CASE REPORT

Proliferative Verrucous Leukoplakia: Benignly progressing towards malignancy

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ABSTRACT

The condition, OPVL arises as clinical foci of hyperkeratosis that progressively spread and become multifocal. Many potential etiologies have been hypothesized, but little has been roved about the origin of this disease process. We herein present a case of oral proliferative verrucous leukoplakia (OPVL) and discuss this so called rare entity in light of current information.

Keywords: Hyperkeratosis, Oral proliferative verrucous leukoplakia (OPVL)

INTRODUCTION

In 1985, Hansen et al[1] coined the term "proliferative verrucous leukoplakia" (PVL) after a long-term study of 30 patients with this disease. The condition arises as clinical foci of hyperkeratosis that progressively spread and become multifocal. The lesions eventually assume an exophytic, verrucous appearance and are extremely resistant to treatment. Ultimately, many progress to invasive cancer, and 30% or more of patients with PVL die of this disease[2]. Many potential etiologies have been hypothesized, but little has been roved about the origin of this disease process. We herein present a case of oral proliferative verrucous leukoplakia (OPVL) and discuss this so called rare entity in light of current information.

CASE REPORT

A 56 year old woman presented with a slowly progressive whitish plaque at left residual alveolar ridge of lower jaw since 3 years and right alveolar ridge and the right comissure since 8 months.

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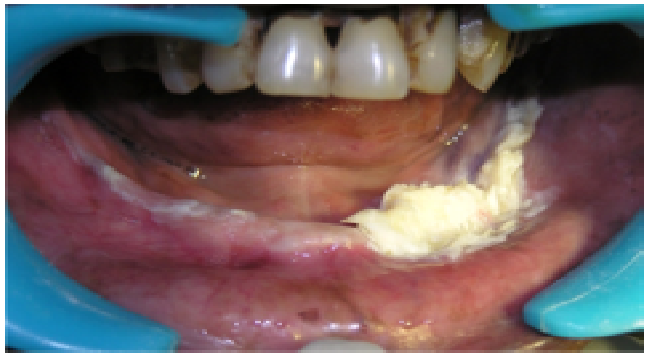

Figure 1

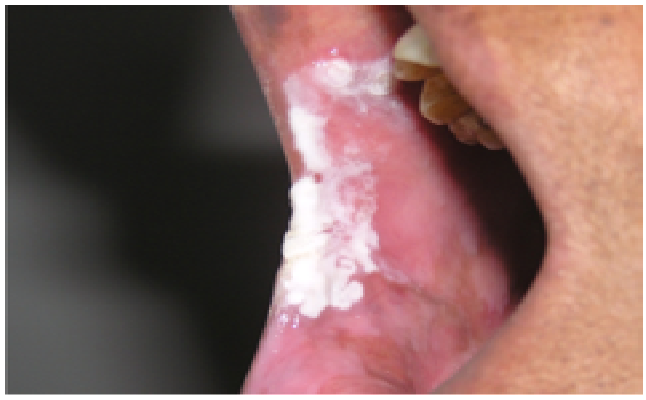

Figure 2

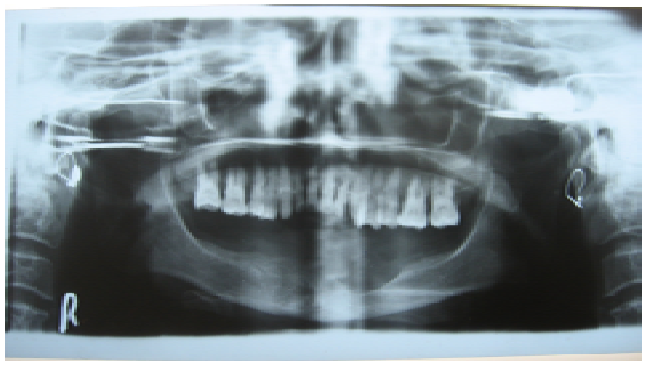

Figure 3.

An incisional biopsy was performed and histopathological examination was done.

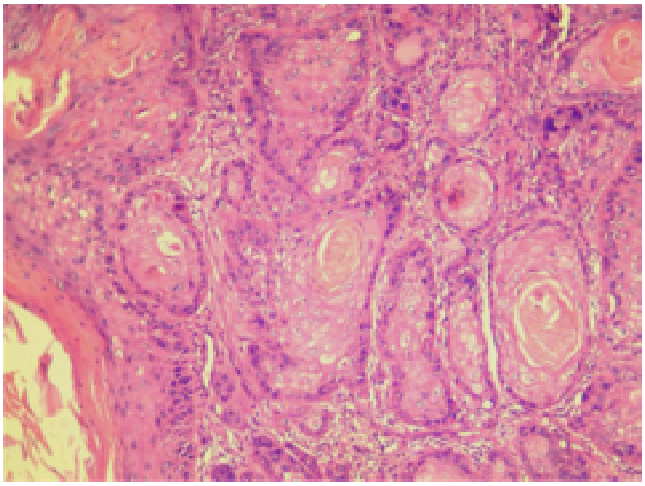

Figure4. left alveolar ridge of lower jaw.
(Hematoxylin and Eosin stained section, 10X, well differentiated squamous cell carcinoma)

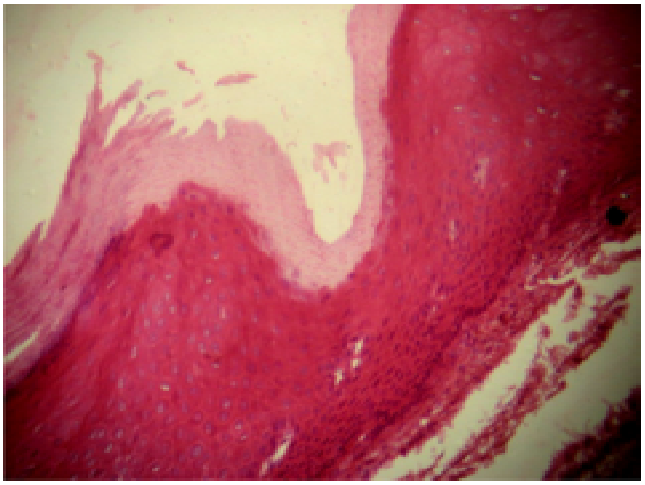

Figure 5. Right comissure
(Hematoxylin and Eosin stained section, 10X, shows acanthosis and hyperkeratosis)

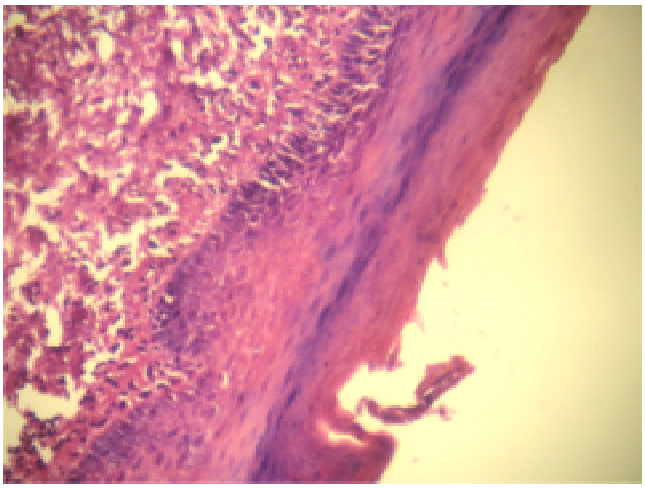

Figure 6. Right alveolar ridge.
(Hematoxylin and Eosin stained section, 10X, shows acanthosis and hyperkeratosis)

Her past medical history, including her family history, was unremarkable. There was no history of using tobacco in any form. In addition to her poor oral hygiene, she was a chronic betel nut chewer. Radiograph showed a well defined radioluscency with irregular margins and loss of crest of alveolus on left side of mandible.

Culture for Candida albicans was found to be negative.

Later the follow up was not possible as the patient didn't report back.

DISCUSSION

PVL is a unique type of oral leukoplakia, usually begins as a simple hyperkeratosis that spreads locally or to other sites to become multifocal and proliferative. Lesions of PVL tend to be slow-growing, persistent and irreversible which in time, become exophytic and wart like, display verrucal projections and areas of erythematous change within white patches, and have the appearance of verrucous and nodular leukoplakia.[1] Unlike other forms of leukoplakia, PVL exhibits a strong female predilection, with a female-to-male ratio of approximately 4:1. Although approximately 5% of all dysplastic leukoplakias transform to cancer over an average period of 5 years, PVL has an almost 100% rate of malignant transformation,[3] but this can occur over an extended follow-up period of 5 to 20 years.[4] Most commonly affected oral sites are alveolar ridge, gingiva, buccal mucosa.

Many potential etiologies have been hypothesized, but little has been proved about the origin of this disease process. The disease seems to be idiopathic. There is frequent absence of commonly known risk factors (up to 80% cases). Literature shows neither the role of immunodeficiency nor any associated syndrome. The proliferative effect of PVL was explained on basis of the high rate of field cancerization existing in PVL patients (Bagan et al. 2004)[5]. It was noted that there is usually a time lag between the appearances of new tumors in the same patient. This suggests that PVL might have an infectious etiology- possibly a viral infection. Although several workers[6,7,8] have suggested that HPV might have a role in the pathogenesis of PVL. Bagan *et al*.[9] failed to find HPV in their group of patients and suggested that there is no association of PVL with HPV. Rather recently, Bagan *et al*.[10] detected the presence of EBV in a large percent of their patient group suggesting an etiologic role in the pathogenesis and recurrence of PVL. On the other hand, non conclusive result was found regarding the association between candida albicans and HPV.[1,2]

Despite such extensive works, the etiology of PVL is still as enigmatic as the disease itself. However potential biomarkers can be used to predict the prognosis of the existing lesion. Kannan R *et al*.[11] found Transforming growth Factor-alpha over expression in the patients with PVL and SCC.

Immunohistochemical studies by Gopalakrishnan R *et al.*[12] found mutated and wild-type p53 over expression in HPV and oral SCC. Flow cytometric analysis was given by Kahn MA[13], Lowe *et al.*[14] observed the positive association between histopathological severity and nuclear morphometrical alteration in cases of PVL. PVL being an clinical diagnosis, exact nature of the lesion can only be judged by its histopathological evaluation.

Hansen *et al.*[1] suggested histologic stages in the continuum of PVL.

Grade 0: normal mucosa

Grade 2: Hyperkeratosis (Clinical leukoplakia)

Grade 4: Verrucous hyperplasia

Grade 6: Verrucous carcinoma

Grade 8: Papillary squamous cell carcinoma

Grade 10:Less well differentiated squamous cell carcinoma

With intermediates

Our case represented grade 9 at left alveolar ridge, grade 3 at right comissure, grade 2 at right alveolar ridge .

Batsakis *et al.*[3] reduced the number of histologic stages to 4 with intermediates:

Grade 0: Clinical flat leukoplakia without dysplasia

Grade 2: Verrucous hyperplasia

Grade 4: Verrucous carcinoma

Grade 6: Conventional squamous cell carcinoma with intermediates

Our case represented grade 6 at left alveolar ridge, grade 1 at right alveolar ridge and grade 2 at right comissure, thus characteristically showing different grades (spectrum of disease) at different sites in at the same time. The papillary SCC was omitted in the later classification, stating that the oropharynx, not the oral cavity, is the usual site of thatdisease.[3,15] They discussed how PVL and VH are 2 interrelated oral mucosal lesions. Each has shown to have a considerable propensity to progress to malignancy—either verrucous carcinoma or conventional SCC with varying degrees of differentiation.[3] PVL has no single defining histopathologic feature. Therefore, PVL should be used only as a clinical description and not as a definitive diagnosis.3 The diagnosis of VH can only be established through microscopic analysis.[5] Although VH can be a histologic component in the evolutionary spectrum of PVL, it is not exclusive to PVL, nor indeed is VH confined to the oral cavity.[6]

CONCLUSION

Our case represented spectrum of histopathological changes at different sites in the oral cavity, viz, benign lesions at right commisure and alveolar ridge while obvious malignancy on the left side. Both the initial clinical presentation and the early biopsy findings of PVL can lull the clinician into a false sense of comfort. However, over a protracted period of time, there is always possibility of widespread disease and progression to carcinoma.[16] Thus it is imperative to give serious consideration to innocuously appearing white lesion of the oral cavity.

REFERENCES

1. 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.
2. Palefsky JM, Silverman S Jr, Abdel-Salaam M, et al: Association between proliferative verrucous leukoplakia with human papilloma virus type 16. J Oral Pathol Med 1995; 24:193.
3. Batsakis JG, Suarez P, El-Naggar AK: Proliferative verrucous leukoplakia and its related lesions. Oral Oncol 1999; 35:354.
4. Silverman S Jr, Gorsky M: Proliferative verrucous leukoplakia: A follow-up of 54 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 84:154.
5. Bagán JV, Murillo J, Poveda R, Gavaldá C, Jiménez Y, Scully C. Proliferative 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.
6. 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.
7. 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 Radiol Endod. 1997;83:471-7.
8. Eversole LR. Papillary lesions of the oral cavity: relationship to human papillomaviruses. J Calif Dent Assoc. 2000;28:922-7.
9. Bagan JV, Jimenez Y, Murillo J, Gavaldá C, Poveda R, Scully C, et al. Lack of association between proliferative verrucous leukoplakia and human papillomavirus infection. J Oral Maxillofac Surg. 2007;65:46-9.
10. Bagan JV, Jiménez Y, Murillo J, Poveda R, Díaz JM, Gavaldá C, et al. Epstein-Barr virus in oral proliferative verrucous leukoplakia and squamous cell carcinoma: A preliminary study. Med Oral Patol Oral Cir Bucal. 2008;13:E110-3.
11. Kannan R, Bijur GN, Mallery SR, et al. Transforming growth factor-alpha overexpression in proliferative verrucous leukoplakia and oral squamous cell carcinoma. An immuno-histochemical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996; 82:69.
12. Gopalakrishnan R, Weghorst CM, Lehman TA, et al. Mutated and wild-type p53 expression and HPV integration in proliferative leukoplakia and oral squamous cell carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 83:471.
13. Kahn MA, Dockter ME, Hermann-Petrin JM: Proliferative verrucous Leukoplakia: Four cases with flow cytometric analysis.Oral Surg Oral Med Oral Pathol 1994; 78:469.
14. Lowe NP, Cordova SW, Betterman BL, Hodges JS and Rohrer MD. 0312 Computerized nuclear morphometry of PVL.
15. Murrah VA, Batsakis JG. Proliferative verrucous leukoplakia and verrucous hyperplasia. Ann Otol Rhinol Laryngol 103:660, 1994. 1;14 (6): 2009.
16. Bishe KA, Sethi A. Proliferative Verrucous Leukoplakia – diagnostic pitfalls and suggestions. Med Oral Patol Oral Cir Bucal, J 2010; E263-4.