A Case Report on Smoking-Related Pseudo-Epitheliomatous Hyperplasia of the Oral Cavity

Afreen Munir[1**], Ashika.S[2], Abin benny[3], Albin Saji[4], Dr. Sheik Haja Sherief [5]

***Corresponding Author:* Afreen Munir**

[1]Pharm D Intern, Department of Pharmacy Practice, Nandha College of Pharmacy, Erode, Tamil Nadu –INDIA

[2]Pharm D Intern, Department of Pharmacy Practice, Nandha College of Pharmacy, Erode, Tamil Nadu –INDIA

[3]Pharm D Intern, Department of Pharmacy Practice, Nandha College of Pharmacy, Erode, Tamil Nadu –INDIA

[4]Pharm D Intern, Department of Pharmacy Practice, Nandha College of Pharmacy, Erode, Tamil Nadu –INDIA

[5]Head of the department, Department of Pharmacy Practice, Nandha College of Pharmacy Erode, Tamil Nadu- INDIA

[1]EMAIL: afreenmunir22@gmail.com

[3]EMAIL: abinbenny33@gmail.com

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Afreen Munir, Pharm-D Intern, Nandha College of Pharmacy, Erode 638052, Tamil Nadu –INDIA. E-mail: afreenmunir22@gmail.com

ABSTRACT

The condition, known as pseudoepitheliomatous hyperplasia, is a benign disease that causes an overabundance of the epidermis and adnexal epithelium and often mimics squamous cell carcinoma. Therefore, it is sometimes also referred to as pseudocarcinomous hyperplasia, due to its appearance being fairly indistinguishable from well-differentiated squamous cell carcinoma. However, it is a reactive epithelial proliferation with irregular hyperplasia and tongues of epithelium extending into the dermis. Oral pathologists largely overlook PEH, which is of significance in research studies. Due to small sample sizes, incomplete excision, improper orientation, and dense inflammation, the differential diagnosis between PEH lesions and invasive squamous cell carcinoma often becomes challenging. At times, such diagnosis is sometimes difficult as the lesion may mimic other lesions on clinicopathological examination. Excessive sun exposure and tobacco use are risk factors for lip cancer. Most cases of lip cancer occur on the lower lip, are squamous cell carcinomas, and originate from the thin, flat squamous cells found in the middle and outer layers of the skin. Here is a case that initially was diagnosed as lip carcinoma SCC but underwent further wedge biopsy on clinical suspicion to confirm a PEH diagnosis. Proper management calls for the differentiation of PEH from malignancy, as brought out in this case.

KEYWORDS

Pseudoepitheliomatous hyperplasia, squamous cell carcinoma, histopathology, Lip cancer, smoking, oral cancers, tobacco.

INTRODUCTION

PEH of the lower lip primarily affects males, with an incidence rate of 4 per 100,000 people. It most commonly occurs in individuals over 70 years old, usually appearing in the central third of the lip, and rarely exceeds 2 cm in size. The development of lip cancer has been linked to tobacco use and excessive alcohol consumption **[1].** Oral conditions related to PEH include necrotizing sialometaplasia, median rhomboid glossitis, and chronic hyperplastic candidiasis. Tobacco habits are a well-known risk factor for cancer, and both smoking and smokeless forms of tobacco significantly raise the likelihood of tumor formation. Alcohol consumption has also been causally linked to cancers of the oral cavity, pharynx, and larynx. While the exact mechanisms by which alcohol and tobacco induce cancer remain unclear, they are known carcinogens [2]. The risk of cancer is comparable in people who smoke medium tar (15-21 mg), low tar (8-14 mg), or very low tar cigarettes (<7 mg). However, men who smoke non-filtered cigarettes with a tar content of 22 mg are at greater risk of developing PEH of the lips [3]. A beedi, a thin cigarette or mini-cigar filled with tobacco flakes and wrapped in a leaf, is another form of smoking linked to cancer. This case report presents a patient with smoking-induced PEH of the oral cavity, a condition that can be easily misdiagnosed as SCC, thus requiring careful clinical and histological evaluation.

CLINICAL FEATURES OF PEH

PEH typically manifests as a well-defined plaque or nodule, which may show varying degrees of scaling and crusting. The pronounced epithelial hyperplasia gives rise to the "vegetative" or verrucous appearance often observed. Ulceration might accompany the lesion. The size of the papules or nodules can range from under 1 cm, as seen in granular cell tumors, to several centimetres in cases like halogenoderma or deep fungal infections. PEH lesions are generally skin-coloured or pinkish-tan but may appear pigmented when associated with melanoma. They can also develop near ulcers, burn scars, or colostomies. In some instances, PEH may present as a large plaque with central scarring or an active serpiginous border, commonly linked to blastomycosis. These lesions may grow or, in some cases, resolve on their own. PEH can also develop as a hyperplastic response to a long-standing infection or chronic inflammatory condition. The presence of a palpable nodule beneath the skin in association with PEH may suggest an underlying pathology such as lymphoma or carcinoma, and in such cases, a biopsy including the deep dermis or subcutaneous tissue is essential for accurate diagnosis.

Benign hyperplasia of the epithelial rete ridges is more of a microscopic pattern than a specific diagnosis and can sometimes be mistaken for squamous cell carcinoma. This pattern can be observed in a range of conditions, including infections, inflammation, trauma, and neoplasms.

CASE REPORT

Patient information:

A 43-year-old male patient was admitted to Government Erode Medical College and Hospital with lesions on his lower lip for the past 6 months.

Presenting symptoms: His medical history includes H/O swelling in his lip for the past 6 months, which has gradually increased in size to its current proportions. He also experienced pain, weight loss, and a loss of appetite. There was no H/O bleeding due to lesions, fever, or trauma.

Personal history: He is a known case of a chronic smoker (Beedi) with a daily intake of 5 packs and has been an alcoholic for the past 20 years.

General examination: Mild pallor alone was present. No other signs of icterus, cyanosis, clubbing, etc., and vitals were found to be stable.

Systemic examination: found within normal limits.

Local examination of the case:

Clinical examination reveals proliferative lesions in the lower lip along the tubercular boundary extending from the midline to 2 cm from the angle of the mouth, measuring 3*2 cm and pale in color. Smoke tar was abundant throughout the cavity, including the uvula, soft palate, hard palate, buccal mucosa, and floor of mouth. The lesion had a rough, nodular surface, was non-tender, and didn’t bleed on palpation. There were no signs of induration or fixation to underlying structures.

Local examination of the left foot shows an ulcer of size 3*3 cm in the plantar aspect of the non-functioning left great toe.

Investigations:

1. USG Thyroid (On day 5 of admission): showed right lobe thymus normal and left lobe show cystic mass of size 1.2*1.1 cm, which was concluded as mild left thyromegaly with colloid type left lobe. Two sub-mental nodes of size 7*7mm and 6*6mm.
2. CBC was found within normal limits, but CRP was elevated.
3. A wedge biopsy of lesions was sent on day 9 of admission, and findings showed tracing features of pseudoepitheliomatous hyperplasia of the lip.

Table- 1 - Laboratory Investigations of The Case

S. No	PARAMETERS	OBSERVED VALUE	REFERENCE VALUES
1	**Hb (g/dL)**	11.4-*	**12-16**
2	**RBC (10^{12}/L)**	3.86	**3.5-5.5**
3	**WBC (10^9/L)**	5.9	**4-10**
4	**PLT (10^9/L)**	232	**100-300**
5	**RBS (mg/dL)**	77-*	**80-120**
6	**S. UREA (mg/dL)**	17	**10-50**
7	**S. CREATININE (mg/dL)**	0.8	**0.7-1.4**
8	**T. PROTEIN (mg/dL)**	7.5	**6-8.3**
9	**S. ALBUMIN (g/dL)**	3.5	**3.8-5**
10	**T. BILIRUBIN (mg/dL)**	0.6	**<1**
11	**SGOT (IU/L)**	20	**<37**
12	**SGPT (IU/L)**	18	**<40**
13	**ALKP (IU/L)**	63	**60-280**
14	**T3**	2.28	**0.9-2.8**
15	**T4**	13.2	**5.1-14.1**

16	**TSH**	1.21	**0.27-4.20**
17	**Na +(mmol/L)**	128**-***	**135-145**
18	**K +(mmol/L)**	3.9	**3.5-5**
19	**Cl^-**	94**-***	**96-106**
20	**PDW**	9.3*****	**7-9**
21	**PCT**	0.20	**0.108-0.282**

Note : - *: slightly decreased , *: slightly elevated , **: highly elevated

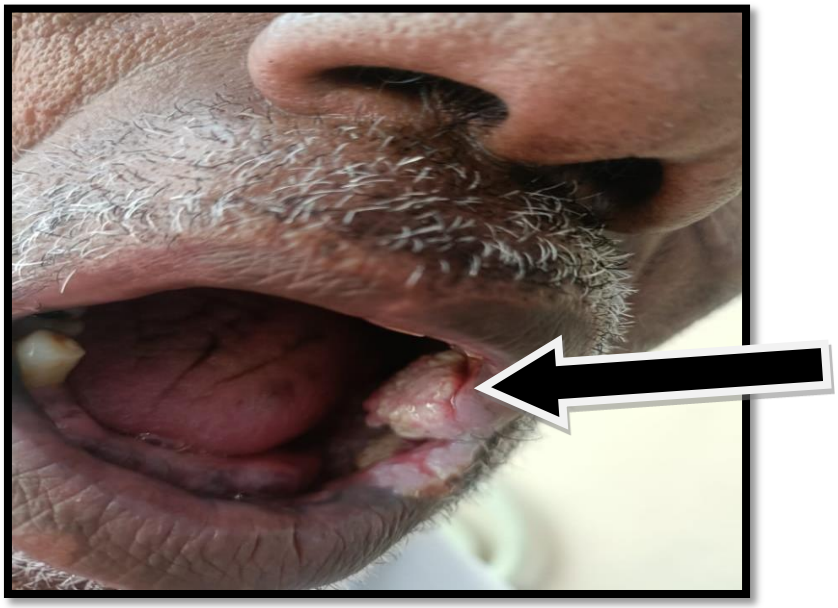

Fig 1 - "Lesions of Pseudoepitheliomatous Hyperplasia of lip"

Differential diagnosis (D/D)

Due to the clinical appearance of the lesion, differential diagnoses included:

- Squamous cell carcinoma
- Verrucous carcinoma
- Chronic traumatic ulcer
- Pseudo-epitheliomatous hyperplasia (PEH)
- Inflammatory hyperplasia [4]

TABLE- 2 -BIOSPY RESULTS

GROSS FINDINGS (H/P)	IMMUNOHISTOCHEMISTRY REPORT
Proliferative lesions in the lower lip along the tubercular boundary extending from the midline to 2 cm from the angle of the mouth, measuring 3*2cm and pale in color.	**P53 test -** Reports showed that there was less stain observed in p53 which indicates that it's PEH and not SCC.
Left foot shows ulcer of size 3*3 cm in the plantar aspect of non-functioning left great toe. The left lobe shows a cystic mass of size 1.2*1.1 cm. Impression shows mild left thyromegaly with colloid-type left lobe [5]	**The e-Catherin test** showed a more intense stain, confirming the diagnosis of PEH. [6]

DIAGNOSIS:

Based on clinical, histological, and immunohistochemical findings, the lesion was diagnosed as smoking-induced pseudo-epitheliomatous hyperplasia of the oral cavity along with mild left thyromegaly (colloid type left lobe).[7]

MANAGEMENT OF THE CASE

Medical Treatment:

1. **Pre-operative medications** like (Acetaminophen 500mg, Ranitidine 150mg, Multivitamin, Cefixime 200mg) twice daily.
2. Advised patient to take a **High protein Bland diet** (avoid spicy foods) and follow proper oral hygiene.
3. Glycerine for local application and povidone iodine mouthwash.
4. **Smoking Cessation Counselling:** The patient was strongly advised to quit smoking, with support offered in the form of nicotine replacement therapy and counselling.

Surgical Treatment:

- **Surgical Excision:** A wide local excision of the lesion was performed, ensuring clear margins to prevent recurrence. The excised tissue was sent for histopathological confirmation, which again showed features consistent with PEH without dysplasia or malignancy.[8]
- **Flap Coverage:** If the excision leaves a wound too large for direct closure, a flap technique is employed. This involves relocating a nearby piece of tissue that retains its own blood supply to cover the wound.
- **Closure and Healing:** The flap is meticulously positioned and sutured in place, followed by dressing the area and monitoring for proper healing.
- **Regular follow-up –**The patient was discharged on the 20th day and followed up for the recurrence of the lesion

DISCUSSION

From the data obtained during our present study, we analysed that exposure to tobacco and smoking was significantly responsible for pseudo epitheliomatous hyperplasia in the lower lip. A vast number of literature depicts that smokers are exposed to these carcinogens and their metabolites have also been found in the urine of individuals in higher concentrations than that of nonsmokers.[9] Chronic irritation, especially from tobacco smoking has been the significant cause for the production of reactive hyperplastic lesions in the oral cavity. Probably, in this case, chronic smoking could have led to chronic irritation of the oral mucosa, thus contributing to the abnormal epithelial growth seen in PEH. The lack of dysplasia and atypical features during histopathological analysis was critical for determining the difference between PEH and SCC, which might otherwise result in extremely aggressive treatment. Studies into the mechanisms of tobacco-induced cancer laid an excellent groundwork for how tobacco carcinogens work. We have now identified the carcinogens in cigarette smoke, their metabolism to DNA adducts, and the competing detoxification pathways. At the same time, there is an increased consciousness of the complex pathways that lead to genomic instability resulting in cancer, from the accumulation of unrepaired DNA adducts in the tissues of smokers. Such findings can be very useful in exploring the avenues towards directing critical steps in the cancer induction process, with such mechanistic insights being developed into practical strategies against the prevention and treatment of tobacco-induced cancer. [10]

Diagnosis of PEH needs considerable caution because making a diagnosis of PEH would require a biopsy combined with clinicopathologic correlation, often including the review of multiple tissue levels. Atypical epithelial processes such as verrucous carcinoma, proliferative verrucous leukoplakia, and squamous cell carcinoma can look very much alike. Misdiagnosis of PEH may occur and result in unnecessary radical surgery or surgery-related complications. A second opinion or double reporting may prevent misdiagnosis of PEH and squamous cell carcinoma. Special stains may sometimes be necessary to establish infection. Tobacco-induced oral cavity lesions, such as PEH, are poor candidates for diagnosis by mimicking neoplastic lesions. Proper diagnosis could be achieved by thorough clinical evaluation, histological examination, and application of immunohistochemical procedures in this context. Early detection, hence early differentiation from SCC, would ensure that unnecessary treatment is negated and the patients receive proper care. This case emphasizes the importance of considering benign reactive conditions like PEH for an exophytic lesion in a chronic smoker. Educational intervention coupled with smoking cessation prevents such conditions and decreases the likelihood of oral cancer.

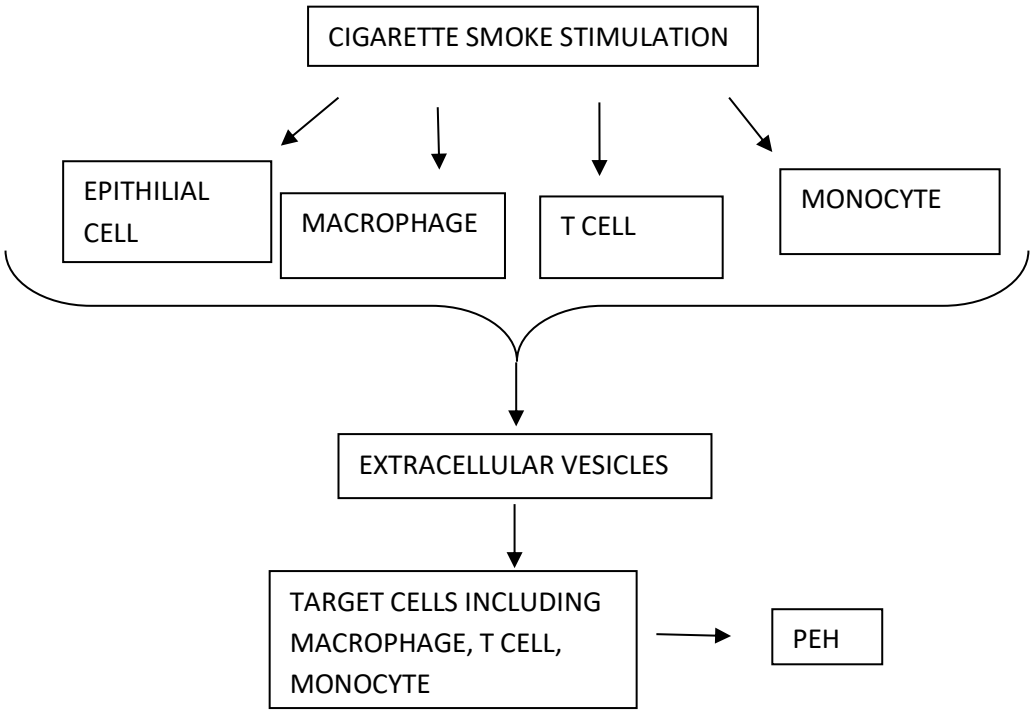

Fig 2 - Mechanism of Action of Tobacco-induced Oral Leukoplakia

CONCLUSION

PEH is a benign epithelial hyperplasia that has been microscopically linked to a wide range of skin disorders. The pathophysiology of PEH has not yet been explained by scientific data. The histopathologic analysis of samples containing PEH should follow a methodical procedure. It could be harmful to the patients' care if these results are misinterpreted as SCC. Being conscious of the chance that the initial diagnosis that springs to mind may not be correct also helps to avoid many mistakes. PEH should be taken into account in a well-differentiated SCC diagnosis in order to potentially prevent needless surgery. The entities mentioned in the review that follows are not meant to be a comprehensive list of the topic; rather, they are offered solely for the lessons they can impart regarding the dangers that are associated with them. The gold standard for making the correct diagnosis is still hematoxylin and eosin microscopic analysis and clinicopathologic correlation. In challenging situations, tissue culture, immunohistochemistry, and direct immunofluorescence can frequently be useful diagnostic adjuncts[6].This case underlines the necessity of suspicion of benign conditions like pseudo-epitheliomatous hyperplasia (PEH) in chronic smokers who present with exophytic oral lesions. Since PEH is benign, a differential diagnosis must be made between squamous cell carcinoma; hence detailed histopathological and immunohistochemical examination is required. [11]Smoking cessation is still one of the preventive measures as well as part of management; however, early diagnosis is necessary to prevent overtreatment and to minimize the possibility of the disease turning malignant.[12]

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