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ORIGINAL ARTICLE

PROGNOSTIC INDICATORS OF VERRUCOUS CARCINOMA - A SEVEN YEAR INSTITUTIONAL STUDY

Priyadharshini Muthumanickam[1], Abilasha Ramasubramanian[2], Pratibha Ramani[3]
[1]Pg Resident , Department of Oral Pathology, Saveetha institute of medical and technical sciences, Chennai, India,
[2]Professor Department of Oral Pathology, Saveetha institute of medical and technical sciences, Chennai, India,
[3]Professor & Head Department of Oral Pathology, Saveetha institute of medical and technical sciences, Chennai
Corresponding author*: Abilasha Ramasubramanian , Department of Oral Pathology, Saveetha institute of medical and technical sciences, Chennai, India, priyavignesh1451996@gmail.com
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Verrucous carcinoma (VC), a rare subtype of squamous cell carcinoma (SCC), is distinct due to its unique clinical and histopathological characteristics Unlike conventional SCC, VC is characterized by a slow growth rate, locally aggressive behaviour, and a limited tendency for distant metastasis. However, it remains a clinical concern due to its potential to transform into invasive SCC. Materials and Methods:The research focused on cases diagnosed between 2017 and 2024, involving patients with verrucous carcinoma (VC), verrucous carcinoma transforming into squamous cell carcinoma (SCC), and proliferative verrucous leukoplakia. The hospital's database served as the primary source of patient data for this study, offering access to clinical records, histopathological findings, and other relevant diagnostic information.Results : Out of 60 cases in the dataset, 58 (96.7%) were valid and included in the analysis, while 2 cases (3.3%) had missing data. This high percentage of valid cases ensures the reliability of the findings.

Keywords*:* Verrucous carcinoma, oral cancer, prognosis

INTRODUCTION

Head and neck cancers constitute a significant global health challenge, ranking as the seventh most prevalent cancer worldwide. Approximately 90% of these malignancies arise within the oral cavity, predominantly affecting the squamous epithelium. Verrucous carcinoma (VC), a rare subtype of squamous cell carcinoma (SCC), is distinct due to its unique clinical and histopathological characteristics[1]. Unlike conventional SCC, VC is characterized by a slow growth rate, locally aggressive behaviour, and a limited tendency for distant metastasis. However, it remains a clinical concern due to its potential to transform into invasive SCC. Understanding the prognostic factors associated with VC is critical for guiding treatment approaches and improving patient outcomes [2].

The incidence of verrucous carcinoma is relatively low, accounting for less than 5% of all oral cancers. It is most commonly diagnosed in individuals over the age of 40, with a slight male predominance. Its geographic distribution is influenced by cultural and lifestyle factors, such as the use of smokeless tobacco and betel quid chewing. In regions like Southeast Asia and the Indian subcontinent, these habits significantly contribute to the prevalence of VC. Conversely, in Western countries, the use of smokeless tobacco products plays a prominent role in its etiology. Though typically observed in older adults, occasional cases in younger individuals highlight the need for awareness across all age groups [3].

VC is primarily associated with chronic mucosal irritation. Tobacco use, both in smoked and smokeless forms, remains the most significant risk factor. Other contributory factors include areca nut chewing, alcohol consumption, and poor oral hygiene[3].Human papillomavirus (HPV) infection has emerged as a potential etiological agent, with studies reporting varying prevalence rates depending on the diagnostic techniques used, such as polymerase chain reaction (PCR) or immunohistochemistry. The interaction between HPV and host cellular mechanisms is believed to play a role in the development and progression of VC. Additionally, genetic predispositions and chronic inflammatory conditions may further exacerbate its pathogenesis[4].

Clinically, VC often presents as a slow-growing, exophytic lesion with a warty or cauliflower-like surface.

Verrucous carcinoma lesions are almost always large, exophytic, soft, fungating, slow growing neoplasms with a pebbly mamillated surface. These lesions commonly involve the buccal mucosa, gingiva, tongue, and other areas of the oral cavity. Early-stage VC may mimic benign conditions such as verrucous leukoplakia, making accurate diagnosis challenging. Patients are typically asymptomatic in the initial stages, delaying diagnosis until the lesion becomes extensive. Differential diagnoses include papillomas, leukoplakia, and conventional SCC, necessitating a thorough clinical and histopathological evaluation [5,6].

Histologically, VC is characterized by hyperkeratosis, papillomatosis, and a pushing border of invasion without infiltrative growth. Cellular atypia is minimal, and mitotic activity is generally absent, reflecting the tumours well-differentiated nature[7]. Immunohistochemical markers such as p53, Ki-67, and cytokeratins can assist in distinguishing VC from other oral lesions. The unique histopathological features underscore the importance of expert pathology review for accurate diagnosis and effective management [8,9].

The prognosis for VC is generally favourable when detected early and managed appropriately. The absence of metastatic potential to regional lymph nodes and distant organs distinguishes VC from other forms of SCC. Prognostic factors influencing outcomes include tumor size, depth of invasion, anatomical location, and HPV status. Overexpression of molecular markers such as p53 and high Ki-67 proliferation indices has been linked to aggressive disease behaviour. Additionally, host- related factors such as age, immune competence, and the presence of comorbidities play crucial roles in determining prognosis [10].

Recent advancements in diagnostic techniques have improved the detection and management of VC. High-resolution imaging modalities, including magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET-CT), provide detailed insights into tumor extent and involvement of adjacent structures[11]. Molecular profiling has enabled the identification of genetic and epigenetic alterations, offering potential biomarkers for targeted therapy. These innovations have enhanced diagnostic accuracy and facilitated personalized treatment planning [12].

Surgical excision with clear margins remains the cornerstone of VC management. In cases where complete excision is challenging, adjunctive therapies such as radiotherapy and chemotherapy may be employed. However, the role of these therapies is limited due to the tumours low radio sensitivity and chemo resistance[13]. Emerging treatments, including targeted therapy and immunotherapy, are being explored in clinical trials, showing promise in improving outcomes for specific patient subsets. The integration of these novel approaches into clinical practice could revolutionize the management of VC in the future [14].

This study aims to investigate the prognostic indicators of verrucous carcinoma through a comprehensive analysis of cases diagnosed at Saveetha Dental College and Hospitals between 2017 and 2024.

MATERIALS AND METHODS

This study was a retrospective analysis conducted at the Department of Oral Pathology, Saveetha Dental College and Hospitals. The research focused on cases diagnosed between 2017 and 2024, involving patients with verrucous carcinoma (VC), verrucous carcinoma transforming into squamous cell carcinoma (SCC), and proliferative verrucous leukoplakia. The hospital's database served as the primary source of patient data for this study, offering access to clinical records, histopathological findings, and other relevant diagnostic information.

The study included patients diagnosed histopathologically with oral VC, cases showing a transformation from VC to invasive SCC, and proliferative verrucous leukoplakia. Patients with incomplete medical records, those whose diagnosis was not confirmed by histopathological analysis, and those undergoing treatment outside the hospital were excluded to ensure consistency and reliability in data collection.

Clinical data, including patient demographics (age, gender, and lifestyle habits such as tobacco or areca nut use) , lesion characteristics (site, size, and clinical presentation), and duration of symptoms, were extracted. Information regarding treatment modalities, recurrence rates, and follow-up outcomes was also gathered. Provided in Table 1.

The data were compiled and tabulated using Microsoft Excel.

All cases were reviewed by a team of experienced pathologists to confirm the diagnosis of VC and related conditions. Histopathological analysis focused on key features, including hyperkeratosis, exophytic growth, papillomatosis, and the characteristic "pushing" border of invasion. Data were analyzed using SPSS software. Descriptive statistics were calculated to summarize patient demographics and clinical features. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as means and standard deviations.

Comparative analyses were conducted to evaluate the correlation between clinical features and prognostic outcomes. Statistical significance was determined using appropriate tests, such as the chi-square test for categorical variables and t-tests for continuous variables, with a p-value of <0.05 considered statistically significant.

Table 1. Clinical features

Variable	Category	No. of Patients
Gender	Male	39
	Female	7
Age	≤50 years	16
	≥51 years	37
Habits	With Habits	35
	Without Habits	26
Laterality	Left	29
	Right	19
	Bilateral	0
Lymph Node Metastasis	Yes	41
	No	20
TNM Stage	T1	2
	T2	2
	T3	1
	T4	11
Invasion	Maxilla	5
	Mandible	3
	Skin	1

RESULTS

The statistical analysis of verrucous carcinoma and related conditions provides significant insights into the relationships between demographic factors and clinical outcomes. Out of 60 cases in the dataset, 58 (96.7%) were valid and included in the analysis, while 2 cases (3.3%) had missing data. This high percentage of valid cases ensures the reliability of the findings. The analysis revealed a strong association between age and advanced disease features such as metastasis and extranodal extension (ENE), with older patients showing a higher likelihood of presenting with these characteristics ($p < 0.001$). This suggests that disease progression and spread are more prevalent in older individuals, underscoring the need for vigilant monitoring and aggressive management in this group. Additionally, a significant relationship was identified between gender and habits like smoking or chewing tobacco ($p = 0.045$), indicating that these behaviours, known risk factors for carcinogenesis, are more prevalent in one gender. However, no significant associations were found between age and diagnosis type, suggesting that the type of verrucous carcinoma or related condition is distributed uniformly across different age groups. Similarly, no significant correlations were observed between age and habits, or gender and clinical outcomes such as metastasis or ENE. The analysis also found no gender-specific differences in biopsy results or diagnosis types, indicating that the patterns of disease presentation and diagnostic findings are similar across genders.

These findings have important clinical and public health implications. The strong association between age and advanced disease characteristics highlights the importance of early detection and tailored treatment plans for older patients, who are at greater risk of

metastasis and ENE. Targeted interventions, such as more frequent screenings and comprehensive management approaches, could help mitigate disease progression in this high-risk group. The significant link between gender and habits underscores the need for gender-specific public health strategies, such as tobacco cessation programs, to address modifiable risk factors and reduce disease burden.

In contrast, the absence of significant associations between other variables, such as age and diagnosis type or gender and metastasis, suggests that certain factors may not play a pivotal role in disease progression or outcomes.

DISCUSSION

Verrucous carcinoma (VC) is a rare variant of squamous cell carcinoma (SCC) that predominantly affects the oral cavity, particularly the buccal mucosa, gingiva, and tongue. Our study, comprising 61 cases, revealed a male predominance (44 males, 13 females), consistent with previous literature indicating that VC is more common in males, particularly in regions with high tobacco consumption. Another study conducted between 2018 and 2022, involving 5,469 biopsy-proven head and neck cancer patients, found a male-to-female ratio of 4.2:1. The study highlighted that men constituted 80.80% of the study population, with oral cavity lesions being the most common site. The higher prevalence in males was linked to greater exposure to risk factors such as tobacco and alcohol[15]. Similarly, a study by Batsakis et al. (2019) reported that male patients accounted for approximately 75% of VC cases, aligning with our findings[16].

Similarly, a study focusing on oral verrucous carcinoma over a ten-year period reported that 83% of the patients were male, resulting in a male-to-female ratio of 5:1. The mean age at presentation was 49 years. In this cohort, 33.3% of patients chewed tobacco, 26.6% both chewed and smoked tobacco, and 10% only smoked tobacco. This further underscores the significant role of tobacco use in the etiology of VC, especially among males17.

Our data showed 35 cases (57.3%) with a history of deleterious habits, with pan chewing (11 cases), gutka (3 cases), and smoking (2 cases) being the most frequently reported. The association of VC with tobacco and areca nut has been well documented in prior studies. Ackerman first provided a comprehensive description of verrucous carcinoma in 1948, highlighting its association with tobacco use. In his study of 31 patients, Ackerman noted that many were elderly men with a history of chewing tobacco[18]. This led him to postulate a link between tobacco use and the development of verrucous carcinoma[19].

More studies by Munde et al. (2013) reinforced that 80-90% of patients with VC have a history of tobacco use, either in the form of chewing or smoking[20].

A study by Ackerman found that habit-associated VC cases showed a higher prevalence of field cancerization, where multiple lesions develop due to long-term carcinogen exposure[21]. Our findings support this, as many patients with habitual risk factors presented with lesions in high-risk areas such as the buccal mucosa and gingiva. In contrast, a study by Hashibe et al. (2003) demonstrated that alcohol alone is not a strong independent risk factor, but when combined with tobacco, it significantly increases the risk[22].

This was evident in our cohort, where alcohol use was observed in some cases, often alongside tobacco chewing.

VC is characterized by a papillary, well-differentiated epithelial proliferation with minimal dysplasia. Our cases frequently showed verrucous hyperplasia with minimal nuclear atypia and a pushing rather than infiltrative growth pattern, which aligns with previous histopathological descriptions. A study by Kraus and Perezmesa (1966) emphasized that VC lacks the usual features of SCC, such as nuclear pleomorphism and increased mitotic activity, making it distinct in its behavior and response to treatment[23].

Radiographically, 9 cases (14.8%) in our study showed evidence of bone invasion, reinforcing findings by Shear and Pindborg (1980), who reported that VC can cause underlying bone destruction in advanced cases, despite its slow-growing nature[24].A study published by Bansal et Al noted that while VC is generally a benign lesion with minimal aggressive potential, long- standing cases can show transformation into squamous cell carcinoma[25]. Additionally, a case report *samira et Al* discussed squamous cell carcinoma arising in a multiple verrucous epidermal nevus, emphasizing the importance of monitoring for malignant transformation in such lesions[26].These studies suggest that while VC typically remains confined to the epithelium, there is a potential for transformation into more invasive forms like SCC, underscoring the need for careful monitoring and management.

In our study , metastasis was observed in 3 cases (4.9%), while extranodal extension (ENE) was also noted in 3 cases (4.9%). Historically, VC has been considered non-metastatic or minimally metastatic. Ackerman initially classified VC as a locally aggressive but non-metastasizing tumor, an assertion supported by many subsequent studies. However, some cases of lymph node involvement and distant metastasis have been reported in more recent studies. For instance, a case report discussed a 67-year-old male patient with hybrid verrucous carcinoma exhibiting bone invasion and bilateral lymph node metastasis, despite the absence of a clear SCC

component.

This suggests that even minimal invasive characteristics within VC can lead to metastatic behaviour[27].

Another study highlighted that hybrid verrucous carcinoma, characterized by the coexistence of verrucous and conventional SCC histological features, can exhibit more aggressive behaviour, including lymph node metastasis[28].

This underscores the importance of thorough histopathological evaluation to identify any conventional SCC areas within VC, as their presence may necessitate more aggressive management. These findings emphasize the need for careful assessment of VC cases, particularly those with hybrid histology, to determine the appropriate therapeutic approach and predict potential metastatic behavior.

VC is typically a slow-growing, well-differentiated tumor with a low propensity for metastasis. In contrast, hybrid tumors—those exhibiting both VC and conventional squamous cell carcinoma (SCC) histological features—may demonstrate more aggressive behavior, including lymphatic spread. *Another* case report by Cunha et Al of VC with foci of invasive SCC, highlighting the potential for increased metastatic risk in such hybrid lesions[29].

Additionally, a case report described a rare instance of VC of the scalp, noting that while VC typically has low metastatic potential, certain factors may contribute to a more aggressive course[30].

Our findings align with this, as metastatic cases in our cohort were among patients with longstanding habits. Similarly, Shafer et al. (1975) documented ENE in only 2-5% of cases, comparable to our study's 4.9% incidence.These findings underscore the importance of thorough histopathological evaluation to identify any conventional SCC areas within VC, as their presence may necessitate more aggressive management[31].

Another OSCC study found no significant correlation between bone invasion and nodal metastasis, instead highlighting that the worst pattern of invasion (WPOI-4,5) was a stronger predictor of nodal spread. In contrast, the VC dataset reported nodal metastasis in only 3 cases (4.9%), reinforcing the well-documented low metastatic potential of VC. This comparison suggests that while OSCC metastasis is influenced by invasive tumor patterns, VC rarely metastasizes, further distinguishing their biological behavior[32].

One study found a strong correlation between high METTL5 expression and nodal metastasis in OSCC, indicating its role in tumor progression and poor prognosis. In contrast, the VC study reported nodal metastasis in only 3 cases (4.9%), reinforcing its low metastatic potential. This comparison highlights that while OSCC frequently exhibits nodal spread influenced by molecular factors like METTL5, VC remains largely localized with minimal lymphatic involvement[33].

VC is often diagnosed at an early stage (T1 or T2), as it presents as a slow-growing exophytic lesion. However, some cases in our study exhibited advanced-stage disease with T4 classification. Studies by van der Waal et al. (2011) suggested that delayed diagnosis, particularly in habitual tobacco users, often results in T3 or T4 staging at presentation. This emphasizes the importance of early detection and regular screening in high-risk populations[32].

Prognosis of VC varies with the stage at diagnosis. National survey of head and neck verrucous carcinoma reported that survival rates significantly decreased from 86.7% for Stage I to 46.8% for Stage IV, emphasizing the importance of early detection and treatment[33]. Additionally, Kademani et al. (2005) conducted a retrospective study on intraoral squamous cell carcinoma, identifying stage and grade as significant prognostic factors. While this study focused on squamous cell carcinoma rather than VC, it highlights the impact of disease stage on patient outcomes[34].

These findings underscore the critical role of early diagnosis and intervention in improving survival rates for patients with verrucous carcinoma.This is particularly relevant to our dataset, where a small subset of cases showed aggressive behavior, correlating with more advanced staging.

The primary treatment modality for VC is surgical excision with adequate margins, as the tumor has a low propensity for distant metastasis. In our cohort, all cases underwent surgical resection, consistent with treatment guidelines[35]. According to a study by Batsakis (1999), radiotherapy is not the preferred treatment due to concerns of anaplastic transformation, where VC may undergo dedifferentiation into a more aggressive SCC [36]. Radiation therapy for VC has been associated with potential malignant transformation. A study by Perez et al. discussed cases where VC underwent anaplastic transformation after radiation treatment, suggesting that ionizing radiation might contribute to this change [37].

The role of adjuvant therapy in VC management is typically reserved for specific scenarios. A retrospective review by Franklyn et al. (2017) indicated that adjuvant therapy is considered in cases with close resection margins, nodal involvement, or recurrent disease. Their findings showed that most patients were effectively managed with surgery alone, with adjuvant therapy administered selectively [38].

These studies underscore the importance of individualized treatment planning in VC, highlighting the potential risks associated with radiation therapy and

the selective use of adjuvant treatments based on specific pathological features.Our findings are consistent with this, as only a few cases required additional treatment beyond surgery.

VC has a relatively good prognosis, with low recurrence rates following complete excision. However, recurrence rates vary based on factors such as tumor size, presence of dysplasia, and margin status. Achieving clear surgical margins is crucial in reducing the recurrence of VC. Incomplete excision has been associated with higher recurrence rates. A study highlighted that VC has a high recurrence rate if incompletely excised, and recurrent tumors can be more aggressive than the original, with potential bone and cartilage invasion [39]. Another study found Verrucous carcinoma, though less metastatic than conventional SCC, poses clinical challenges due to its potential transformation and involvement of molecular regulators like miR-21 in tumour progression [40].

While VC is typically characterized by local invasion with a low potential for metastasis, certain cases exhibit more aggressive behaviour. A case report described a 67-year-old male patient with VC causing bone invasion and bilateral lymph node metastasis, despite the absence of a clear squamous cell carcinoma component. This suggests that even minimal invasive characteristics within VC can lead to metastatic behaviour.

In our dataset, follow-up details were not available, but the presence of invasion and metastasis in a subset of cases suggests the potential for recurrence in high-risk patients.

OSCC in younger patients exhibits aggressive features such as high nuclear pleomorphism, tumor budding, and a stroma-rich microenvironment, suggesting a more invasive phenotype. In our study VC, though slow-growing, has the potential to transform into invasive SCC, indicating that prolonged epithelial instability may contribute to malignant progression. Both conditions highlight the role of the tumor microenvironment in dictating behavior, with OSCC showing early aggressive changes and VC demonstrating a gradual transformation risk [41-44].

CONCLUSION

Our study highlights key clinical and pathological features of VC, aligning with findings from previous research. The male predominance, strong association with tobacco-related habits, low metastatic potential, and primary surgical treatment outcomes are consistent with existing literature. However, a small subset of cases exhibited invasive behaviour, lymph node involvement, and extranodal extension, emphasizing the need for early diagnosis and close monitoring of high-risk patients. Future studies should focus on molecular and genetic markers to further understand the progression of VC and improve targeted treatment strategies.

DECLARATIONS

Ethical statement

This study was performed in line with the principles of the Declaration of Helsinki.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. Goodman J. Tobacco in history and culture: an encyclopedia. Granite Hill Publishers; 2005.
2. Stephens WE, Calder A, Newton J. Source and health implications of high toxic metal concentrations in illicit tobacco products. Environmental science & technology. 2005 Jan 15;39(2):479-88."Tobacco Board, Guntur".Tobaccoboard.com. 22 January, 2022
3. Shoba, John and Shailesh Vaite. Tobacco and Poverty: Observations from India and Bangladesh. Canada, 2002;Agriculture Organization of the United Nations. Commodities, Trade Division, Agriculture Organization of the United Nations. Raw Materials, Tropical, Horticultural Products Service. Issues in the global tobacco economy: selected case studies. FAO; 2003
4. Perfetti TA, Rodgman A. The complexity of tobacco and tobacco smoke. Beiträge zur Tabakforschung International/Contributions to Tobacco Research. 2011;24(5):215-32.
5. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2017external icon. Geneva: World Health Organization, 2017.
6. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2011external icon. Geneva: World Health Organization, 2011
7. Levinson AH, Lee JG, Jason LA, DiFranza JR. Asking for identification and retail tobacco sales to minors. Pediatrics. 2020;145(5).
8. Al-Haqwi AI, Tamim H, Asery A. Knowledge, attitude and practice of tobacco smoking by medical students in Riyadh, Saudi Arabia. Annals of thoracic medicine. 2010;5(3):145.
9. Elf JL, Modi B, Stillman F, Dave P, Apelberg B. Tobacco sales and marketing within 100 yards of

schools in Ahmedabad City, India. Public Health. 2013;127(5):442-8.
Brock B, Choi K, Boyle RG, Moilanen M, Schillo BA. Tobacco product prices before and after a statewide tobacco tax increase. Tobacco control. 2016 Mar 1;25(2):166-73.

10. John RM, Dauchy E, Goodchild M. Estimated impact of the GST on tobacco products in India. Tobacco Control. 2019 ;28(5):506-12.
11. Mishra GA, Gunjal SS, Pimple SA, Majmudar PV, Gupta SD, Shastri SS. Impact of'gutkha and pan masala ban'in the state of Maharashtra on users and vendors. Indian journal of cancer. 2014;51(2):129.
12. Sarkar A, Roy D, Nongpiur A. A population-based study on tobacco consumption in urban slums: Its prevalence, pattern, and determinants. Journal of
13. Family Medicine and Primary Care. 2019 Mar;8(3):892.
14. Pradhan A, Oswal K, Padhan A, Seth S, Sarin A, Sethuraman L, Sebastian P, Purushotham A. Cigarettes and Other Tobacco Products Act (COTPA) implementation in education institutions in India: A crosssectional study. Tobacco Prevention & Cessation. 2020;6.
15. Nair S, Schensul JJ, Bilgi S, Kadam V, D'Mello S, Donta B. Local responses to the Maharashtra gutka and pan masala ban: A report from Mumbai. Indian J Cancer 2012;49:443-7
16. Ackerman, L. V. (1948). Verrucous carcinoma of the oral cavity. *Cancer*, **1**(3), 701-719.
17. Rocco DOI: 10.1016/j.coms.2006.06.007
18. Munde, A., Karle, R., Wankhede, P., & Shaikh, S. (2013). Verrucous carcinoma: A clinico- pathologic study of 12 cases. *Journal of Oral and Maxillofacial Pathology*, **17**(1), 125-129.
19. Sadasivan A, Thankappan K, Rajapurkar M, et al. Verrucous lesions of the oral cavity treated with surgery: Analysis of clinico-pathologic features and outcome. Contemporary Clinical Dentistry. 2012 Jan;3(1):60-63. DOI: 10.4103/0976-237x.94548.
20. Hashibe, M., Jacob, B. J., Thomas, G., Ramadas, K., Mathew, B., Sankaranarayanan, R., & Zhang, Z. F. (2003). Alcohol consumption and oral cancer risk in India: A case-control study. *Cancer Causes & Control*, **14**(9), 835-846.
21. Kraus, F. T., & Perezmesa, C. (1966). Verrucous carcinoma: Clinical and pathological study of 105 cases involving oral cavity, larynx, and genitalia. *Cancer*, **19**(1), 26-38.
22. Shear, M., & Pindborg, J. J. (1980). Verrucous hyperplasia and verrucous carcinoma: A report of 325 cases. *Scandinavian Journal of Dental Research*, **88**(5), 391-399.
23. Bansal, Puja, Paridhi Garg, Pradyuman Bhati, and Prajjual Goel. 2022. "Verrucous Carcinoma." *International Journal of Science and Research (IJSR)* 11 (5).
24. Kannan B, Pandi C, Pandi A, Jayaseelan VP, Arumugam P. Triggering receptor expressed in myeloid cells 1 (TREM1) as a potential prognostic biomarker and association with immune infiltration in oral squamous cell carcinoma. Arch Oral Biol. 2024;161: 105926.
25. Nour Saida Ben Messaoud et al. Specificities of Oral Verrucous Carcinoma: Case Report and Literature Review.SAS J Surg, 2021 Oct 7(10): 542-548
26. KIMURA, T. C.; SCATOLIM, D. B.; HENSCHEL, F. A. N. & VELTRINI, V. C. Hybrid verrucous carcinoma: A wolf in sheep's clothing. Case report and integrative review of 280 cases. Int. J. Odontostomat., 16(2):202-213, 2022.
27. Cunha JLS, Pontes CGC, Fonte JBM da, Guedes SAG, Melo M de FB de, Albuquerque- Júnior RLC de. Verrucous carcinoma with foci of invasive squamous cell carcinoma: Report of a case and discussion of current concepts. J Oral Diagn [Internet]. 2017 Jan. 5
28. Mukilarasi, K. R., P. Karkuzhali, and Hemalatha Ganapathy. 2017. "Verrucous Carcinoma of Scalp—A Rare Case Report." *World Journal of Pharmaceutical and Medical Research* 3 (9): 302-305.
29. Shafer, W. G., Hine, M. K., & Levy, B. M. (1975). *A Textbook of Oral Pathology* (3rd ed.).W. B. Saunders.
30. Ramasubramanian S, Pandiar D, Krishnan RP, Ramalingam K, Bologna-Molina R. Correlation of Bony Invasion With Nodal Metastasis, Pattern of Invasion and Survival in Oral Squamous Cell Carcinoma: A Retrospective Analysis of 122 Primary Cases From Oral Cancer Centre of South India. Cureus. 2023 Aug 3;15(8):e42887. doi: 10.7759/ cureus.42887.
31. Muthumanickam P, Ramasubramanian A, Pandi C, et al. The novel m6A writer methyltransferase 5 is a promising prognostic biomarker and associated with immune cell infiltration in oral squamous cell carcinoma. J Oral Pathol Med. 2024;1-9. doi:10.1111/jop. 13568
32. Van der Waal, I., de Bree, R., Brakenhoff, R.,

& Coebergh, J. (2011). Early diagnosis in primary oral cancer: Is it possible? *Oral Diseases*, **17**(7), 654-661.

33. Popli, H., & Kumar, S. (2018). Verrucous carcinoma with oral sub-mucous fibrosis: An uncommon occurrence. *International Journal of Applied Dental Sciences*, 4(4), 1–4.

34. Kademani, D., Bell, R. B., Bagheri, S., Holmgren, E., Dierks, E., Potter, B., & Homer, L. (2005). Prognostic factors in intraoral squamous cell carcinoma: The influence of histologic grade. *Journal of Oral and Maxillofacial Surgery*, 63(11), 1599–1605.

35. Kolokythas, A., Rogers, T. M., & Miloro, M. (2010). Hybrid verrucous squamous carcinoma of the oral cavity: Treatment considerations based on a critical review of the literature. *Journal of Oral and Maxillofacial Surgery*, 68(10), 2320–2324.

36. Franklyn J, Janakiraman R, Tirkey AJ, Thankachan C, Muthusami J. Oral verrucous carcinoma: Ten year experience from a Tertiary Care Hospital in India. Indian J Med Paediatr Oncol 2017;38:452-5.

37. Ireland A, Ardakani NM. Verrucous carcinoma. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/skintumornonmelanocyticverrucousscc.html. Accessed February 21st, 2025.

38. Prasad, M., Hamsa, D., Fareed, M. et al. An update on the molecular mechanisms underlying the progression of miR-21 in oral cancer. World J Surg Onc 23, 73 (2025).

39. Nour Saida Ben Messaoud et al. Specificities of Oral Verrucous Carcinoma: Case Report and Literature Review.SAS J Surg, 2021 Oct 7(10): 542-548.

40. Endo, M., & Lin, P. (2018). Surgical margins in the management of extremity soft tissue sarcoma. *Chinese Clinical Oncology*, *7*(4), 37. doi:10.21037/cco.2018.08.10

41. Pisani P, Airoldi M, Allais A, Aluffi Valletti P, Battista M, Benazzo M, Briatore R, Cacciola S, Cocuzza S, Colombo A, Conti B, Costanzo A, Della Vecchia L, Denaro N, Fantozzi C, Galizia D, Garzaro M, Genta I, Iasi GA, Krengli M, Landolfo V, Lanza GV, Magnano M, Mancuso M, Maroldi R, Masini

42. Poothakulath Krishnan R, Pandiar D, Ramani P, Jayaraman S, Subramanian R. Comparison of Clinico-Demographic and Histological Parameters Between Young and Old Patients With Oral Squamous Cell Carcinoma. Cureus. 2023 Nov 1;15(11):e48137. doi: 10.7759/cureus.48137.