

Signet-ring Change in Cells of Oral Squamous Cell Carcinoma: Important and Ignored Factor

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ABSTRACT

Introduction: Oral squamous cell carcinoma (OSCC) is one of the most common tumors any dentist can encounter; still the histopathology of this much commonly encountered malignancy has not evolved much. Many histopathological variants of OSCC are established entities in the literature but not many of these are reported. Signet-ring cell variant is one such extremely rare variant of OSCC of which only two cases are reported in the literature till date. The present article sheds light on the etiopathogenesis and management of this unconventional variant.

Discussion: The signet-ring variant of SCC, although is rare in the oral mucosa, manifests itself at least as a focal change in many cases of SCC at other locations such as SSC of skin as well as pulmonary SSC. The morphological change seen in signet-ring cells probably reflects a degenerative phenomenon related to anaplastic progression. Although the presence of signet-ring cells in conventional OSCC is established as a distinct feature, commenting on the biological behavior and prognosis of such cases is difficult due to less number of reported cases; hence the need of more such articles.

Conclusion: The unconventional variants of very common tumors need to be studied and should be given attention as these can give us the clue for the overall behavior and outcome of such entities.

Keywords: Histopathological variants, Human papillomavirus, Hydropic degeneration, Oral squamous cell carcinoma, Signet cells, Signet-ring variant.

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most common tumors any dentist can encounter. But, still the histopathology of this much commonly encountered malignancy has not evolved much. Especially, apart from mentioning the tumor differentiation into well-differentiated, moderately differentiated, or poorly differentiated one in the histopathology report, many a times reporting of certain unconventional features that may have a prognostic impact is not taken into consideration. The present article aims to shed light on one such unconventional feature of squamous cell carcinoma (SCC), which deserves our attention.

DISCUSSION

The signet-ring variant of SCC, although is rare in the oral mucosa, manifests itself at least as a focal change in many cases of SCC at other locations such as SSC of skin as well as pulmonary SSC.^{1,2} The term "signet-ring cell morphology" describes a cell with a large intracytoplasmic vacuole, resulting in compression and eccentric displacement of the nucleus¹ (Figs 1 and 2). Electron microscopy reveals that most of the vacuoles contained moderate amounts of electron-dense flocculent material, while the others are empty. Further studies demonstrate that inciting factors may promote the formation of dilated endoplasmic reticula, and that the dilated endoplasmic reticula are among the most important components of these vacuoles.²⁻⁴

The morphological change seen in signet-ring cells probably reflects a degenerative phenomenon related to anaplastic progression. Many researchers have stated that the reason for the signet-ring morphology of the cells is hydropic degeneration in the cells, which causes their progression toward dedifferentiation.^{4,5} However, not all signet-ring formations have a degenerative origin and can be secondary to the production of mucin, immunoglobulin accumulation, or deposition of thyroglobulin, among others.⁵ Wang

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et al. in one of their published case reports on cutaneous SCC have put forth that UV rays and the presence of human papillomavirus (HPV) are among the causative factors for signet ring-like changes in the malignant squamous cells of cutaneous SCC especially of the head and neck region.² One more interesting finding of the case reports is the association of diabetes mellitus (DM) with this variant of SCC. Authors have put forth this primary verification after studying the p63/FGFR2 axis of the cells that DM may be an etiological factor in the development of clear cell/signet-ring cell cutaneous SCC. This hypothesis can further be explained by the fact that metabolic disorders including hyperinsulinemia and immune disorders in patients with DM increase the risk of malignant

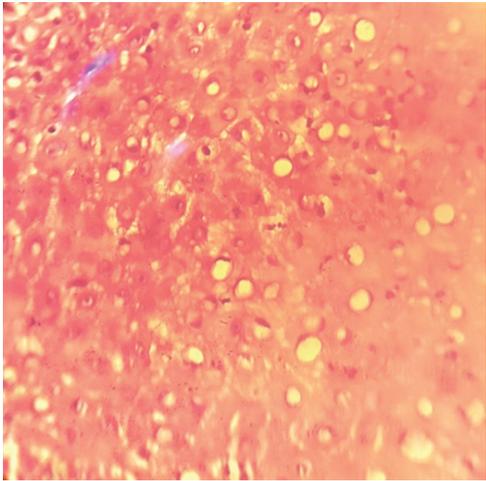


Fig. 1: Signet-ring-shaped cells (H and E stain, 10× magnification)

transformation in dysplastic ulcers by enhancing the p63 that further enhances the expression of fibroblast growth factor receptor 2 (FGFR2). As also, DM increases the risk of HPV infections in the cells. The study supports the fact as the signet cells demonstrated strong positivity for FGFR2 immunohistochemically.² In some cases, cells may appear as signet rings as a result of artifact caused due to the use of Lugol's iodine.⁴

Although the presence of signet-ring cells in conventional OSCC is established as a distinct feature, commenting on the biological behavior and prognosis of such cases is difficult as till date only 12 cases of this variant have been reported. Among these 12 cases, only 2 were intraoral. However, almost in all these 12 cases that show this change the patient either showed local recurrences or distant metastasis of the tumor with compromised prognosis.⁵ According to the case description of signet-ring variant of SCC of upper lip published by Demellawy et al., it has been clearly mentioned that due consideration to this rare and unconventional variant of SCC should be given so that its significance could be established with more clarity.⁶ The literature search also did not yield many cases of signet-ring variant, which further raises the notion that whether the cases of such unconventional variant are diminishing or whether these cases are ignored and not reported.

The signet-cell variant of OSCC warrants attention while reporting as it can get misinterpreted as other tumors including adenocarcinomas of the salivary glands, basal cell carcinomas, melanomas, and lymphomas and as other metastatic tumors.^{5,7} This can further lead to wrong treatment and compromised prognosis of the patient.

Hence, documentation and reporting of such unconventional variants of common malignancies should be done as a routine practice so as to generate more and more information regarding their behavior, impact on diagnosis, prognosis, and treatment of these rare variants.

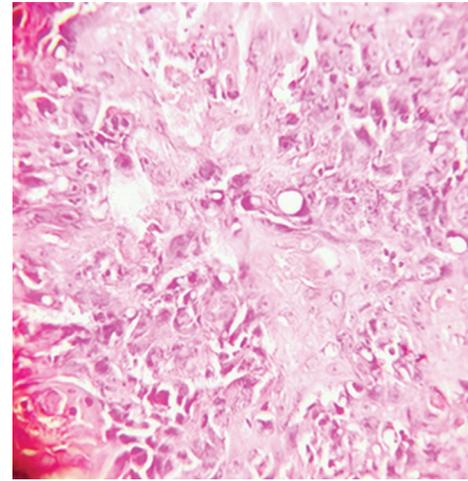


Fig. 2: Signet-ring-shaped cells with clear cytoplasm and eccentrically displaced nucleus (H and E stain, 40× magnification)

CONCLUSION

The unconventional variants of very common tumors need to be studied and should be given attention as these can give us the clue for the overall behavior and outcome of such entities. As also, these can bring down the diagnostic dilemmas and misinterpretations, thereby cutting-edge diagnosis and treatment can be provided.

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