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Specificities of Oral Verrucous Carcinoma: Case Report and Literature Review

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Abstract | **Case Report**

Introduction: Verrucous carcinoma of the oral mucosa recurs locally but does not metastasize in the absence of an invasive squamous cell carcinoma component. ***Clinical Observation***: We report a case of an oral verrucous carcinoma in 67-year-old male patient causing bone invasion and bilateral lymph node metastasis despite the absence of a clear squamous cell carcinoma component. ***Discussion:*** Some verrucous carcinomas show dysplasia with very minor component of conventional squamous cell carcinoma. Currently, there is great challenge in diagnosing those "in between" tumor type because of the lack of standard nomenclature and studies assessing their clinical behavior.

Keywords: Verrucous Carcinoma Literature Review oral mucosa recurs.

1. INTRODUCTION

Oral verrucous carcinoma (OVC) presents predominantly as an exophytic growth with a pebbly micronodular surface, a slow growing rate and becomes locally invasive if not treated properly.

The first ever documented evidence of a verrucous carcinoma dates back to 1941 when Fridell and Rosenthal reported a case of well-differentiated squamous cell carcinoma (SCC) of the oral cavity as "papillary verrucous carcinoma."

Verrucous carcinoma as a variant of well-differentiated squamous cell, carcinoma was defined by Ackerman in 1948 as a diagnostically challenging squamous cell neoplasia involving lip, oropharyngeal, and laryngeal mucosa.

Various synonyms used to describe this tumor, including Ackerman's tumor, Buschke Lowenstein tumor, florid oral papillomatosis, epithelioma cuniculatum, and carcinoma cuniculatum [1].

The most common site is the oral cavity involving buccal mucosa, mandibular alveolar crest, gingiva, and tongue. The glottic larynx is the most frequent nonoral site.

Verrucous carcinoma of the oral mucosa recurs locally but does not metastasize in the absence of an invasive squamous cell carcinoma component. Some verrucous carcinoma shows dysplasia with very minor component of conventional squamous cell carcinoma. Currently, there is great challenge in diagnosing those "in between" tumor type because of the lack of standard nomenclature and studies assessing their clinical behavior[2].

A Hybrid Verrucous Carcinoma (HVC) is characterized by the coexistence of histological diagnostic verrucous carcinoma (VC) and a non-verrucous squamous cell carcinoma arising synchronously from the same maternal field. The published literature suggests that 20 % of initially Diagnosed VC patients contained hybrid variety.

Regional lymph node metastasis is uncommon and related the presence of SCC foci. Distant metastasis have not been reported yet[3].

We report a case of an oral verrucous carcinoma causing bone invasion and bilateral lymph node metastasis despite the absence of a clear squamous cell carcinoma component.

2. OBSERVATION

A 76-year-old male patient came to the Department of Oral Medicine Oral Surgery Monastir University Dental Clinic with a chief complaint of mandibular pain localized in the symphyseal median area lasting for several weeks. The patient had the habit of smoking and chewing Tunisian smokeless Tabaco (Neffa) for nearly 54 years.

Clinical examination

The Extra-oral examination showed hypoesthesia in the area over the chin and the lower lip and bilateral submandibular painful on palpation lymph nodes which were around 2 cm. The intra-oral examination has particularly revealed a verrucous proliferative growth in the anterior mandibular ridge extending to the gingivo-buccal sulcus with 4 cm × 6 cm in diameter *(Fig 1)*.

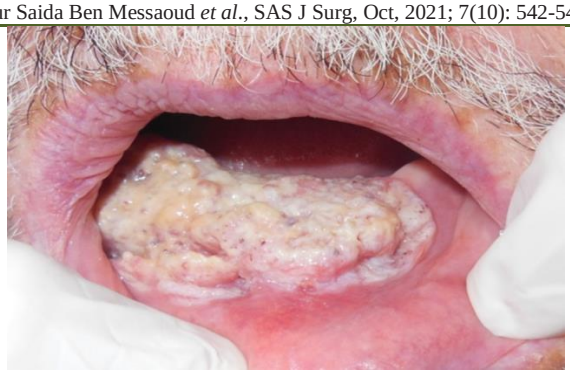

Fig-1: Inhomogeneous verrucous proliferative growth in the anterior mandibular ridge extending to the gingivo-buccal sulcus with 4 cm × 6 cm in diameter

Radiological assessment

A CT scan was performed and showed ill-defined osteolytic lesion of the symphyseal median mandibular bone, rupture of both buccal and lingual cortex. *(Fig 2)*. The lesion was mild enhanced on iodinated contrast media administration. Narrow window CT- scan axial sections showed invasion of the buccal space as well as the oral floor *(Fig 3)*.

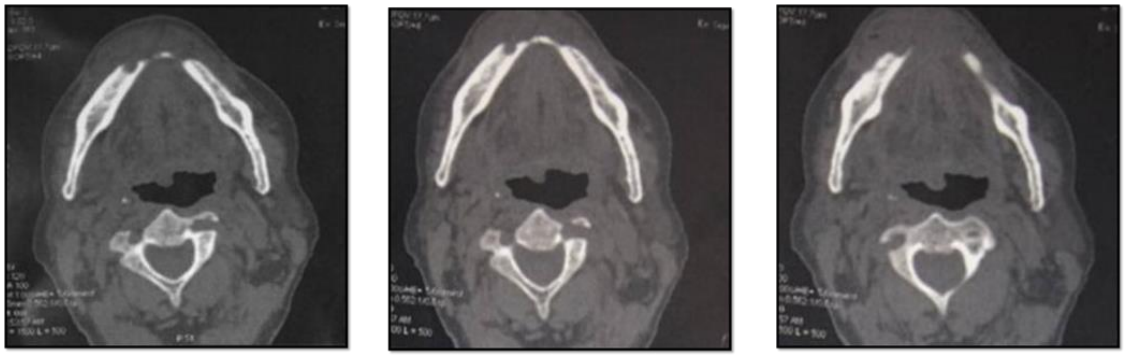

Fig-2: Wide windows CT- scan axial section showing ill-defined osteolytic lesion that destroy the buccal and lingual cortex.

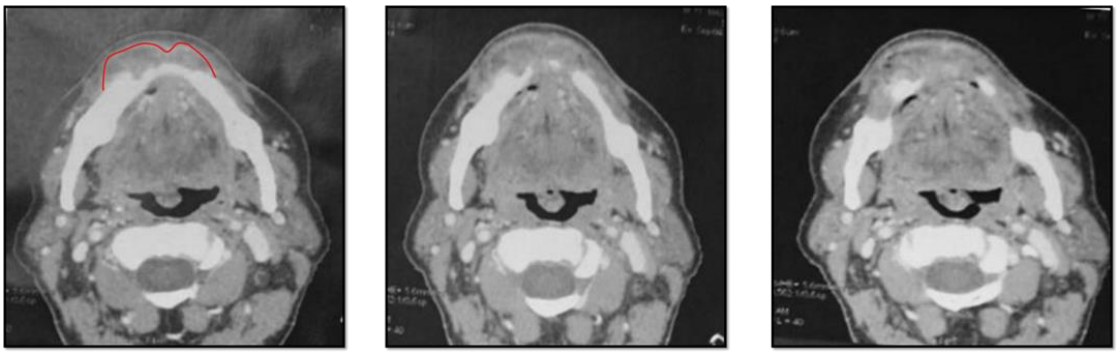

Fig-3: Enhanced CT- Scan axial sections showing invasion of the buccal space as well as the oral floor

Preoperative diagnosis

The Clinical and the radiological features suggested an invasive malignant tumor. A gingivo-mandibular squamous cell carcinoma was retained as preoperative diagnosis with T4N2cM0 staging.

Treatment

The patient was referred to the department of maxillo-facial surgery, Sahloul University Hospital; where a marginal mandibulectomy was performed under general anesthesia associated to left functional neck dissection and right supra-omohyoide neck dissection. The post-operative course was marked by unfortunate consequences including pathological fracture with overlap of the remaining mandibular bone in the operated area associated to a serious medical condition that the patient had died off few weeks later (Fig 4).

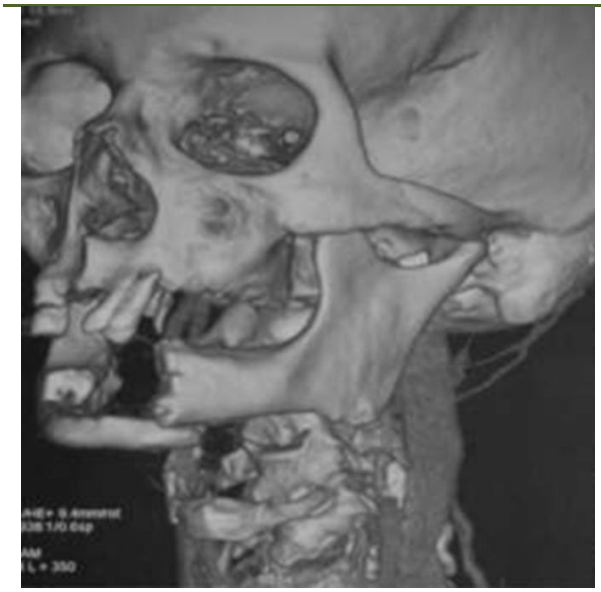

Fig-4: Post-operative CT scans: 3 D reconstruction showing pathological fracture in the operated site

Histopathological diagnosis

The histopathological examination of the exicised specimen showed epithelial proliferation with down growth into connective tissue but usually without the pattern of true invasion *(Fig 5)*. The epithelium was well differentiated with little mitotic activity. At the tumor base, irregular nests of tumor with angulated edges, cells with hyperchromatism were present associated to chronic inflammatory cell infiltration in the underlying connective tissue *(Fig 6)*. The histopathological removed lymph node examination showed right metastatic submandibular lymph node (level Ib) and left jugular upper metastatic lymph node (Level II) of a less differentiated carcinoma. Basing on these features the histopathological diagnosis was an oral hybrid verrucous carcinoma.

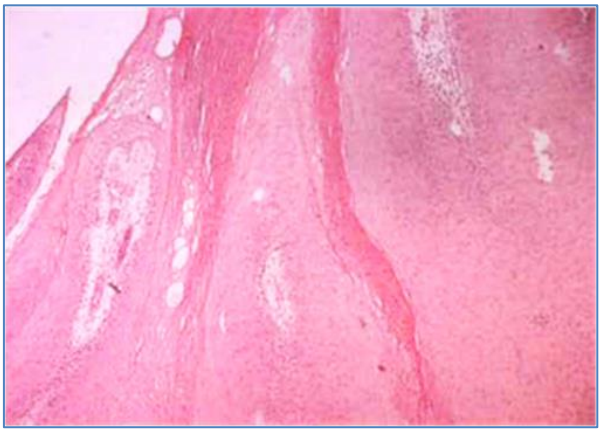

Fig-5: Photomicrograph showing typical verrucous carcinoma features with papillomatosis and hyperkeratosis (HE×40)

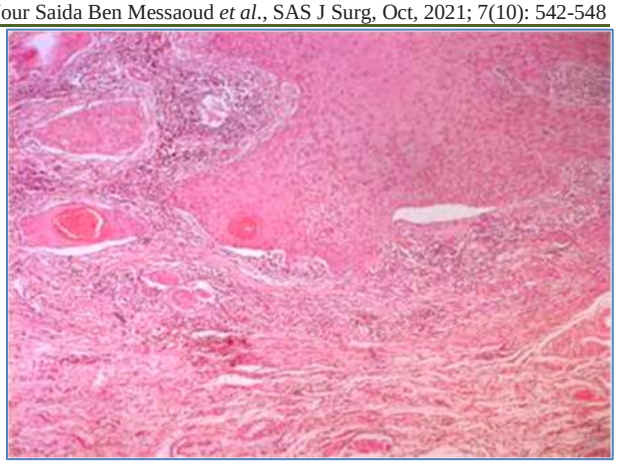

Fig-6: Medium power view photomicrograph showing at the tumor base, irregular nests of tumor with angulated edges, cells retaining abundant cytoplasm (HE×200).

3. DISCUSSION

3.1 Physiopathology

The pathogenesis of VC of the oral cavity is not clear. HPV, chewing tobacco, alcohol use, use of snuff, and poor oral hygiene are predisposing factors of OVC development [4].

HPV types six and 11 are the most common pathogens for oral squamous papillomas, but there is controversy regarding the evidence of HPV infection in the pathogenesis of oral verrucous carcinoma[5].

Kalyani *et al*. in a series of 36 cases of verrecous carcinoma including 18 VC, 13 atypical VC, and 5 SCC arising in VC Demonstrated that Although a minority of VC are p16 and HPV DNA positive (for cases), transcriptionally active high-risk HPV is uniformly absent. These findings argue that verrucous carcinoma and its related SCC are not HPV-driven tumors[6].

3.2. Clinicopatholigical features

3.2.1 Verrucous carcinoma

VC represents 2–12 % of oral cancers, occurring mainly in olderly men; mean age of presentation is 69 years. The most common site of occurrence is buccal mucosa followed by mandibular alveolar ridge and gingiva. VC is a slow-growing tumor that enlarges with direct extension rather than frank invasion. They are exophytic, do not metastasize, but can invade and destroy deeper tissues.

The clinical behavior of VC can be, at times, destructive despite its deceptively benign microscopic appearance: papillomatosis, acanthosis, dysplasia in variable degrees [7].

Contradictory observations have been published concerning the metastatic potential of OVC. Some authors describe an invasive growth with disconnected islands and groups of invading tumoral cells and therefore possible metastasis and described sporadic cases of metastatic VC, while others insist that VC is locally invasive and cannot metastasize.

Inflammatory lymph node involvement is frequent, consequent to the inflammatory reaction seen at the invasive front of the tumor, however less differentiated VC metastatic lymph nodes are uncommon findings [8].

3.2.2 Hybrid VC

A hybrid VC is a non-verrucous SCC that arises synchronously with the VC. There is a profound difficulty in diagnosing these lesions which show subtle differences in clinical appearances.

Medina *et al*. in 1984 reported coexistence of foci of SCC in VC for the first time. Incidence of these lesions was 20 %in their clinicopathologic study of 104 cases[9]. Gokavarapu S *et al*. reported in a series of 55 patients with oral verrucous lesions 49 % showed VC and 51% HVC on final histopatholigcal examination. Invasive foci of SCC were missed in 51% of cases on incision biopsy [10].

VC irrespective of size does not metastasize to regional lymphatics .Hybrid VC may metastasize to regional lymph nodes [3]. In the reported case the presence of submandibular lymph node metastasis was suggestive of HVC although final histopothological examination felt to identify clear SCC foci.

Currently there is evidence that local recurrence of VC in a form of a less- differentiated carcinomas and lymph node metastasis are related to foci of SCC arising in VC that may be unrevealed by preoperative biopsy and even final histopathologic examination.

These foci of less differentiated carcinoma were in previous literature attributed to called ‘radiotherapy induced anaplastic transformation of VC’, currently there is no evidence to attribute anaplastic transformation of VC to radiotherapy[3, 11].

3.2.3 SCC

VC with a component of conventional invasive SCC is not well described in the literature so there are no guidelines to clinical management. However, when any component of invasive SCC is present, tumors are treated clinically just as conventional SCC. These patients get surgical resection associated to neck dissection and, if indicated by overall pathologic stage, adjuvant radiation therapy[12]. However, some VCs show dysplasia without any conventional invasive SCC or have just a minor component of invasive SCC. Currently, there is great challenge in diagnosing tumors with these limited changes, and the terminology is widely variable. Pathologists use various descriptive terms such as ‘verrucous carcinoma with focal dysplasia and/or invasion’, ‘well differentiated squamous cell carcinoma with verrucous features’, ‘focus of squamous cell carcinoma arising within a verrucous carcinoma’, ‘verrucous squamous cell carcinoma, and hybrid verrucous carcinoma. There is a distinct lack of standard nomenclature[2].

Kaylani R *et al*. have recently reported that VC with dysplasia or minimal invasion (foci of SCC less than 2 mm in depth) is a variant of VC with an extremely favorable prognosis including no relapse neither lymph nodes metastasis comparing to SCC arising in VC (SCC greater than 2 mm in depth)[13].

Recent genetic and molecular studies focused to distinguish VC and conventional SCC. VC unlike conventional SCC exhibited cells with S-phase confined to basal layers. Flow cytometry has prouved that it is a diploid lesion unlike SCC which is an aneuploid lesion. CD44v9 was detected in VC more frequently than conventional SCC which possibly explains the low incidence of metastasis to lymphatics. Expression of Ki-67, p53 was significantly higher in SCC, but VC showed higher expression of Ki-67 and p53 in comparison to verrucous hyperplasia[14].

Recently Samman M *et al*. investigate genomic analysis of oral VC comparing to oral SCC and they lead to conclusion that oral VC is not a subtype of oral SCC as VC samples lacked mutations in genes commonly associated with oral SCC (TP53, NOTCH1, NOTCH2, CDKN2A and FAT1) [15].

Valuable information has been gathered by all these studies, but until now there is no method to derive these results into clinical applicability. Cost of these investigations limit their routine use in developing and underdeveloped countries.

3.3 Management of VC/HVC

3.3.1 Surgical excision

Nowadays, no one doubts that the most effective treatment of OVC is complete removal by local excision, marginal or segmental resection for a tumor showing invasion of the underlying bone, and neck dissection for cervical metastasis or when there is suspicion of metastasis as a SCC counponent may coexist with an OVC unrevealed by the initial biopsy [11]. The indication of systematic neck dissection is still controversary[16].

3.3.2 Radiotherapy

There have been ongoing discussions regarding the optimal therapy for OVC when complete surgical excision is impossible. The main point of this

discussion has focused on anaplastic transformation after radiotherapy that was clearly stressed in the older literature.

Nowadays radiotherapy has gained credibility in the treatment of OVC. Recent articles show rather better results than earlier reports, with disease-free 5-year Survival of 49% to 66% in many case series [11].

3.3.3 Chemotherapy

Chemotherapy, including cytotoxic drugs such as 5fluorouracil, bleomycin, and methotrexate, has had positive reports as an efficient OVC treatment. These drugs showed clear beneficial effects, particularly in reducing tumor size, but have generally failed to produce complete remission [2, 17].

3.3.4 Specific treatment modalities

Specific treatment modalities for VC are reported in the literature, such as photodynamic therapy, cryosurgery, Laser surgery, and the administration of recombinant alfa interferon. These methods may be acceptable for proliferative oral verrucous hyperplasia, but their efficiency has yet to be established for the management of VC[18, 19].

3.4 Differential diagnosis of oral verrecous lesions

An accurate diagnosis of oral VC could be challenging and requires an adequate biopsy specimen[10]. Diagnosis also requires experience and close collaboration between surgeon and pathologist. The differential diagnosis should include lesions of similar clinical features such as verrucous hyperplasia, papilloma, proliferative verrucous leukoplakia, SCC, chronic candidiasis, and condyloma accuminatum.

Differential histopathological diagnosis would require the presence of normal margins and is still considered as the 'gold standard' while immunohstochemical investigations have been considered as adjuncts for difficult cases diagnosis.

Discriminating these lesions histologically by incisional biopsy remains a challenge especially in poorly orientated specimens and where the adjacent normal margins were missed[20].

3.4.1 Oral squamous papillomas

May affect any intraoral site and are usually less than 10 mm in size. They usually have a narrow base and a broad papillary surface. They tend to lack much keratinization, contain prominent fibrovascular cores and exhibit minimal cytological atypia[4].

3.4.2 Oral verrucous hyperplasia (OVH)

OVH presents as a whitish or pink elevated oral mucosal plaque or mass with a verrucous or papillary surface and classified into two variants namely the sharp and the blunt variety. The sharp variety comprising of long, narrow, and heavily keratinized verrucous processes appears white as a result of heavy keratinization while the blunt variety consists of verrucous processes that are broader, flatter, and not heavily keratinized.

The most affected site is the buccal mucosa. A study on Taiwanese patients reported a strong association between OVH and areca quid as well as smoking habits[21].

A malignant transformation rate of 3.1% and mean malignant transformation duration of 54.6 months was reported in their series of cases[22]. For this reason OVH is considered a potentially malignant disorder.

Wang *et al*. reclassified OVH into a plaque type and mass type primarily based on their histopathological features. The histopathological positive diagnosis of OVH includes epithelial hyperplasia with parakeratosis or hyperkeratosis with absence of down growth of hyperplastic epithelium into the lamina propria as compared with adjacent normal mucosal epithelium. A surface keratin layer of >40 microns was used to differentiate the mass and the plaque types. Epithelial dysplasia was uniformly present in both the variants of OVH. It was reported that the mass type of OVH described by Wang *et al*. exhibited a greater tendency to malignant transformation[22].

Based on the available literature, it is apparent that the terminologies used to describe these lesions are confusing and there is a need to standardized terminology and diagnostic criteria[21].

3.4.3 Proliferative verrucous leukoplakia (PVL)

Aggressive form of oral leukoplakia that has a protracted growth phase PVL and OVH are interrelated lesions and both may progress to malignancy. However, these terminologies are neither clinically and histopathologically interchangeable since PVL does not have a single defining histopathology and is more a clinically preferred term whereas, OVH has to be diagnosed histopathologically[21].

4. CONCLUSION

Verrucous carcinoma is a rare, low-grade well-differentiated form of squamous cell carcinoma seen on skin and mucosa. It is slow-growing and locally aggressive. A case of strongly invasive oral verrucous carcinoma is presented with the medical history, management and outcome. Thus, the importance of knowing the malignant potential of this lesion is stressed. Indeed, in 20 % of verrucous carcinoma, foci of squamous cell carcinoma could be found suggesting hybrid verrucous carcinoma.

A review of literature and differential diagnosis critiria of oral verrucous lesions were discussed. Based on the available literature, we conclude that

- The terminologies used to describe verrucous lesions of the oral mucosa are confusing and there is a need to standardized terminology and diagnosis criteria
- Oral verrucous carcinoma is a rare tumor, locally invasive with excellent prognosis if removed in totality by surgery
- The presence of Squamous cell carcinoma foci in typical verrucous carcinoma is frequent. The prognosis may still favorable in cases of minimal invasion (less than 2 mm in depth)
- The possibility that the majority of oral verrucous carcinoma do not manifest foci of cellular atypia or mild dyplasia may be the result of a non-representative biopsy or incomplete sampling.
- Verrucous carcinoma associated to deep invading foci of squamous cell carcinoma, lymph node metastasis, or distant metastasis exhibit poor

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- Verrucous carcinoma associated to deep invading foci of squamous cell carcinoma, lymph node metastasis, or distant metastasis exhibit poor prognosis and should be managed as a conventional squamous cell carcinoma

Abbreviation's list

1. HPV : Human papilloma virus
2. HVC : Hybrid verrucous carcinoma
3. OVH : oral verrucous hyperplasia
4. OVC : Oral verrucous carcinoma
5. PVL: Proliferative verrucous leukoplakia
6. SCC: squamous cell carcinoma
7. VC: verrucous carcinoma

REFERENCES

1. Rao, D. S., Kalappanavar, A. N., Ali, I. M., & Annigeri, R. G. (2016). Verrucous carcinoma-an enigma: Case report and review. *Contemporary clinical dentistry*, *7*(3), 391.
2. Shergill, A. K., Solomon, M. C., Carnelio, S., Kamath, A. T., Aramanadka, C., & Shergill, G. S. (2015). Verrucous carcinoma of the oral cavity: Current concepts. *Int J Sci Study*, *3*, 114-8.
3. Gokavarapu, S., Tantravahi, U. S., Gundimeda, S. D., Rao, T. S., & Murthy, S. (2014). Oral hybrid verrucous carcinoma: A clinical study. *Indian journal of surgical oncology*, *5*(4), 257-262.
4. Alan, H., Agacayak, S., Kavak, G., & Ozcan, A. (2015). Verrucous carcinoma and squamous cell papilloma of the oral cavity: Report of two cases and review of literature. *European journal of dentistry*, *9*(03), 453-456.
5. Samman, M., Wood, H., Conway, C., Berri, S., Pentenero, M., Gandolfo, S., ... & Rabbitts, P. (2014). Next-generation sequencing analysis for detecting human papillomavirus in oral verrucous carcinoma. *Oral surgery, oral medicine, oral pathology and oral radiology*, *118*(1), 117-125.
6. Patel, K. R., Chernock, R. D., Zhang, T. R., Wang, X., El-Mofty, S. K., & Lewis Jr, J. S. (2013). Verrucous carcinomas of the head and neck, including those with associated squamous cell carcinoma, lack transcriptionally active high-risk human papillomavirus. *Human pathology*, *44*(11), 2385-2392.
7. Walvekar, R. R., Chaukar, D. A., Deshpande, M. S., Pai, P. S., Chaturvedi, P., Kakade, A., ... & D'Cruz, A. K. (2009). Verrucous carcinoma of the oral cavity: A clinical and pathological study of 101 cases. *Oral Oncology*, *45*(1), 47-51.
8. Sonalika, W. G., & Anand, T. (2016). Oral verrucous carcinoma: A retrospective analysis for clinicopathologic features. *Journal of cancer research and therapeutics*, *12*(1), 142.
9. Medina, J. E., Dichtel, W., & Luna, M. A. (1984). Verrucous-squamous carcinomas of the oral cavity: a clinicopathologic study of 104 cases. *Archives of Otolaryngology*, *110*(7), 437-440.
10. Gokavarapu, S., Rao, L. C., Patnaik, S. C., Parvataneni, N., Raju, K. V. V. N., Chander, R., & Kumar, K. J. (2015). Reliability of incision biopsy for diagnosis of oral verrucous carcinoma: A Multivariate clinicopathological study. *Journal of maxillofacial and oral surgery*, *14*(3), 599-604.

11. Yoshimura, Y., Mishima, K., Obara, S., Nariai, Y., Yoshimura, H., & Mikami, T. (2001). Treatment modalities for oral verrucous carcinomas and their outcomes: contribution of radiotherapy and chemotherapy. *International journal of clinical oncology*, *6*(4), 192-200.
12. Vidyasagar, M. S., Fernandes, D. J., Kasturi, D. P., Akhileshwaran, R., Rao, K., Rao, S., ... & Solomon, J. G. R. (1992). Radiotherapy and verrucous carcinoma of the oral cavity: a study of 107 cases. *Acta Oncologica*, *31*(1), 43-47.
13. Patel, K. R., Chernock, R. D., Sinha, P., Müller, S., El-Mofty, S. K., & Lewis, J. S. (2015). Verrucous carcinoma with dysplasia or minimal invasion: a variant of verrucous carcinoma with extremely favorable prognosis. *Head and neck pathology*, *9*(1), 65-73.
14. Hosseinpour, S., Mashhadiabbas, F., & Ahsaie, M. G. (2017). Diagnostic biomarkers in oral verrucous carcinoma: A systematic review. *Pathology & Oncology Research*, *23*(1), 19-32.
15. Samman, M., Wood, H. M., Conway, C., Stead, L., Daly, C., Chalkley, R., ... & Rabbitts, P. (2015). A novel genomic signature reclassifies an oral cancer subtype. *International journal of cancer*, *137*(10), 2364-2373.
16. Kang, C. J., Chang, J. T. C., Chen, T. M., Chen, I. H., & Liao, C. T. (2003). Surgical treatment of oral verrucous carcinoma. *choice*, *1*, 2.
17. Karagozoglu, K. H., Buter, J., Leemans, C. R., Rietveld, D. H. F., Van den Vijfeijken, S., & Van Der Waal, I. (2012). Subset of patients with verrucous carcinoma of the oral cavity who benefit from treatment with methotrexate. *British Journal of Oral and Maxillofacial Surgery*, *50*(6), 513-518.
18. Yu, C. H., Lin, H. P., Cheng, S. J., Sun, A., & Chen, H. M. (2014). Cryotherapy for oral precancers and cancers. *Journal of the Formosan Medical Association*, *113*(5), 272-277.
19. Lin, H. P., Chen, H. M., Yu, C. H., Yang, H., Wang, Y. P., & Chiang, C. P. (2010). Topical photodynamic therapy is very effective for oral verrucous hyperplasia and oral erythroleukoplakia. *Journal of oral pathology & medicine*, *39*(8), 624-630.
20. Mehrotra, D., Goel, M., Kumar, S., Pandey, R., & Ram, H. (2012). Oral verrucous lesions: Controversies in diagnosis and management. *Journal of oral biology and craniofacial research*, *2*(3), 163-169.
21. Zain, R. B., Kallarakkal, T. G., Ramanathan, A., Kim, J., Tilakaratne, W. M., Takata, T., ... & Jalil, A. (2016). Exophytic verrucous hyperplasia of the oral cavity–application of standardized criteria for diagnosis from a consensus report.
22. Wang, Y. P., Chen, H. M., Kuo, R. C., Yu, C. H., Sun, A., Liu, B. Y., ... & Chiang, C. P. (2009). Oral verrucous hyperplasia: histologic classification, prognosis, and clinical implications. *Journal of Oral Pathology & Medicine*, *38*(8), 651-656.