Enigma of oral potentially malignant disorders - A brief overview

N. K. Priya¹, R. Shruthy¹, Ashwini Ramakrishna¹, N. K. Sowmya², G. S. Madhushankari¹

¹Department of Oral Pathology and Microbiology, College of Dental Sciences, Davangere, Karnataka, India; ²Department of Periodontics, Bapuji Dental College and Hospital, Davangere, Karnataka, India

Abstract
Oral cancer is a unique cancer, nevertheless detected at the later stage. It is of note that oral cancer develops from oral potentially malignant disorders (OPMDs) that comprises premalignant lesions and conditions. Dearth of awareness and lack of knowledge in the detection of oral cancer along with patients presenting in the advanced stage of cancer have led to delay in diagnosis. Present treatise consideration will be mainly on the malignant potentiality of rare OPMDs, especially dyskeratosis congenital, epidermolysis bullosa, lupus erythematosus, Plummer-Vinson syndrome, and xeroderma pigmentosum. An English literature search engine was done for articles relating to OPMDs using Medline journals and National Library of Medicine.

Keywords
Lupus erythematosus, malignant transformation, oral potentially malignant disorders, xeroderma pigmentosum

Correspondence
N. K. Priya, Department of Oral Pathology and Microbiology, College of Dental Sciences, pavilion Road, Davangere - 577 004, Karnataka, India. E-mail: priya77mds@rediffmail.com

Received 01 April 2016; Accepted 28 May 2016
doi: 10.15713/ins.jcri.127

Introduction
Oral cancer, being the sixth most common cancer worldwide, accounting around 3% of all malignancies and 90-95% of different oral malignancy.¹,² More than a million fresh cases are detected per annum in the Indian scenario. Survival rate has not significantly improved over the past decades.³

It is a known fact that most of the oral squamous cell carcinoma (OSCC) are preceded by or coexist with potentially malignant disorders (PMDs).³ PMDs are heterogenous group of lesions and conditions which are cautioned for future occurrence of oral cancer especially OSCC. Wide array of PMDs is implicated in the development of oral cancer.³ Proper clinical assessment and histological judging of PMDs may help to prevent the occurrence of OSCC. Death due to oral cancer remains high either due to fact that the patients approach to treatment at the advanced stage with the resultant delay in diagnosis, in spite of lesions presenting in an accessible area.⁴ Earlier literature suggested that occurrence and increased rate of malignant transformation (MT) in PMDs were habit related.⁵

Habits such as tobacco or beetle quid chewing, smoking with the synergistic effects were considered to be the important etiologies of PMDs and OSCC in Asia and its subcontinent. Though numerous articles have reported that PMDs and oral cancer can occur at the normal sites or in the absence of habit.⁴,⁵

Sir James Paget was the first to describe MT of an oral lesion into carcinoma. 1877 Schwimmer reported the similar findings. Later, in 2005, WHO coined the term “potentially malignant disorders” to describe such lesions.⁶ Buccal mucosa followed by tongue, gingiva and the floor of the mouth are the most site for the occurrence of PMD’s with a prevalence of 1-5%.⁵ Present article enlightens the malignant potentiality of certain rare PMDs [Table 1].

Lupus Erythematosus
Lupus erythematosus is an immunologically-mediated collagen vascular disorder.⁷

“Lupus” is a Latin word meaning “Wolf” and “erythematous” resembling reddish used to describe erosive skin lesions evocative of a “wolf’s bite.”⁸

Basically, two forms of lupus are described, discoid LE (DLE), affecting skin and mucous membranes, and systemic LE (SLE), affecting joints, visceral organs and other tissues. Bulloous form, acute cutaneous form, subacute cutaneous form chronic cutaneous form, and a neonatal form are the different forms of LE.
Etiopathogenesis

The etiology of LE is attributed to genetic as well as environmental components influencing the pathogenesis leading to an irreversible break in immune responses against endogenous nuclear antigens. [8]

Ultraviolet (UV) light, demethylating drugs, or endogenous viruses, and epigenetic factors have a role in etiology of SLE. [8]

Clinical features

Clinical manifestation includes butterfly rash on the face, vasculitic dermatitis, maculopapular eruptions, Raynaud’s phenomenon, and alopecia. Cutaneous lesions reveal well-defined erythematous patches with adherent scaling. SLE may swan array of features such as fatigue, involvement of the kidneys, the heart, lungs and brain, joint and muscle pain. [6]

Oral lesions are more often seen on palate, buccal, and vestibular mucosa. Mucosa typically comprises central erythematous area surrounded by a slightly elevated white border with fine perpendicular "paint-brush"-like lines. Lesions in the palate are quite ill-defined with superficial ulcerations. Most of the patient complains of burning sensation, dryness, and soreness while having hot and spicy food. [9]

Malignant potential

Malignant changes in DLE were first reported by Field and Longman. The incidence of malignant lesions in individual affected with SLE was around 5%. Discoid oral lesions have been considered to be potentially malignant disorder. SCC and less commonly basal cell carcinoma (BCC) arises from skin damaged by actinic rays have a more aggressive behavior than the conventional one. SCC developing in a lesion of DLE is very rare with incidence being 3.3-3.4%. [7,10]

Epidermolysis Bullosa (EB)

EB is characterized by blistering and increased fragility of the skin. EB exhibit an incredible variation in genetic heterogeneity and clinical phenotypes, especially in multiple EB disorders. [14]

Basically, there are four major types and over more than 30 subtypes in EB. The four major types include intra-epidermal, junctional, dystrophic, and mixed EB, they differ genotypically, phenotypically, and by the site of ultrastructural disruption or cleavage. The character and the severity of craniofacial as well as oral manifestations of the different EB varies distinctly. [14]
and skin. The proteins transcribed from these genes play a role in cell adhesion in the oral mucosa and during developing tooth bud.\(^{[14]}\)

**Oral manifestations**

Increased tissue fragility of oral and perioral part, oral ulcerations, healing with scarring, blister formation, gingivitis and gingival hyperplasia, periodontal disease, ankyloglossia, and microstomia can be seen as one of the oral manifestations in EB.\(^{[14,15]}\)

**Malignant potential**

Individuals affected with EB are at higher risk of developing SCC, especially of hard and soft palate and lower lip.\(^{[15]}\)

**Plummer-Vinson Syndrome (PVS)**

PVS was described by Paterson and Kelly in 1919, later termed by Henry Stanley Plummer and Porter Paisley Vinson.

Microcytic hypochromic anemia, atrophic glossitis, and esophageal webs or strictures are the characteristic of this syndrome and is associated with iron deficiency anemia.\(^{[16]}\)

**Etiopathogenesis**

Etiopathogenesis of PVS is uncertain. Severe iron deficiency, malnutrition, and autoimmune processes are the contributory factors in this syndrome.\(^{[17]}\)

**Clinical features**

PVS is more common in females.\(^{[17]}\) Syndrome is characterized by atrophic changes in the oral mucosa, pharynx and esophagus, dysphagia, and hypochromic anemia. Other symptoms such as angular cheilitis, glossitis, early loss of teeth, web formation, achlorhydria, nail deformation, hyperkeratosis, conjunctivitis, and visual disturbances.\(^{[17]}\) Weakness, fatigue, and dyspnea are secondary to iron deficiency anemia.\(^{[17]}\)

**Malignant potential**

PVS is associated with a high risk of OSCC, esophagus, and pharynx. Anemia in PVS results in epithelial atrophy, changes in cell kinetics with resultant decreases in the repairing ability of the mucosa, thus making a way to carcinogens and co-carcinogens and thus predisposing the entire oral mucosa to more prone for malignancy. About 3-15% of the individual develop SCC of the upper GIT. PVS is a major risk factor presented with esophageal or pharyngeal cancer.\(^{[17]}\)

**Xeroderma Pigmentosum (XP)**

XP an uncommon genetic autosomal recessive, progressive, degenerative disease with extreme photosensitivity to radiation. XP was first described by Dr. Moriz Kaposi and Herba in 1874, a dermatologist in Vienna, later James Cleaver in San Francisco reported defective DNA repair in XP cells.\(^{[14]}\) The term “xeroderma or parchment skin” was initially described and in 1882 later the term “pigmentosum” was added to emphasize the striking pigmentary abnormality.\(^{[19]}\)

**Etiopathogenesis**

XP is mainly caused due to the defect in the nucleotide excision repair mechanism with defective repair of DNA and damage to various cell UV radiation. Many XP patients with tumors show mutations in the p53 gene, indicating the mutation is characteristic of UV exposure. Consanguinity as well as certain drugs and chemicals has also been implicated to play a role in the etiology of XP.\(^{[19]}\)

**Clinical features**

Clinical manifestation of XP usually starts at the earlier age. Extreme photosensitivity and burning sensation after minimal exposure to sun are the usual presentation in the individual. Individual can present with dryness of skin, hyperpigmentation, freckling in sun-exposed areas such as nose, zygoma, and forehead, and telangiectasia. Avoidance to exposure to sunlight results in aged appearance of skin, dry, rough, and atrophic. This lesion is characterized by mottled hyper-pigmented and hypopigmented areas.\(^{[18,19]}\)

Ocular manifestations such as photophobia, conjunctival infection, ocular lesion with erythema, and loss of lashes. Individual with XP have increased risk of SCC of eyes, oral mucosa and skin, melanoma, and multiple BCC. One-fifth of individual have an associated abnormalities such as difficulty swallowing, deafness, delay in growth, and low intelligence.\(^{[19]}\)

Oral leukoplakia, erythroplakia, actinic cheilitis, and SCC of the tip of the tongue and lips in younger individual and are presumed to be induced by UV radiation. Individuals with XP are more prone for fibrosis and stretching of this fibrosed areas result in pain while performing action of speech, while having food, and oral hygiene maintenance. Hence, individuals have poor oral hygiene, increased accumulation dental plaque, caries, and periodontal disease.\(^{[19]}\)

**Malignant potential**

BCC, SCC, and melanoma are most commonly seen in XP. BCC and SCC destroy local skin and underlying tissues but do not spread to internal organs. Melanoma can spread to internal organs and can be fatal. XP patients have an increased frequency of BCC and SCC up to 97% and malignant melanomas up to 65% compared to individual not affected with XP.\(^{[18]}\)

**Conclusion**

Dentists play a vital role in monitoring the mucosal changes as do the clinician. Dentists should take care not to overlook any of the PMD while they come across any oral lesions in a young individual without any habit history. Proper history, clinical
examination with relevant investigations, and biopsy will suffice to diagnosis. Persistent monitoring is necessary in each individual affected with OPMDs owing to the possibility of MT can greatly enrich the life expectancy of the individual.

Acknowledgment

I acknowledged my family and colleagues for their support, contribution, and help.

References
