cytokeratin-expressions. Cytoplasmatic immunoreaction for γ2-chain in ASCC and expression of Fli-1 in angiosarcoma and are the main distinguishing features of both entities.[7]

Pseudovascular adenoid SCC or angiosarcoma- like SCC, a variant of the ASCC has been reported in the skin of the head and neck, as well as in other organs, such as the lungs, breast, vulva, urinary bladder, and uterine cervix, but not in the upper aerodigestive tract. [1]

Squamous cell carcinoma: ASCC differs from typical squamous cell carcinoma both regarding histology and also by its aggressive nature. ASCC in the oral cavity has the poor prognosis. [7]The ASCC tumor shows glandular lumen. [8]Most authors now regard ASCC as a variant of SCC rather than a sweat gland tumor. It usually has a typical SCC pattern in combination with glandular formations, dyskeratotic cells, and acantholysis. Classic SCC may also show cleft formation with dyskeratosis and acantholysis, but it does not have a definite wall or cohesive layer of cells surrounding the acantholytic cells, as seen in ASCC. It was thought at first that ASCC had less potential to metastasize to lymph nodes than did de novo SCC. [5]

Adenosquamous carcinoma: ASCC is different from adenosquamous carcinoma because the adenoid elements are negative for mucins and also because acantholytic features of squamous cell carcinoma are present In ASCC. [14]

PseudovascularAdSCC: This tumor is unlike the pseudovascularAdSCC as the adenoid elements show no features of vasculature [14]

Basaloid squamous cell carcinoma: Absence of the basaloid cells makes ASCC tumor different from basaloid squamous cell carcinoma. [14]

Eccrine adenocarcinomas: In the eccrine adenocarcinoma, the glandular spaces are lined with periodic acid-Schiff (PAS)-positive cells, whereas in ASCC, the cells are PAS negative. Likewise, ASCC lacks the production of carcinoembryonic antigen, S100 protein, and amylase, which can be seen in glandular malignancies. [5]

Epithelioidangiosarcomas: The red blood cells were seen in the vascular spaces of the Epitheloidangiosarcomas whereas in ASCC it was filled up with the atypical keratinocytes. But in some cases, the ASCC may show the presence of the red blood cells within the pseudoglandular spaces in which case, immunohistochemical stains may be required to distinguish between the two lesions. Angiosarcomas are typically positive for vimentin and CD-34, whereas ASCC is positive for cytokeratin (CK) and epithelial membrane antigen (EMA). [5]

Metastatic adenocarcinomas: [13, 5]Absence of positivity for glandular features using immunohistochemical markers helps in differentiating this tumor from metastatic adenocarcinoma.

The inadequate data regarding this lesion size and the settings of the patients in several of these reviews makes it problematic to analyze the potential of ASCC to metastasize; accurately. Although there has been conflicting

literature, it is to be considered that the malignant potential of ASCC is no greater than that of a typical invasive SCC.

CASE REPORT

Figure 1: Clinical appearance of the lesion

An emaciated female patient, 64 years of age, presented to a dental hospital in Karnataka, INDIA (**Figures 1, 2**) with a chief complaint of pain and discomfort in the lower left back teeth region for the past 5 months. The pain was described as dull and it aggravated during mastication. She was otherwise asymptomatic. She gave a 40-year history of chewing paan with tobacco, at a count of 4-5 paans/ day. Her family history, medical history and history of allergy were non-contributory.

Clinical examination:

Extraoral findings: revealed a swelling of around 3x5 centimeters in size, (**Figure 3)**; located in front of the tragus of the ear and extending to the corner of the mouth. The swelling was firm in consistency and tender on palpation. The lymph node on the same side was firm, palpable and movable over the deeper structures.

Intraorally: there was an ulcero-proliferative growth measuring about 2x3 centimeters in size, extending from the 35 to the 38 regions. **(Figures 2, 3**) The surrounding area was erythematous, and the base of the ulcer showed a yellowish necrotic slough. On palpation, the firm and tender swelling were appreciated. The border of the ulcer was everted. Hard tissue examination revealed a grade II mobility with 35 and grade lll mobility with 37 and 38. There was a grade III level of stains and calculus.

Figure 2: Ulceroproliiferative growth 2x3 cm in size and extending from 35 to 38 regions

Figure 3: Surrounding area was erythematous and ulcer base showed a yellow necrotic slough

The patient was advised an orthopantomogram (OPG). The OPG showed a bony extension of the lesion and radiolucency was observed in the distal and lower part of the ramus of the mandible. A pathological fracture was observed on the left side of the mandible. **(Figure 6**)

The provisional diagnosis of Squamous cell carcinoma of the oral cavity was given. Blood examination was non-specific and unrelated to the findings. An incisional biopsy was done.

The Hematoxylin and eosin stained sections of the tissue revealed a large collection of basaloid cells with angular nuclei. Cystic glandular spaces were present. The basaloid cells showed dysplasia and mitosis. (**Figures 5, 6,7, 8, 9, 10)**A confirmatory histopathological diagnosis of the Adenoid squamous cell carcinoma was made after observing the characteristic SCC features with duct-like structures without any secretory component within it.Patient was referred to a higher cancer center for treatment in January 2015 and due to high rate of metastasis into visceral organs she succumbed to her illness in March 2015

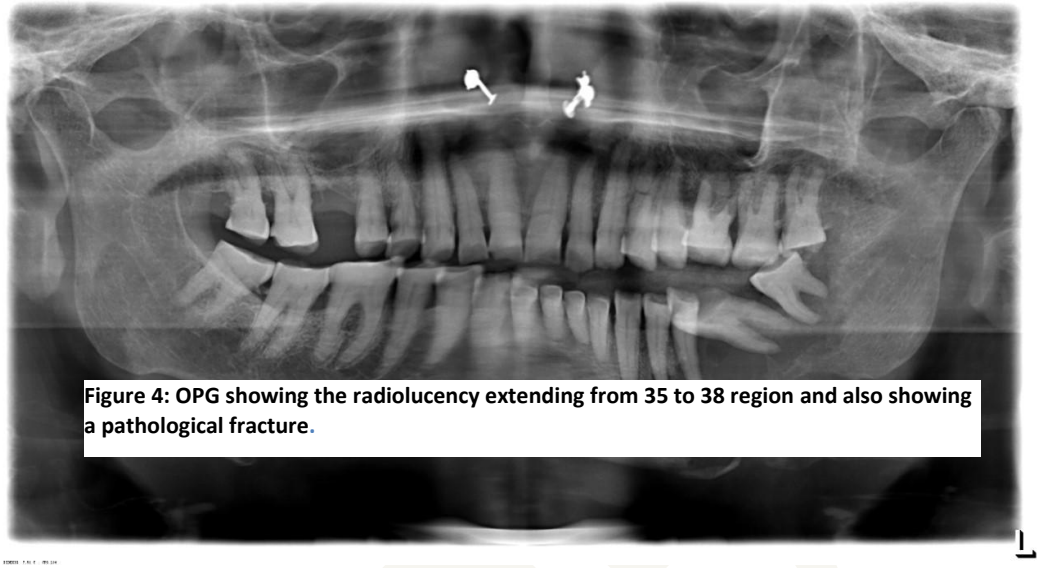

Figure 4: OPG showing the radiolucency extending from 35 to 38 region and also showing a pathological fracture.

Figures 5: Incisional biopsy procedure in progress. Lesional tissue measuring 2x3 cm in size.

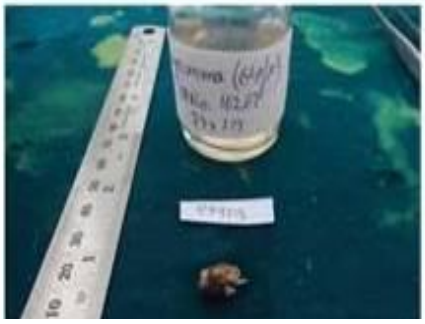

Figure 6: Pathological specimen

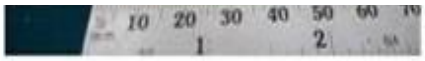

Figure 7 and 8: Epithelial cells enclosing the acantholytic areas

Figures 9, 10 and 11: Epithelial cells surrounding the glandular spaces. Acantholytic process resulting in gland like areas

Figure 12 and 13: Dysplastic areas confirming a squamous cell carcinoma or its variant. Keratin pearl formation is visible. (45x view of the same tissue)

.

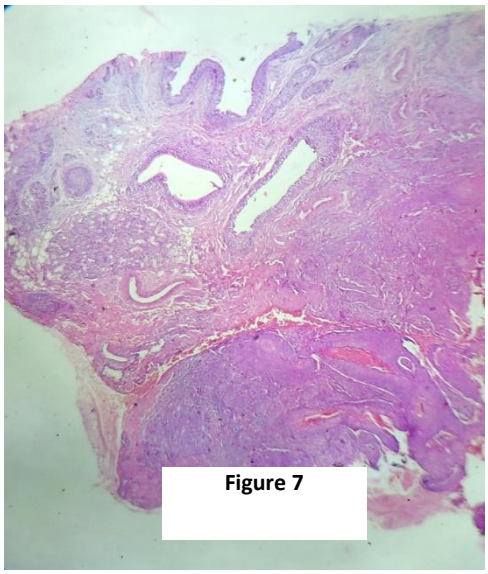

Figure 7

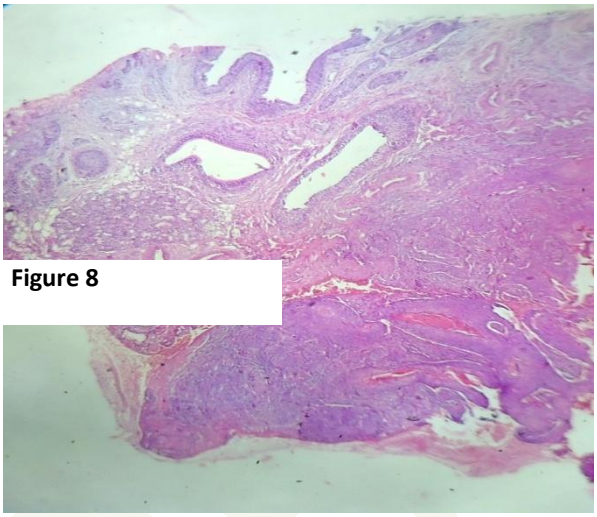

Figure 8

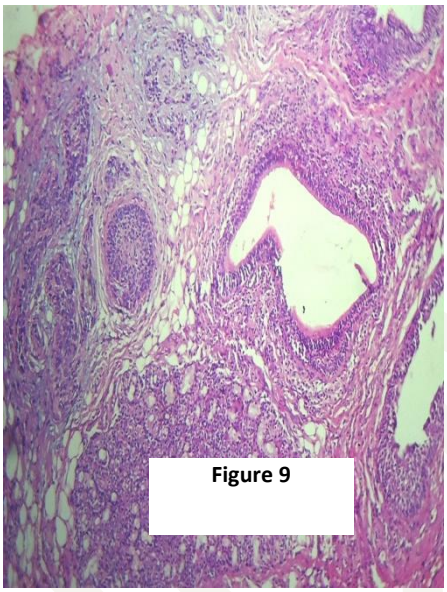

Figure 9

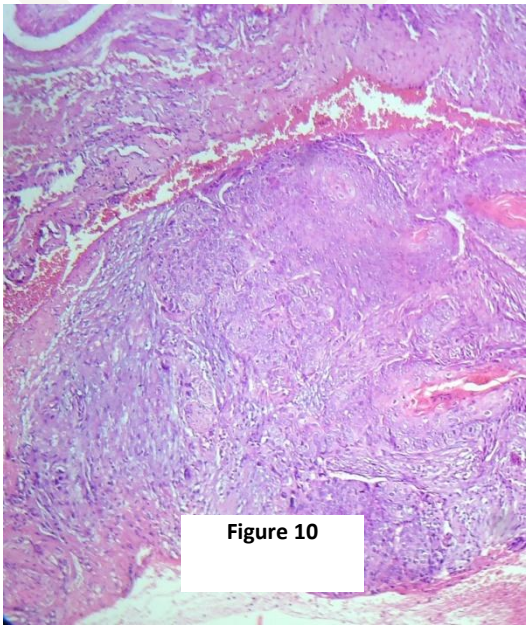

Figure 10

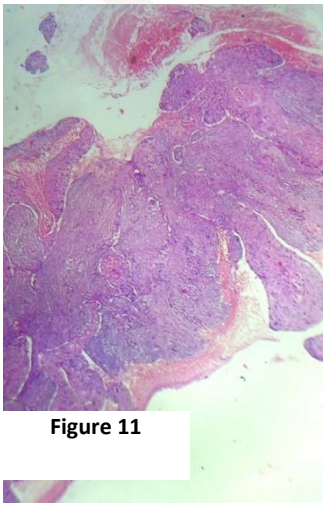

Figure 11

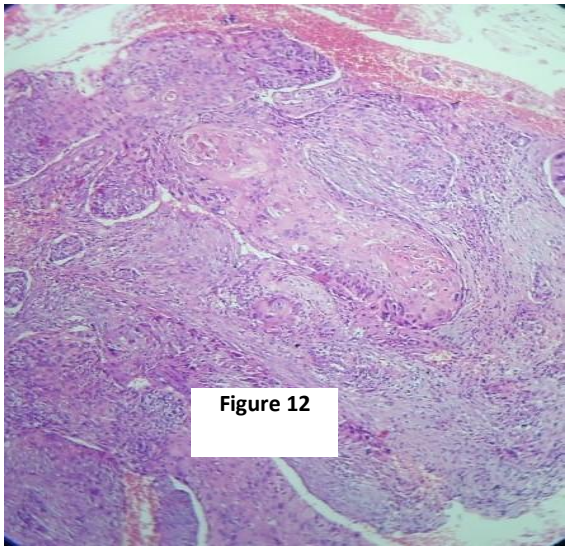

Figure 12

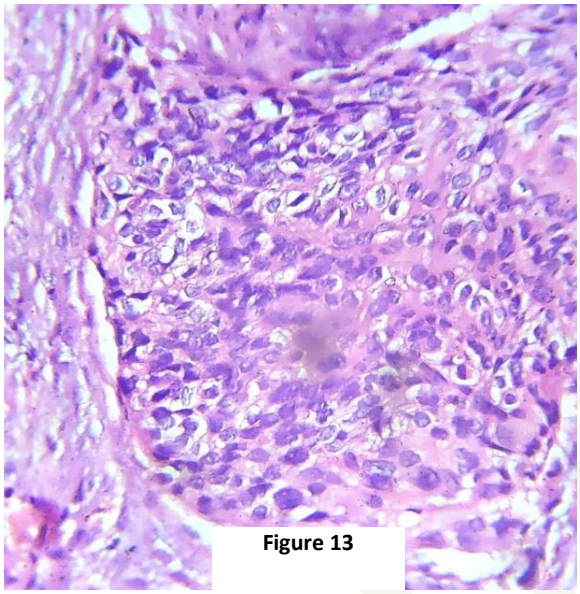

Figure 13

CONCLUSION

ASCC is an uncommon variant of SCC with a poor prognosis and therefore, making the differential diagnosis by immunohistochemistry to exclude eccrine neoplasms, salivary gland neoplasms, epithelial neoplasms and vascular sarcomas is considered mandatory.

FOOTNOTES

Competing interests: None declared.

Informed consent of the patient was received for publication of this case study.

REFERENCE

1. N Zidar, N Gale, AŽupevc, and D Dovšak. Pseudovascular adenoid squamous- cell carcinoma of the oral cavity—a report of two cases. J ClinPathol. 2006 Nov; 59(11): 1206–1208.
2. JiYeon Lim, Mi Ok Do, Seong Hyun Kim, JeongHeeHahm, and KyuKwangWhang. A Case of Acantholytic Squamous Cell Carcinoma. Ann Dermatol. 2008 Dec; 20(4):267-270.
3. Tumors and cysts of Epidermis. Page 821. Lever's Histopathology of the Skin. David E. Elder, Rosalie Elenitsas, Bernett L. Johnson, George F. Murphy. Lippincott Williams & Wilkins, 2009 - Medical - 1257 pages
4. S Akeesha A. Shah, Susanne K. Jeffus, Edward B. Stelow. Squamous Cell Carcinoma Variants. of the Upper Aerodigestive Tract. A Comprehensive Review with a Focus on Genetic Alterations. Arch Pathol Lab Med. June 2014; 138: 731-744
5. Margaret H. Rinker, Neil A. Fenske, Leigh Ann Scalf, and L. Frank Glass. Histologic Variants of Squamous Cell. Carcinoma of the Skin. S. 4 Cancer Control July/August 2001.8(4): 354-357
6. Douglas R. Gnepp. Squamous Cell Carcinoma of upper aerodigestive tract. Pages 88, 89. Diagnostic Surgical Pathology of the Head and Neck. Elsevier Health Sciences, 07-Apr-2009 - Medical - 1224 pages
7. Mardi K, Singh N. Acantholytic squamous cell carcinoma of the oral cavity: A rare entity. J Oral MaxillofacPathol 2014. 18, Suppl S1:128-30

8. Sook-Bin Woo. .Leucoplakia, Oral Dysplasia and Squamous Cell Carcinoma. Page 254. Oral Pathology: A Comprehensive Atlas and Text. Elsevier Health Sciences, 07-Feb-2012 - Medical - 464 pages
9. Oliver Driemel, Urs DA Müller-Richter, Samer G Hakim, et al. Oral acantholytic squamous cell carcinoma shares clinical and histological features with angiosarcoma. Head Face Med. 2008; 4: 17.
10. A Sigfrid, A. Muller, Charles M. Wilhelmj Edgar G. Harrison, R. K. Winkelmann. Adenoid Squamous Cell Carcinoma (Adenoacanthoma of Lever) Report of Seven Cases and Review. Arch Dermatol. 1964; 89(4):589-597.
11. Kusafuka K1, Ebihara M, Ishiki H, et al. Primary adenoid squamous cell carcinoma of the oral cavity. Pathol Int. 2006 Feb: 56(2):78-83.
12. Leslie Michaels, Henrik B. Hellquist. Unusual form of Squamous cell carcinoma. 2001. Page 410. Ear, Nose and Throat Histopathology. Doi 10.1007/978-1-4471-0235-9
13. Antonio Cardesa, Pieter J. Slootweg. Lesions of squamous epithelium. Page 22. Pathology of the Head and Neck. Springer Science & Business Media, 02-Aug-2006 - Medical - 316 pages.
14. Tadashi Terada. Adenoid squamous cell carcinoma of the oral cavity. Int J ClinExpPathol. 2012; 5(5): 442–447
15. Margaret H. Rinker, MD, Neil A. Fenske, MD, Leigh Ann Scalf, MD, and L. Frank Glass. Histologic Variants of Squamous Cell. Carcinoma of the Skin. S. 4 Cancer Control July/August 2001; 8(4) : 354-357