An adamant entity of oral cavity – A case report of Proliferative verrucous leukoplakia with review of literature

Versha Rani Giroh[1,*], Manjula Hebbale[2], Amit Mhapuskar[3], Nisha Singh[4]

[1,4]PG Student, [2]Associate Professor, [3]Professor & HOD, Bharati Vidyapeeth Deemed University, Dental College & Hospital, Pune

***Corresponding Author:**
Email: vershagiroh98@gmail.com

Abstract

Hansen et al first described proliferative verrucous leukoplakia (PVL) in the year of 1985. It is a rare form of oral leukoplakia which occurs as a slow growing and becomes multifocal and as the time progresses it becomes exophytic, wart like and ultimately transforms to squamous carcinoma. It has a high recurrence rate and also high malignant transformation rate. Etiology is still under the sheets. Though there has been association of human papilloma virus with its occurrence. The diagnosis and the management is still unclear.

A case of proliferative verrucous leukoplakia has been discussed with its etiology, diagnosis, management and prognosis.

Keywords: Verrucous leukoplakia, Proliferative

Access this article online

Website:
www.innovativepublication.com

DOI:
10.5958/2395-6194.2016.00040.0

Introduction

Proliferative verrucous leukoplakia is a form of oral leukoplakia with a white component, dominated by papillary projections.[1] The term was coined by Hansen et al and defined as a single white lesion which grows slowly with time and becomes multifocal.[2] The lesion is persistent and irreversible and resistant to any sort of treatment[3]. Generally, an erythematous area and /or verrucous areas are present as initial manifestation which progress to verrucous carcinoma or squamous cell carcinoma.[4] According to the World health organization nomenclature, oral PVL comes under the category of "potentially malignant disorders"[5,6]. The etiology is still unknown. Tobacco use does not seem to play a significant role in the etiology, occurs in both smokers and non -smokers.[7] Palefsky JM et al (1995), Gopalakrishnan et al (1997), Eversole et al (2000) found the association of PVL and human papilloma virus[8,9,10]. Began et al (2004) found the association of Epstein-Barr virus and PVL.[11]

Case Report

A 48-year-old female patient reported to department of oral medicine and radiology with a chief complaint of burning sensation in the mouth since 3 months. Burning sensation occurred during and after meals which gradually increased over the period of time. No other significant history was reported by her. Her medical, social, dental and family history was non-contributory. She gave a positive history of mishri application (burnt tobacco which is applied over the teeth)2-3 times a day for around 10-15 minutes and then rinse her mouth with water since last 13 years. Extra-oral examination was non-contributory.

On intraoral examination, multifocal whitish homogenous plaques were seen involving the entire right and left buccal mucosa. On upper labial mucosa, a whitish plaque was seen extending from 21 -25 and from the labial mucosa to the buccal vestibule. Few whitish specks were seen on the lower labial mucosa mainly on the left side. No involvement of palatal mucosa was seen. Areas of hyperpigmentation were seen on the right and left buccal mucosa and upper and lower labial mucosa. The lesion appeared to be wrinkled without any erythematous areas. The lesion was non tender, non-scrapable and non-stretchable. The consistency of lesion was leathery. There was no bleeding on provocation. Both the upper and the lower labial gingiva were also involved. Multiple whitish thick homogenous plaques were seen extending from the marginal gingiva, interdental papillae, attached gingiva to the vestibule. The plaques appeared to be wrinkled with no sign of erosive areas. The lesions were non tender, non-scrapable, and was leathery in consistency. The Visual analogue scale(VAS) score found to be 7. (Fig. 1, 2, 3, 4)

On the basis of clinical findings and the history, a provisional diagnosis of proliferative verrucous leukoplakia was made as the lesions were multifocal involving the buccal mucosa, labial mucosa and the gingiva.

Incisional biopsy was performed from right and left buccal mucosa which revealed stratified squamous hyperparakeratinised epithelium with broaden rete ridges. Few dysplastic features such as basal cell hyperplasia, acanthosis with prominent intercellular

bridges were observed. The overall picture was suggestive of verrucous leukoplakia. (Fig. 5)

Patient was advised and counselled to quit the habit of mishri application. Symptomatic treatment was given to her which included the following:

- Cap.Aquasol (topical application over the lesions 2-3 times a day after meals)
- Mucopain gel (topical application over the lesions 2-3 times a day before meals)

Patient was recalled after one month; the VAS score was reduced to 2. (Fig. 6 and Fig. 7). Patient is under constant follow up of 3 months' interval.

Fig. 1: Upper labial mucosa and gingiva

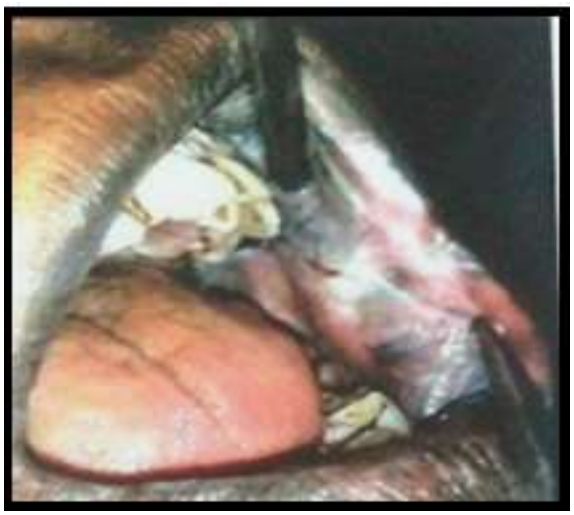

Fig. 2: Left buccal mucosa

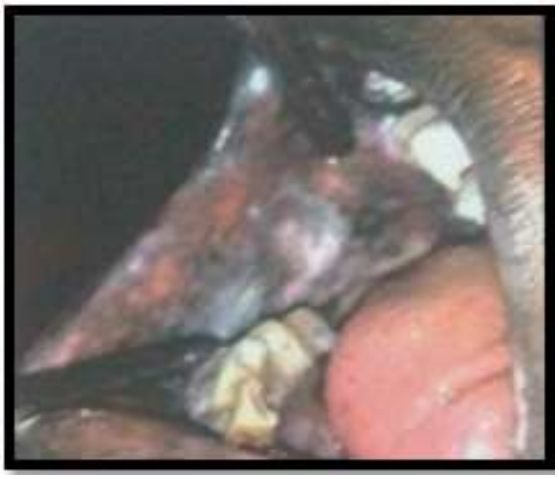

Fig. 3: Right buccal mucosa

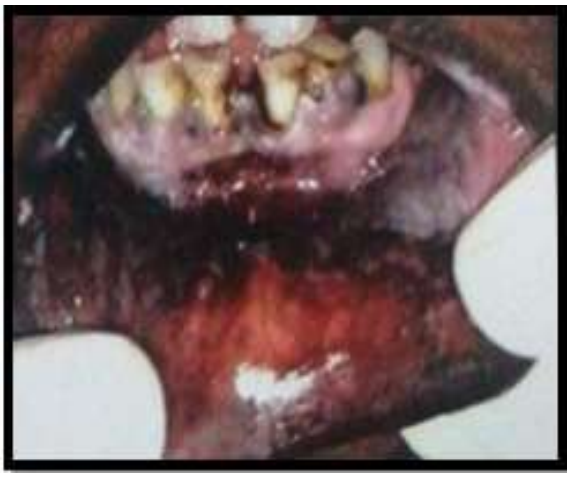

Fig. 4: Lower labial mucosa and gingiva

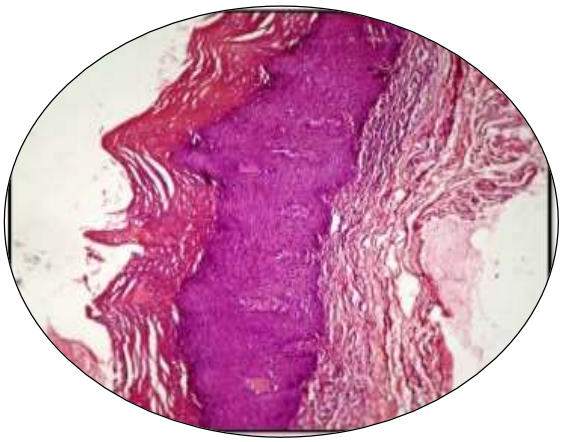

Fig. 5a

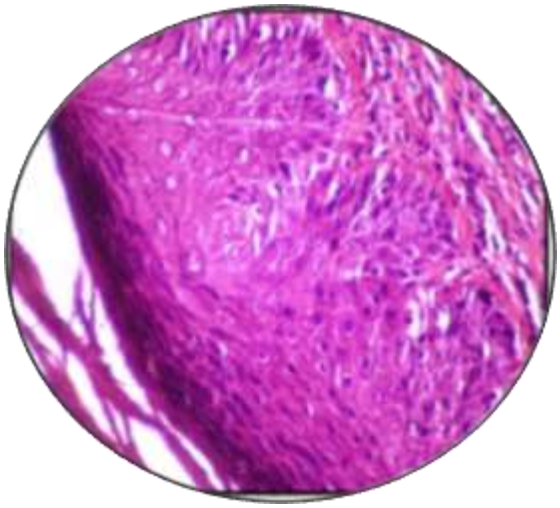

Fig. 5b

Fig. 5: Histopathological image a) 10x b) 40x

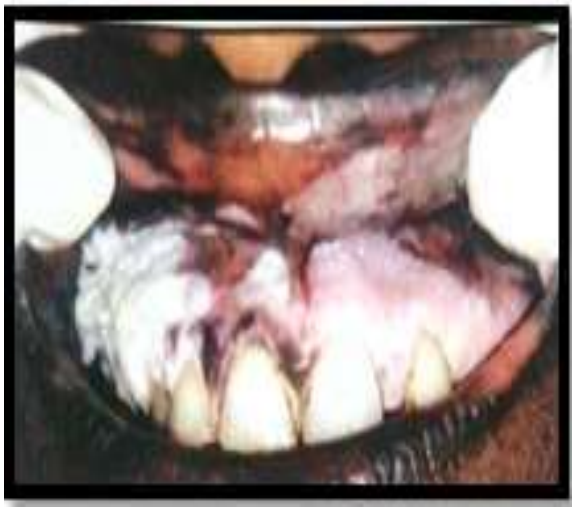

Fig. 6a

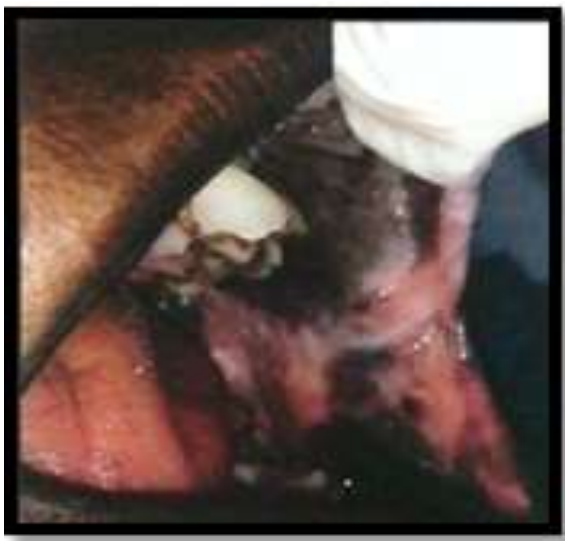

Fig. 6b

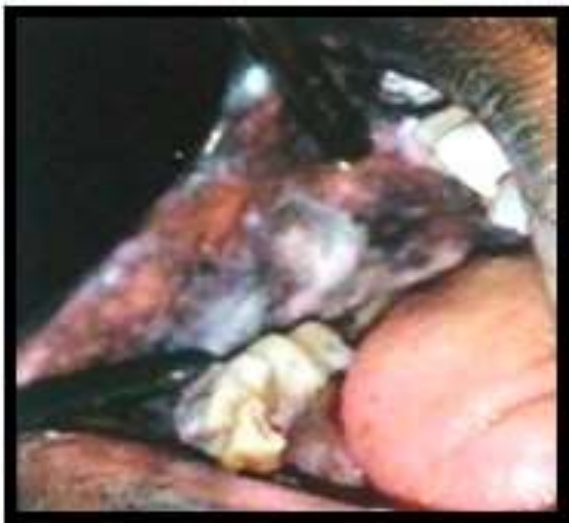

Fig. 6c

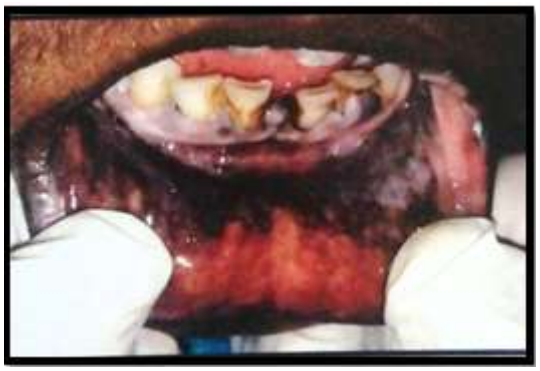

Fig. 6d

Fig. 6: First follow up (A, B, C, D)

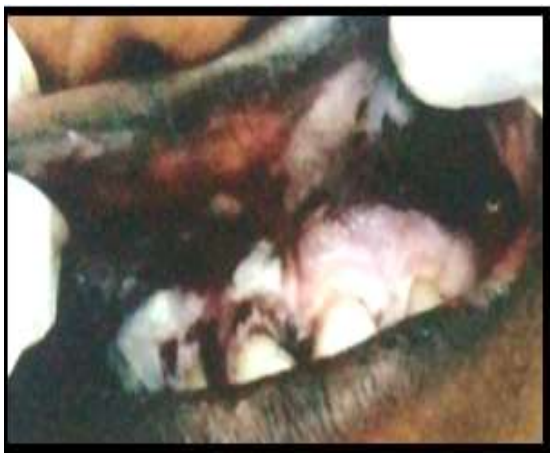

Fig. 7a

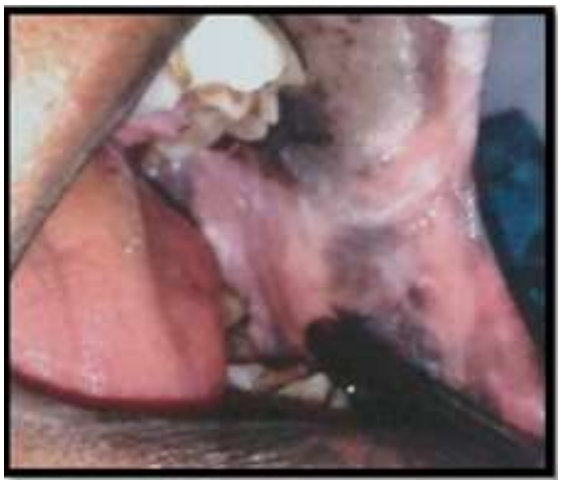

Fig. 7b

Fig. 7c

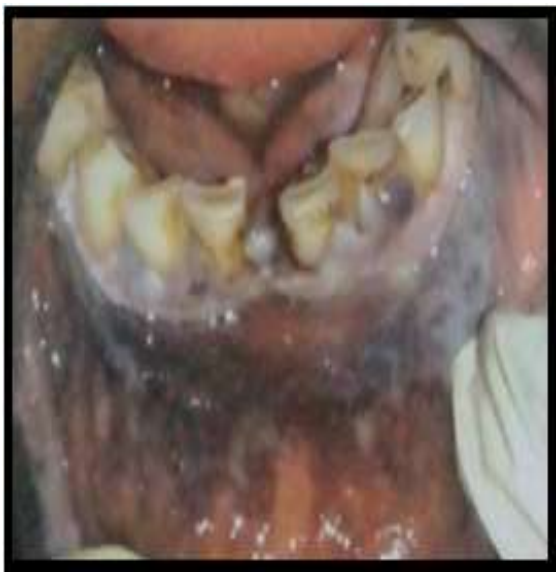

Fig. 7d

Fig. 7: Second follow up (A, B, C, D)

Discussion

PVL is a slow growing, multifocal and persistent lesion with or without being exophytic. It has a tendency to recur with a higher malignant potential of about 70-100%[4]. In 2007, Cabay et al defined as a distinct clinical form of oral leukoplakia which in turn is defined by its progressive clinical course, changing clinical and histopathologic features, and potential to develop into cancer[19]. Etiopathogenesis is uncertain but an association of human papilloma virus has been suggested by Eversole et al in 2000[20]. Began et al (2007) does not found any association with human Papilloma virus and PVL[21]. In 2008, he also tried to established a relation between Epstein -Barr virus.[22] Also, Kresty et al in 2008 found aberrations in the genes p161NK4a and P14ARF[23]. The proliferative nature of PVL could be due to an increased TGF-alpha (Transforming growth factor-alpha), as suggested by Kannan et al.[24]

There is a distinct female preponderance and mean age at the time of diagnosis is over 60 years. The sites involved are masticatory mucosa, gingiva, palate, alveolar ridge and buccal mucosa.

Two studies conducted by Ghazali et al(12) and Gandolfo et al(13) proposed a set of diagnostic criteria to their respective cases. They proposed that one of the following combinations of criteria mentioned below should be met.

General diagnostic criteria for PVL[2]

- The lesion starts as homogenous leukoplakia
- With time, some areas of leukoplakia become verrucous
- The disease progresses to the development of multiple isolated or confluent lesions at the same or different site
- With time, the disease progresses through the different histopathological stages reported by Hansen et al.[14]
- The appearance of new lesions after treatment
- A follow-up period of no less than one year

In 2009, Gandolfo et al modified the criteria as:

1. An initially innocuous lesion characterized by a homogenous plaque that progresses over time to an exophytic, diffuse, usually multifocal lesion with a verrucous epithelial growth pattern; and
2. Histopathologically, PVL changes gradually from a simple plaque of hyperkeratosis without dysplasia to verrucous hyperplasia, verrucous carcinoma, or OSSC.

Cerero-Lapiedra et al in 2010 have proposed minor and the major criteria for the diagnosis of PVL. For the diagnosis, the following criteria should be met.[4, 5, 15, 16]

- Three major criteria (being E among them) or
- Two major criteria (being E among them) + two minor criteria

A. Major criteria

a. leukoplakia lesion with more than two different oral sites, which is most frequently found in the gingiva, alveolar processes and palate
b. The existence of a verrucous area
c. That the lesions have spread or engrossed during development of the disease
d. That there has been a recurrence in a previously treated area
e. Histopathologically, there can be simple epithelial hyperkeratosis without dysplasia to verrucous hyperplasia, verrucous carcinoma or oral squamous cell carcinoma, whether in situ or infiltrating

B. Minor criteria
a. An oral leukoplakia lesion that occupies at least 3 cm when adding all the affected areas
b. That the patient be female
c. Nonsmoker
d. A disease evolution higher than 5 years

More recently, Carrad et al, 2013[15] stated that the major criteria A should not include keratinized mucosa as the most frequently site but also consider any site of the oral mucosa in the criteria.

In the present case report, three major criteria viz. A, C and E and minor criteria viz. a, b and c as laid down by Cerero-Lapiedra et al. were met, suggestive of proliferative verrucous leukoplakia.

Management of PVL has been described difficult with poor prognosis. Therapeutic approaches found to be less effective. Treatment modalities includes carbon dioxide laser vaporization, cryotherapy, radiation, chemotherapy and retinoid. Schoelch et al[17] used CO_2 and nd: YAG lasers but the recurrence rate reported were high (83%). Due to the widespread extent of the lesions, complete excision is impossible. It has been found that the lesions recurred even after using scalpel or laser excision.[18] Vitamin A, vitamin A analog, and antioxidant nutrients (vitamins C, E, and beta carotene), have shown no beneficial effects when used in therapeutic doses.[4]

Poor prognosis with high recurrence and 86.7% rate of malignant transformation is seen with PVL[4].

Conclusion

PVL is a difficult lesion to diagnose and manage due to the varying clinical presentation, histological characteristic and resistance to treatment. Early and aggressive treatment of this lesion is recommended because of the growth pattern, recurrence rate and high malignant transformation rate. A long and thorough follow-up for these patients, rule out for any changes in shape, size, color, as well as the appearance of new lesions are required. More randomized controlled studies are required in the field of management for PVL.

References

1. Burket's oral medicine 11th edition .by Greenberg, glick, ship.
2. Raghuvanshi V, Srivastava K, Handa H. Proliferative verrucous leukoplakia: Case report and a comprehensive review of literature. Saudi J Oral Sci 2015;2:103-5.
3. García-Chías B, Casado-De La Cruz L, Esparza-Gómez GC, Cerero-Lapiedra R. Diagnostic criteria in proliferative verrucous leukoplakia: Evaluation. Med Oral Pathol Oral Cir Bucal. 2014 Jul 1;19 (4): e335-9.
4. Silverman S Jr, Grosky M. Proliferative verrucous leukoplakia: a follow up study of 54 cases. Oral Surg Oral Med Oral Pathol Oral RadiolEndod1997;84:154-157.
5. Cerero-Lapiedra R, Baladé-Mar nez D, Moreno-López LA, Esparza-Gómez G, Bagán JV. Proliferave verrucous leukoplakia: A proposal for diagnostic criteria. Med Oral Patol Oral Cir Bucal 2010;15:e839-45.
6. Scheifele C, Reichart PA. Is there a natural limit of the transformation rate of oral leukoplakia? Oral Oncol 2003;39:470-5.
7. Van der Waal I, Reichart PA. Oral proliferative verrucous leukoplakia revisited. Oral Oncol. 2008;44:719-21.
8. Palefsky JM, Silverman S Jr, Abdel-Salaam M, Daniels TE, Greenspan JS. Association between proliferative verrucous leukoplakia and infection with human papillomavirus type 16. J Oral Pathol Med 1995;24:193-7.
9. Gopalakrishnan R, Weghorst CM, Lehman TA, Calvert RJ, Bijur G, Sabourin CL, et al. Mutated and wild-type p53 expression and HPV integration in proliferative verrucous leukoplakia and oral squamous cell carcinoma. Oral Surg Oral Med Oral Pathol Oral RadiolEndod1997;83:471-7.
10. Eversole LR. Papillary lesions of the oral cavity: Relationship to human papillomaviruses. J Calif Dent Assoc 2000;28:922-7.
11. Bagán JV, Murillo J, Poveda R, Gavaldá C, Jiménez Y, Scully C. Proliferave verrucous leukoplakia: Unusual locations of oral squamous cell carcinomas, and field cancerization as shown by the appearance of multiple OSCCs. Oral Oncol 2004;40:440-3.
12. Ghazali N, Bakri MM, Zain RB. Aggressive, multifocal oral verrucous leukoplakia: proliferative verrucous leukoplakia or not? J Oral Pathol Med. 2003;32:383-92.
13. Gandolfo S, Castellani R, Pentenero M. Proliferative verrucous leukoplakia: a potentially malignant disorder involving periodontal sites. J Periodontol. 2009;80:274-81.
14. Hansen LS, Olson JA, Silverman S Jr. Proliferative verrucous leukoplakia. A long-term study of thirty patients. Oral Surg Oral Med Oral Pathol 1985;60:285-98.
15. Carrard VC, Brouns EREA, van der Waal I. Proliferative verrucous leukoplakia; a critical appraisal of the diagnostic criteria. Med Oral Patol Oral Cir Bucal. 2013;18: e411-e413.
16. Bagan JV, Jimenez-Soriano Y, Díaz-Fernández JM, Murillo Cortés J, Sanchís-Bielsa JM, Poveda-Roda R, et al. Malignant transformation of proliferative verrucous leukoplakia to oral squamous cell carcinoma: A series of 55 cases. Oral Oncol. 2011;47:732-735.
17. Schoelch ML, Sekandari N, Regezi JA, Silverman S Jr. Laser management of oral leukoplakia: A follow-up study of 70 patients. Laryngoscope 1999;109:949-53.
18. Fettig A, Pogrel MA, Silverman S Jr, Braman TE, Da Costa M, Regezi JA. Proliferative verrucous leukoplakia of the gingiva. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 2000;90:723-30.
19. Cabay RJ, Morton TH Jr, Epstein JB (2007). Proliferative verrucous leukoplakia and its progression to oral carcinoma: a review of the literature. J Oral Pathol Med 36:255–261.

20. Eversole LR (2000). Papillary lesions of the oral cavity: relationship to human papillomaviruses. J Calif Dent Assoc 28:922–927.
21. Bagan JV, Jimenez Y, Murillo J et al (2007). Lack of association between proliferative verrucous leukoplakia and human papillomavirus infection. J Oral Maxillofacial Surg 65:46–49.
22. Bagan JV, Jime´ nez Y, Murillo J et al (2008). Epstein–Barr virus in oral proliferative verrucous leukoplakia and squamous cell carcinoma: a preliminary study. Med Oral Patol Oral Cir Bucal 13: E110–E113.
23. Kresty LA, Mallery SR, Knobloch TJ et al (2008). Frequent alterations of p16INK4a and p14ARF in oral proliferative verrucous leukoplakia. Cancer Epidemiol Biomarkers Prev 17:3179–3187.
24. Kannan R, Bijur GN, Mallery SR, Beck FM, Sabourin CL, Jewell SD, et al. Transforming growth factor-alpha overexpression in proliferative verrucous leukoplakia and oral squamous cell carcinoma: An immunohistochemical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;82:69-74.