# Oral Squamous Cell Carcinoma associated with Papillon-Lefevre Syndrome: Systematic Review and the first reported case

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## 1. Background:

Papillon–Lefèvre syndrome (PLS) is a rare genetic disease that was so-called as it was first described by French physicians, Papillon and Lefèvre. PLS is caused by a defect in CTSC gene located on chromosome 11q14.1-q14.3 expressed mainly by epithelial cells and some immune cells. It is an inherited as an autosomal recessive trait [1, 2] with the increased risk occurs in association with consanguineous marriage [1, 3].

The pathoetiology of PLS may not be clearly understood but it is well known that clinical features vary with the genetic defect and body responses to bacterial and viral infections [1].

Clinically, cutaneous or skin lesions and oral manifestations are observed simultaneously between the ages of 6 months and 4 years, coinciding with the eruption of deciduous teeth [1].

First, thickening of skin occurs followed by a well demarcated palmo-planter hyperkeratosis. The dorsal surface of hands and feet, elbows, knees, legs, and thighs are also affected but with less severity. The trunk is rarely affected. These lesions vary in their presentation ranging from scaly patches, crusted lesions, skin cracking and deep fissuring. Sometimes, the diseased skin may be superimposed infection leading to formation of abscesses. A color changes either depigmentation or hyperpigmentation may be also detected [1, 2].

Intraorally, the main feature of PLS is the severe and early-onset periodontitis. It starts as early as the eruption of deciduous teeth occurs. The gingiva becomes inflamed and swollen, followed by rapid destruction of periodontium leading to premature loss of deciduous teeth. This cycle occurs again with the eruption of permanent teeth causing looseness, hypermobility, drifting and teeth loss. Most of the permanent teeth are lost in the second decade [1-7].

However, Ikeshima (2006) previously reported a PLS case with intact alveolar bone around the permanent posterior teeth [8]. On the other hand, different treatment modalities in the form of scaling and root planning, oral hygiene measures and regular follow-up can eliminate the reservoir of causative organisms, minimize the destruction of periodontium and delay teeth loss [1].

Despite rarity, the patients with PLS may develop different types of mucocutaneous cancers including skin squamous cell carcinoma [4], malignant melanoma [5-7] and eye lesions [9].

## 2. Objective:

This study aims to perform a systematic review on the possibility of the association between Papillon-Lefevre syndrome and oral squamous cell carcinoma (OSCC) and to introduce the first case report.

## 3. Methodology:

### 3.1. Search Method for Identification of Studies:

This systematic review was conducted depending on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Equity 2012 Extension checklist. A comprehensive electronic search without date and language restrictions was performed in August 2018 using three electronic databases: PubMed, Google Scholar and Cochrane Database. One or a combination of the following search terms was used: (Oral squamous cell carcinoma), (OSCC), (Human oral squamous cell carcinoma), (Human OSCC), (Oral cancer), (Head and neck squamous cell carcinoma), (HNSCC), (Papillon Lefevre syndrome), (Papillon-Lefevre syndrome), (Papillon Lefvre) and (PLS) and the Studies detecting the occurrence of OSCC in patients suffering from this Papillon-Lefevre syndrome were considered. The hand-searching was also done. The reference lists of any relevant study and the reviews on the subject were also evaluated for possible additional studies.

### 3.2. Study selection and data extraction:

Two authors (M. A), (M. S), independently performed the electronic search and evaluated the resultant data.

## 4. Results:

The electronic search using all combinations, except one, showed no entries. The combination of (PLS) and oral cancer resulted in 17 studies. However, all of these studies were excluded after the initial screening of the titles and abstracts. This is because; some studies reported the association of this syndrome with skin and ocular carcinomas while others were totally unrelated to our subject. Such studies did not use PLS as a synonym or abbreviation for Papillon Lefevre syndrome but for other issues such as plasma lipid.

Therefore, the review of the current literature revealed that the association between the Papillon-Lefevre syndrome and OSCC has not been previously reported.

## 5. Case report:

A thirty-six years old male patient came to the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, complaining of a large painful swelling in the left side of his palate interfering with deglutition and speech. The duration of this swelling was about 25 days as reported by patient.

Extraoral examination revealed presence of keratotic thickenings in both aspects of patient's hands and feet soles. Pitting of some fingernails was detected. Hyperpigmented spots and infectious blister-like foci in his feet were also seen (Fig. 1). Peeling of these scales leaves slight erythema. Patient stated that these thickenings worsen in some months of the year but could not correlate this sign with certain season.

Regarding his lifestyle, the patient works as a driver and he is a heavy smoker for more than 20 years. Upon asking him about his family history, he stated that his parents are relatives but they did not complain of such lesions before.

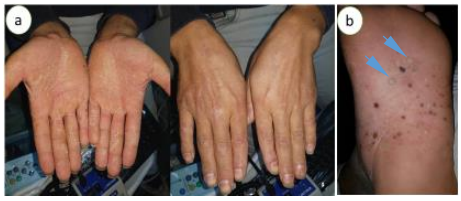


**Figure 1:** Clinical pictures showing (a) hyperkeratosis of dorsal and palmar aspects of patient's hands and nail abnormalities (b) hyperkeratosis of plantar aspects of patient's foot, hyperpigmented spots and infectious foci (arrows).

Intraoral examination revealed a well circumscribed pink nodule, approximately 1.5 x 1.5 cm in size and round in shape located on the left side of the palate. Surface ulcer oozing white cheesy necrotic material was also observed (Fig. 2).

The underlying palatal bone appeared normal in the radiograph (occlusal radiograph and computed tomography). In addition, some missing teeth, drifting in anterior teeth in addition to periodontitis and deep pockets were noticed.

Lab investigations revealed normal blood picture. Magnetic resonance imaging (MRI) was done and revealed absence of any metastatic foci.

The excisional biopsy with safety margins was performed at the Oral and Maxillofacial Surgery Department and the surgical specimen was submitted for microscopic examination in the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Cairo University (Fig. 3).

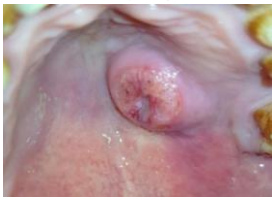

**Figure 2:** Intra-oral picture showing palatal swelling with central ulceration.

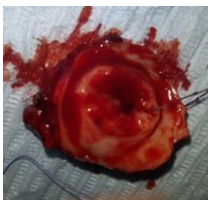

**Figure 3:** Immediate macroscopic picture of the excised specimen.

Histopathological examination of H&E stained tumor sections revealed a surface stratified squamous epithelium showing signs of dysplasia. Malignant epithelial cell nests with keratin pearls were seen invading through the connective tissue. A chronic inflammatory cell infiltrate was also observed. Safety margins showed normal stratification of surface epithelium with slight hyperplasia, hyperkeratosis and prominent granular cell layer. No dysplastic features were seen (Fig. 4).

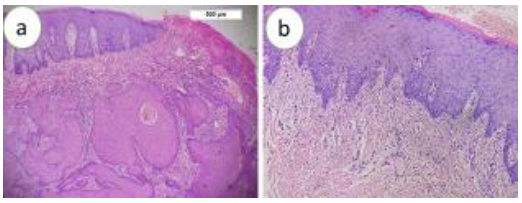


**Figure 4:** Photomicrographs of the oral lesion showing **(a)** Well differentiated OSCC formed of epithelial cell nests invading through the C.T (H&E x40) and **(b)** Safety margin showing non-dysplastic surface epithelium (H&E x100)

## 6. References:

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