CASE REPORT

MANAGEMENT OF PROLIFERATIVE VERRUCOUS LEUKOPLAKIA BY DIODE LASER THERAPY – A CASE REPORT

1."Mahendra Patait, 1Pooja Kulkarni, 1Ashwin Thakare, 2Kedar Saraf and 2Mahesh Ghabne

1Professor and HOD, Dept. of Oral Medicine and Radiology, SMBT Dental College and Postgraduate Research Institute, Sangamner
2PG Student, Dept. of Oral Medicine and Radiology, SMBT Dental College and Postgraduate Research Institute, Sangamner,

ABSTRACT

Proliferative verrucous leukoplakia (PVL) is a rare form of oral leukoplakia, which was first described in 1985 by Hansen et al. Proliferative verrucous leukoplakia is a multifocal and progressive lesion of the oral mucosa, with unknown etiology, and commonly resistant to all therapy attempts with frequent recurrences. It is characterized by a high rate of oral squamous cell carcinoma and verrucous carcinoma transformations. The buccal mucosa and tongue are the most frequently involved sites. It develops initially as a white plaque of hyperkeratosis that eventually becomes a multifocal disease with confluent, exophytic and proliferative features with a progressive deterioration of the lesions, making it more and more difficult to control. Tobacco use does not seem to have a significant influence on the appearance or progression of PVL and may occur both in smokers and nonsmokers. The use of lasers in different dental procedures has become very common. Lasers have obvious benefits for all the patients without administering anesthetic shots and that means less time spent in the dental chair. Procedures were performed more conservatively, with less trauma for patients. This paper reports the management of a proliferative verrucous leukoplakia in a 56-year-old female with a 940 nm diode laser.

Key words: Proliferative Verrucous leukoplakia, Hyperkeratosis, Diode LASER.

INTRODUCTION

Proliferative verrucous leukoplakia (PVL) is a rare oral leukoplakia, principally characterized by chronic proliferation, multiple occurrences, and refractoriness to treatment. Its rate of malignant transformation is extremely high (Hansen et al., 1985). The characteristics of its clinical and pathological progress are considered vital bases for the diagnosis of PVL because there are no particular differences between the pathological changes of PVL and those of oral verrucous leukoplakia (OVL) (Gale et al., 2005). PVL grows slowly and can take up to 7.8 years to become cancerous. The process is irreversible and usually progresses to cancer.

According to the study by Bagan, PVL quickly becomes malignant, on average within 4.7 years (Bagan et al., 2003), whereas Hansen reported an average time to cancer of 6.1 years high (Hansen et al., 1985). However, Silverman and Gorsky reported a longer mean malignant process of 11.6 years (Silverman et al., 1997). According to the latest World Health Organization nomenclature, OPVL conforms to the new terminology of “potentially malignant disorders” given that it is neither a delimited lesion nor a condition (Cerero et al., 2010). It is best-defined as a continuum of oral epithelial disease with hyperkeratosis at one end of a clinical and microscopic spectrum and verrucous carcinoma or squamous cell carcinoma at the other (Gree et al., 1999). It is a long-term progressive condition, which develops initially as a white plaque of hyperkeratosis that eventually becomes a multifocal disease with confluent, exophytic and proliferative features1 and behaves in a more aggressive and relentless
manner than the more innocuous white oral lesions that it can resemble clinically (Cabay et al., 2007). Owing to the progressive nature of OPVL, many forms of therapy used for the management of traditional leukoplakia have been disappointing. Laser ablation reportedly has been successful; it causes relatively low morbidity and no scarring and multiple mucosal sites can be treated simultaneously. However multiple treatments over the course of the disease progression may be required (Azfar and Elston, 2012). The role of lasers in dentistry is well-established in conservative management of oral diseases and also in effectively eliminating it (Pick and Colvard, 1993; Kafas and Kalfas, 2008). The diode laser system has found wide recognition in the areas of lasers as a result of its practical characteristics and is considered as an important tool for a large number of application (Jackson and Lauto, 2002). Diode laser has shown satisfactory results when used as an adjunct to conservative methods in the management of inflamed periodontal tissues and peri-implant tissue as well (De Souza et al., 2008). According to a Deppe and Horch, the use of diode laser systems for the treatment of oral and maxillofacial diseases has shown efficient removal of premalignant lesion of oral mucosa (Deppe and Horch, 2007).

The diode laser which was introduced in dentistry since 1999 is a solid-state semiconductor laser that typically uses a combination of gallium (Ga), arsenide (Ar), and other elements such as aluminium (Al) and indium (In). It has a wavelength ranging from 810 to 980 nm. This energy level is absorbed by pigments in the soft tissues and makes the diode laser an excellent hemostatic agent. Thereby, it is a tool for soft tissue surgeries as well (Tanuja et al., 2011). The laser surgery can be used for ablation of lesions, incisional and excisional biopsies, gingivectomies, gingivoplasties, soft tissue tuberosity reductions, and certain crown lengthening procedure (Wigdor et al., 1995). This case report shows patient with a PVL on left buccal mucosa, left lateral border of tongue and upper left gingiva with respect to 24,25 of the oral cavity and followed by diode laser application for the PVL excision with infiltrated local anesthesia.

CASE REPORT

A female patient, aged 56 years, attended the Department of Oral Medicine with painless white patches over the left buccal mucosa, left lateral border of tongue and upper left gingiva with respect to 24,25 for over 10 years. The white patches on her left buccal mucosa and tongue, which felt coarse but were painless. On a physical examination, her face was symmetrical and while speaking, it was decided to go for an excisional biopsy performed under LA using a LASER (Fig 4).

Surgical procedure

The treatment plan was explained to the patient and an informed consent was obtained. Local anesthesia infiltration was done and complete excision of the lesion over left buccal mucosa and upper left gingiva was done utilizing a diode laser unit (wavelength 940nm). The procedure was done in contact mode. Surgical assistant grasped the buccal growth with Adson’s tissue holding forceps and retraction was done with minimum tension. The fiberoptic tip was placed at the periphery and gradually moving around the lesion, continuously firing the laser to dissect out the lesions completely (Fig 4). The intraoperative view of the case is shown in fig 5. The excised tissue was immersed in 10% formalin solution and sent for histopathological examination. (Fig 6). The patient was comfortable and no sutures were necessary. Antibiotics were not given postoperatively. Patient was instructed to take analgesics if needed. Patient was recalled after one month to evaluate the healing which was uneventful (Fig 7). Due to the high vascularity of the tongue we opted for the palliative care. The patients immunity was enhanced, and retinoic acid and nystatin were given as topical therapy. Close surveillance was undertaken, with periodic checkups upon request.

Histopathological examination

Histopathological examination revealed hyperkeratotic epithelium showing dysplastic features like basilar hyperplasia and hypochromatic cells extending up to the lower third of epithelium. The stroma was made up of collagen fibers with plump to spindle shaped fibroblasts along with patchy distribution of inflammatory cells predominately lymphocytes and plasma cells seen in the juxta-epithelial region (Fig 8). Histologically, the lesion was diagnosed as hyperkeratosis with mild dysplasia.

DISCUSSION

Etiopathogenesis

PVL has no known origin. Unlike typical oral leukoplakia, PVL is more commonly noted in individuals without the usual risk factors of smoking, other forms of tobacco use, and excess alcohol consumption. Fungal and viral origins have not been proven, although earlier studies suggested that human papilloma virus (HPV) was of significance (Palefsky et al., 2015). More recently, however, the relationship between PVL and oncogenic HPV has been challenged (Campisi et al., 2004). In contrast, Beltiol and colleagues (Beltiol et al., 2012) identified HPV in 100% of the patients with PVL, but in only 8.75% of the group without mucosal lesions. Clearly, the role of HPV in the origin of oral PVL remains undetermined. Any site in the oral cavity may be involved with these lesions, but the most commonly affected Any site in the oral cavity may be involved with these lesions, but the most commonly affected. From a genetic standpoint, PVL has been shown to demonstrate cell cycle alterations secondary to dysregulation of p16INK4a and p14ARF genes. Homozygous deletions, loss of heterozygosity, and mutational changes have been frequently shown.
Fig. 1. Preoperative view (left buccal mucosa)

Fig. 2. Preoperative view (Upper left gingiva)

Fig. 3. Preoperative view (on tongue)

Fig. 4. Excisional biopsy (using LASER)

Fig. 5. Intraoperative view

Fig. 6. Biopsy specimen
Although ploidy alterations have been considered a tool to predict malignant transformation, some have questioned this on the grounds of data validity (Kresty et al., 1998). High expression of cell cycle proteins Mcm-2 and Mcm-5 could help predict the long-term behavior and risk of malignant transformation of PVL. These markers could be useful diagnostic tools, superior to the Ki-67 proliferation marker (Gouvea et al., 2010).

Diagnostic criteria

Because of the lack of specific histological criteria, the diagnosis of PVL is based on combined clinical and histopathologic evidence of progression. In previously published series, diagnosis of PVL was made according to Hansen’s definition. There are few studies that apply a set of diagnostic criteria that are mentioned as follows:

Ghazali et al., established the following criteria (Ghazali et al., 2010).
- The lesion starts as homogenous leukoplakia without evidence of dysplasia at the first visit
- With time, some areas of leukoplakia become verrucous
- The disease progresses to the development of multiple isolated or confluent lesions at the same or a different site with time
- The disease progresses through the different histopathological stages reported by Hansen et al
- The appearance of new lesions after treatment
- A follow-up period of no less than one year.

Gandolfo et al., established the following criteria for diagnosis22.
- 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
- Histopathologically, PVL changes gradually from a simple plaque of hyperkeratosis without dysplasia to verrucous hyperplasia, verrucous carcinoma or OSCC.

Fig. 7. Follow up after 1 month

Although ploidy alterations have been considered a tool to predict malignant transformation, some have questioned this on the grounds of data validity (Kresty et al., 1998). High expression of cell cycle proteins Mcm-2 and Mcm-5 could help predict the long-term behavior and risk of malignant transformation of PVL. These markers could be useful diagnostic tools, superior to the Ki-67 proliferation marker (Gouvea et al., 2010).

Diagnostic criteria

Because of the lack of specific histological criteria, the diagnosis of PVL is based on combined clinical and histopathologic evidence of progression. In previously published series, diagnosis of PVL was made according to Hansen’s definition. There are few studies that apply a set of diagnostic criteria that are mentioned as follows:

Ghazali et al., established the following criteria (Ghazali et al., 2010).
- The lesion starts as homogenous leukoplakia without evidence of dysplasia at the first visit
- With time, some areas of leukoplakia become verrucous
- The disease progresses to the development of multiple isolated or confluent lesions at the same or a different site with time
- The disease progresses through the different histopathological stages reported by Hansen et al
- The appearance of new lesions after treatment
- A follow-up period of no less than one year.

Gandolfo et al., established the following criteria for diagnosis22.
- 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
- Histopathologically, PVL changes gradually from a simple plaque of hyperkeratosis without dysplasia to verrucous hyperplasia, verrucous carcinoma or OSCC.

Fig. 8. Histopathological view

Cerero Lapiédra et al., established the following major and minor criteria (Cerero Lapiédra et al., 2010).

Major criteria
- Leukoplakia lesion with more than two different oral sites, which is most frequently found in the gingiva, alveolar processes and palate
- The existence of a verrucous area
- That the lesions have spread or engrossed during development of the disease
- That there has been a recurrence in a previously treated area
- Histopathologically, there can be from simple epithelial hyperkeratosis to verrucous hyperplasia, verrucous carcinoma or OSCC, whether in situ or infiltrating.

Minor criteria
- An OL lesion that occupies at least 3 cm when adding all the affected areas
- That the patient be female
- That patient (male or female) be a non-smoker
- A disease evolution higher than 5 years.

In order to make the diagnosis of PVL, it was suggested that one of the two following combinations of the criteria mentioned before were met. Three major criteria (E being among them) or Two major criteria (E being among them) + two minor criteria. Nevertheless, at present, there is no criterion that will allow for the early diagnosis of the disease.

Treatment and recurrence

Because of the progressive nature of PVL, many forms of therapy used for the management of traditional leukoplakia have been disappointing. Carbon dioxide laser, radiation, topical bleomycin solution, oral retinoids, beta carotene and systemic chemotherapy have all failed at achieving permanent cure. Methisoprinol is a synthetic antiviral agent capable of inhibiting viral ribonucleic acid synthesis and replication and of stimulating antiviral cell mediated reactions that has been
shown to have some clinical efficacy in HPV induced lesions. Although improvements have been noted with some of these modalities, recurrence rates after cessation of therapy are high, often within months of discontinuation of treatment (Azfar and Elston, 2012; Kharma and Tarakji, 2012). Laser ablation reportedly has been successful in a very small group of patients followed for 6 178 months. Topical photodynamic therapy also may prove useful; it causes relatively low morbidity and no scarring and multiple mucosal sites can be treated simultaneously. However, multiple treatments over the course of the diseases progression may be required24. This lesion is resistant to the presently available treatment modalities; therefore, total excision with free surgical margins is critical combined with a lifelong follow up.

**Malignant transformation**

OPVL is known for its aggressive (Navarro et al., 2004) pathology, given its multifocal involvement, high malignant transformation rates (60-100%), frequent recurrences (87-100%) and high mortality rates (30-50%) (Kresty et al., 2008). The gingiva and palate represented the areas with the highest frequency of these multiple malignant tumors (Cerero-Lapièdra et al., 2010). Given the high tendency for (OSCCs) to appear in these patients, they should be checked for life at least once every 6 months (Bagán et al., 2008).

**Conclusion**

OPVL is a rare, but highly aggressive form of OL, which requires special awareness on the part of the clinician. Therefore, it is recommended to have the earliest possible diagnosis and total excision of this lesion. The aim/intention of reporting this case was to report a case with typical clinical and histologic features of OPVL so as to sensitize the oral physicians. The care should be taken to follow-up these cases for a long time even after surgical management as they have higher recurrence rate and are also known to undergo malignant transformation.

**REFERENCES**


