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RESOLVING DIFFICULT HISTOLOGICAL DIAGNOSIS OF THE RARE ACANTHOLYTIC SQUAMOUS CELL CARCINOMA USING IMMUNOHISTOCHEMISTRY: A CASE REPORT

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ABSTRACT

Background: **Acantholytic squamous cell carcinoma (ASCC), also known as adenoid squamous cell carcinoma, typically affects elderly men in the skin of the head and neck region especially due to exposure to sunlight. It rarely occurs in the oral mucosa but when it does, it is characterized by aggressive biological behaviour and the ability for distant metastasis with very poor prognosis.**

Method: **We report the case of a 73-year-old man diagnosed with ASCC of the left maxillary region who died three (3) months following presentation.**

Result: **Histopathology revealed component cells made up the nests, which were mostly basaloid and slightly pleomorphic with discohesiveness of the epithelial cells at the center of the nest. This histology appearance mimics vascular neoplasms like angiosarcoma with a cellular event like vascular invasion. An immunohistochemistry for AE1/AE3 and CD 34 was employed to resolve the diagnostic challenge encountered within the histology evaluation and distinguish it from other similar entities.**

Conclusion: **This case report highlights the need for immunohistochemical study of the unique and rare oral ASCC whose definitive diagnosis may be missed because of similarities with other entities.**

Keywords: Acantholytic squamous cell carcinoma, Vascular invasion, Angiosarcoma, Immunohistochemistry.

INTRODUCTION

Oral squamous cell carcinoma accounts for over 95% of oral cavity cancers and records one of the lowest five-year survival rates among all cancers.[1,2] According to the World Health Organization (WHO), histological variants of squamous cell carcinoma may be classified as basaloid, acantholytic, adenosquamous, spindle cell/ sarcomatoid, papillary, and lymphoepithelial carcinomas and records up to 95% of all oral cavity cancers.[3] However, the acantholytic squamous cell carcinoma (ASCC) variant carries a significant biological impact due to its aggressive clinical behaviour and very poor prognosis.[4] Notably, only a few cases of acantholytic squamous cell carcinomas have been described in literature with a cumulative incidence of 0.1% of all oral squamous cell carcinomas.[5] Additionally, the rare occurrence and distinct histological features of acantholytic squamous cell carcinoma often present a diagnostic challenge. Hence, in addition to histological diagnosis, the need for reliable molecular markers to improve the accuracy of the diagnosis remains crucial.[6]

In this case report, we present a 73-year-old male who was diagnosed with acantholytic squamous cell carcinoma of the left maxillary region using immunohistochemistry following a histopathological diagnostic dilemma. We believe that this case report will add to existing body of knowledge on the diagnostic challenges associated with ASCC, their morphological differentials or cellular events (E.g., vascular invasion) that may occur on histological evaluation of ASCC. We also intend to detail the

available biological markers that may be employed for resolving these diagnostic conflicts.

CASE REPORT

A 73-year-old male meat-seller presented to our facility with a four-week history of a rapidly growing swelling with associated painful and bleeding ulcers in the left maxillary region. There was a positive history of weight loss and anorexia. There was history of alcohol use and patient consumed at least one bottle of alcohol every week for over 40 years but there was no history of use of any tobacco products. There was no familiar history of similar complaints, and no swellings in any other part of the body. No significant past medical history.

Figure 1: Clinical photograph showing an ulcerative erythematous bucco-lingual swelling in the left maxillary region

Clinical examination revealed a localized, firm swelling on the left cheek, measuring about 3 cm by 3 cm, with intact overlying skin and no evidence of anaesthesia or paresthesia on the cheek region. There was a palpable, tender, hard, and freely mobile enlarged left submandibular lymph node measuring about 2cm in its widest diameter. Intraorally, there was presence of a bucco-palatal swelling measuring about 6cm by 5cm in the region of tooth 21 to 28 with an erythematous surface covered with multiple ulcerations and slough. The floor of the ulcers was indurated and raised. The lesion was firm in consistency, tender, and associated with mobility of the associated teeth 26 and 28 (Figure 1)

A clinical impression of squamous cell carcinoma of the left maxillary region was made, to rule out melanoma. We requested for a craniofacial computerised tomography (C.T) scan to determine the anatomic extent of the tumour (Figure 2) and an incisional biopsy for histological diagnosis (Figure 3).

The incisional biopsy was done on the day of patient's presentation at the clinic, and the histological diagnosis was reported 10 days after the biopsy was taken. Histology revealed a neoplasm composed of epithelial nests within moderately dense fibrous connective tissue stroma. The component cells that make up the nests were mostly basaloid and slightly pleomorphic with discohesiveness of the epithelial cells at the center of the nest (Figure 3). Further, there was an initial opinion that the neoplastic epithelial cells were invading into vascular channels, and another opinion was that it could be an angiosarcoma. To clarify these suggestions

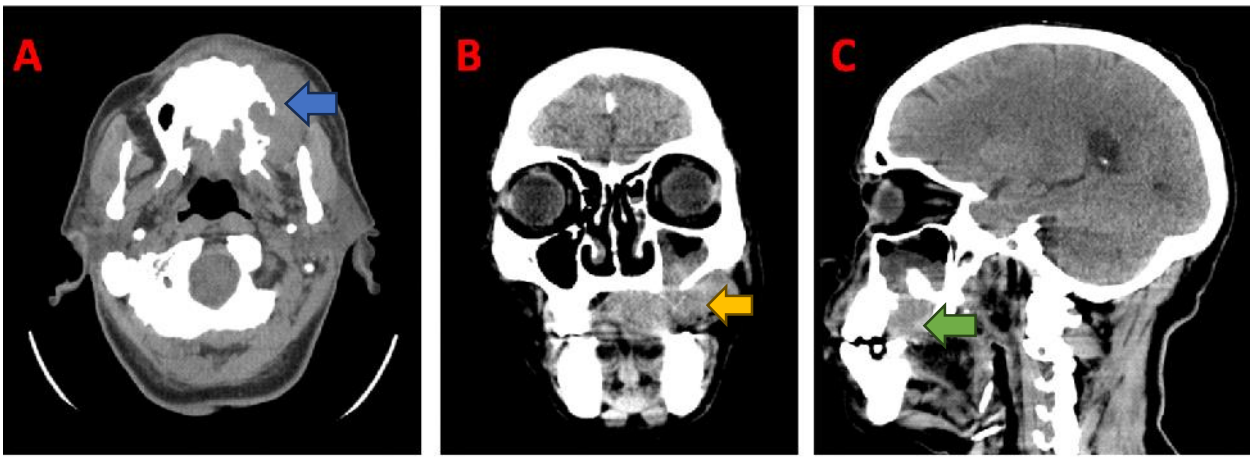

Figure 2: craniofacial C.T scan showing the anatomic extent of the swelling.

A. Axial view shows isodense lesion obliterating the left nasal cavity and left maxillary antrum, extending to the left submasseteric region. (Blue arrow shows the location of lesion)

B. Coronal view shows isodense lesion involving left maxillary antrum, with perforation of the floor of the maxillary antrum, extending to the oral cavity with further involvement of the submasseteric and buccal spaces. (Yellow arrow shows the location of lesion).

C. Sagittal view shows isodense lesion extending from the maxillary antrum with destruction of the floor of the antrum and extension into the oral cavity and retropharyngeal region (Green arrow shows the location of lesion).

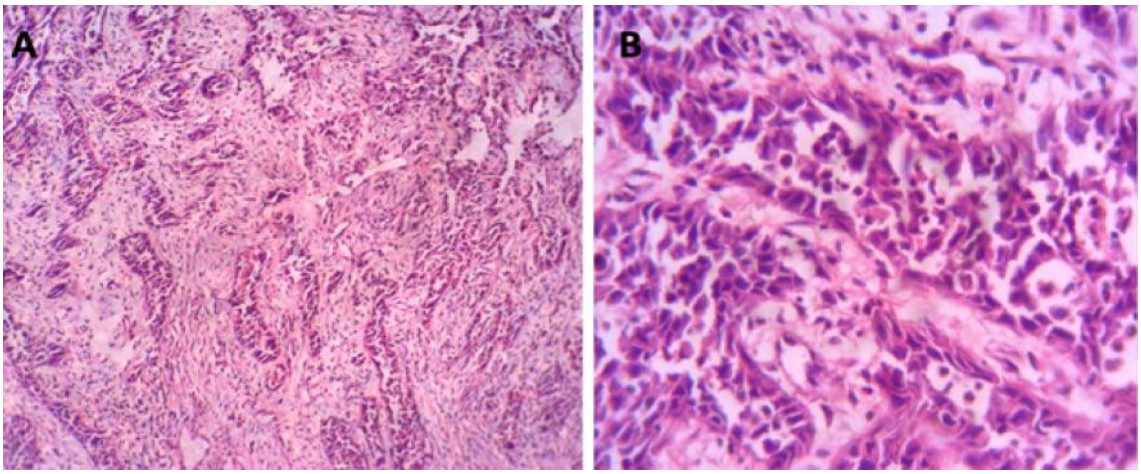

Figure 3: Heamatoxylin and Eosin of ASCC at (A) X 100 magnification and at (B) X 400 magnification.

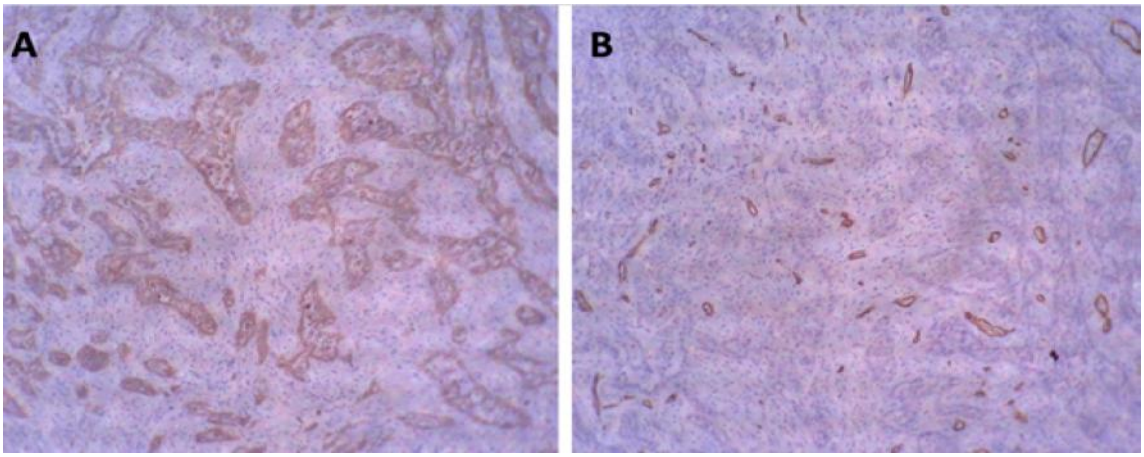

Figure 4: (A) AE1/AE3 positivity of the epithelial neoplastic cell and (B) CD 34 positivity of the vascular channels.

immunohistochemistry was requested for AE1/AE3 and CD34 (Figure 4).

The immunohistochemistry result was then obtained 8 days after the histological diagnosis was made due to the diagnostic dilemma encountered from the histology report. Immunohistochemistry showed positive (++) staining of epithelial islands with AE1/AE3 while CD 34 only stained normal appearing blood vessels (Figure 4). A final diagnosis of acantholytic squamous cell carcinoma was confirmed. Patient was presented immediately at the orofacial tumour group meeting (a multi-disciplinary group meeting involving the oral and maxillofacial surgeons, oncologists, head and neck surgeons, radiation oncologists and oral pathologists) where surgical intervention and adjuvant chemoradiation therapy was decided as treatment modalities for the patient. Unfortunately, patient died before the commencement of any intervention, and this was about three (3) months following his first presentation to our facility from the complications of the disease.

DISCUSSION

Acantholytic squamous cell carcinoma (ASCC) is a rare variant of squamous cell carcinoma that was first described by Lever in 1947 before Muller later redefined the entity.[7,8] ASCC commonly affect males with an average age of occurrence between 38-79 years.[8] ASCC is commonly seen in sun exposed areas especially in the elderly but rarely found in the oral cavity.[9,10] When ASCC occurs in the oral cavity, it is characterized by a more aggressive clinical behaviour[11-13] when compared to those affecting the skin. Though the etiological factors for intraoral ASCC have not been fully elucidated in literature[11,12], tobacco use, alcohol consumption, exposure to sunlight, previous trauma, exposure to Human Papillomavirus, and genetic factors have been identified as notable risk factors of ASCC.[14-16] In this report, however, the patient consumes alcohol consistently for a period of forty (40) years and has regular exposure to ultraviolet radiation from the sunlight through outdoor activities as patient was a meat seller who trades in an open market where exposure to ultraviolet radiation is possible. Additionally, the age of the patient falls within

the peak age of the ASCC.[8] ASCC has diverse clinical presentations ranging from an ulcerative erythematous mass to an ulcero-proliferative mass.[3,9,10] The varying perspectives of different authors on the prognosis of ASCC in the oral cavity are influenced by the limited number of reported cases, which has led to differing opinions on the biological behavior of this condition.[3,17,18]

Histologically, ASCC exhibits cystic degeneration of the neoplastic epithelial cells, resulting in a prominent alveolar pattern and pseudoglandular formations with acantholytic cells.[3,9,10,19] Angiosarcoma, a mesenchymal malignant neoplasm, exhibits a histopathology like that of acantholytic squamous cell carcinoma.[19,20] However, they can be differentiated using vascular immunohistochemical markers like CD 31 and CD 34.[19,20] In this case, we found a morphology which is like that of angiosarcoma. Therefore, immunohistochemistry was helpful in refuting this diagnosis as CD 34 was negative in the neoplastic cells which supports vascular differentiation. Also, the suspicion that epithelial cells were invading the vasculature was resolved with immunohistochemistry as the cells lining the cystic spaces did not stain for CD34. Therefore, we were able to solve the diagnostic dilemma involved in the diagnosis of the rare variant of oral squamous cell carcinoma (the ASCC) using the diagnostic markers.

Furthermore, acantholytic squamous cell carcinoma typically exhibits strong, diffuse positivity for cytokeratin markers (notably CK5/6 and pan-cytokeratin), confirming its epithelial squamous differentiation and effectively ruling out angiosarcoma.[7,8]

In addition, acantholytic squamous cell carcinoma is characterized by aggressive clinical behaviour and very poor prognosis[4] due to early locoregional metastasis, intracranial tumor extension and local recurrence.[21] In fact, ASCC has one of the worst prognoses among all cancers with a reported 0-20% percent survival rate within the first four years of diagnosis.[21] In this case, the patient died three (3) months following presentation to our facility due to suspected distant metastasis and multiple organ dysfunction. This therefore confirms its aggressiveness and poor prognosis, especially following late presentations.

CONCLUSION

ASCC of the oral cavity is rare and may pose a diagnostic challenge with close differentials and a cellular event like vascular invasion, however, such confusion can be solved promptly via use of appropriate immunohistochemistry for more accurate diagnosis. Ensuring an accurate diagnosis for ASCC is crucial due to its aggressive behaviour and associated poor prognosis.

Ethical consideration

Consent was obtained from the patient and relatives for the publication of this report including the use of the clinical pictures.

Conflicts of interest

Afeez Abolarinwa Salami, the corresponding author of this work is a member of Annals of Ibadan Postgraduate Medicine editorial board. To minimise bias, they were excluded from all editorial decision related to the acceptance of this article for publication. Other authors have no conflicts of interest to declare.

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