



ORIGINAL RESEARCH PAPER

Pathology

TOBACCO RELATED ORAL LESIONS – CYTO-HISTOLOGICAL CORRELATION IN A TERTIARY CARE HOSPITAL OF ODISHA.

KEY WORDS:Tobacco related oral lesions ,scrape cytology,verrucous carcinoma,squamous cell

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ABSTRACT

Background: Oral cancer is the commonest malignancy in Indian males. The incidence of oral squamous cell carcinoma appears to be directly related to use of tobacco in various forms .Tobacco related oral lesions have varied presentations like erosive and ulcerative lesions, leukoplakia, proliferative verrucous carcinoma and squamous cell carcinoma.
Aims and objectives: The present study aims to find the correlation between cytological (scrape) analysis and histopathological study in patients with tobacco addiction presenting with oral lesions.
Materials & methods: The study was conducted in S.C.B. Medical College, Cuttack during the period from September, 2012 to August 2016. All the patients were subjected to clinical examination, scrape cytological assessment and histopathological study. The scrape smears were stained with Pap and H&E stain.
Results: Total number of patients in this study was 528 with M:F ratio of 1.65:1. Out of them, 130 cases were correlated with histopathological diagnosis. Maximum number of patients were addicted to Gutka (32.57%) . Majority of patients were in fifth and sixth decades of life(%). Squamous cell carcinoma (SCC) was predominantly seen in 6th decade(%). Alvelolo-buccal complex is the commonest site of SCC of oral cavity. Sensitivity of our study was 97.27%, specificity 95% and positive predictive value (PPV) was 99%.
Conclusion: Scrape cytology is an easy ,rapid, economical and fairly accurate procedure to screen oral lesions. Early diagnosis ,increased awareness will result in effective, early treatment and prevention of complications with downstaging of oral cancers.

Introduction:

Oral cancer is increasing worldwide and it is the sixth most common neoplasm in the world. In developing countries, such as India, Sri Lanka and Pakistan. It is the most common cancer in men accounting for 30% of all new cancer cases. It accounts for 50% - 70% of total cancer mortality.¹

At current rates, approximately 45000 cases in the united states and more than 650,000 cases worldwide are diagnosed each year.² In India and Asia the chewing of betel quid and paan is a major regional predisposing influence.

This habit, considered a delicacy by some, contains ingredients such as areca nut, slaked lime and tobacco, wrapped in betel leaf; many of the ingredients of paan could give rise to potential carcinogens.² Oral carcinogenesis occurs by a step wise accumulation of genetic damage over time. It occurs by a two step procedure –the initial presentation of a precursor (pre-malignant, precancerous) lesions, which subsequently develops into cancer. Precursor lesions progress to squamous cell carcinoma over a period of time if left untreated.

Several oral lesions like leukoplakia, erythroplakia, lichen planus and actinic keratosis are considered to be pre-malignant lesions for oral squamous cell carcinoma.³ In addition to increasing incidence, total cancer mortality due to oral cancers is very high when compared with other cancer related mortality.⁴ Tobacco is a product prepared from the leaves of the tobacco plant by curing them. The plant is part of the genus Nicotiana and of the solanaceae family. More than 70 species of tobacco are known in literature, the chief commercial crop is N. tabacum.⁵

According to mouth cancer foundation approximately 90% of people with mouth cancer are tobacco users. ⁶ The clinical manifestation of many diseases of the oral cavity can be similar to oral manifestation of certain systemic disorders, often making it difficult to establish a correct clinical diagnosis. In some cases, early

stage malignant lesion can be mistaken for benign lesions. This leads to incorrect treatment and potentially dangerous to the patients.⁷ The prognosis for patients with oral squamous cell carcinoma that is treated early is much better , with a 5-year survival rates as high as 80%. The quality of life improves after early treatment because cure can be achieved with less complex and less aggressive treatment.⁸

A significant proportion of oral squamous cell carcinoma develops from pre-malignant lesions. Adjuncts for detection of lesions and selection of biopsy sites include vital tissue staining with toluidine blue and exfoliative cytology. Unfortunately, sensitivity of cytological diagnosis in a meta – analysis of 1306 cases from 14 studies showed an average of only 87.4% (ranging from 73.8 to 100%). Histological examination of tissue remains the gold standard for diagnosis and identification of malignant oral lesion.⁹Even though oral cancer is situated in an accessible position, medical attention is usually sought very late because of its characteristic lack of clinical symptoms; especially pain. This factor contributes greatly to the prognosis of this disease and the high mortality rates associated with it. This calls for a simple, reliable and cost-effective technique in order to differentiate benign lesions from early malignant lesions by scrape cytology.

Materials and methods:

The is a prospective study conducted in the Department of Pathology, S.C.B. Medical College,Cuttack, over a period of 4 years from September, 2012 to August, 2016

Selection of cases:

The study included all patients presenting with whitish and reddish patch ,an ulcerative lesion or a growth in the oral cavity with history of tobacco addiction and referred to the Department of Pathology, S.C.B. Medical College, Cuttack for oral scrape cytological examination. The patients undergoing a scrape cytological examination whose cytodiagnosis were malignant or dysplastic lesion or clinically suspicious lesions were advised for the

histopathological study. The biopsy material from the said lesions were subjected to histotechnical processing and stained with H&E stain at the Department of Pathology. The stained slides were examined by histopathologists without knowledge of scrape cytological findings. The results of cytological and histopathological examinations were recorded and tabulated for a cytohistological correlation.

Prior to the scrape cytology, a detailed clinical history was collected from all patients including history of addiction; followed by a thorough clinical examination in each case. The data recorded were: Name and address, age, sex, clinical diagnosis, past and family history, addiction history :chewing habits, amount consumed daily, duration of addiction (months/years), complaints with duration since onset, site, size, duration of growth, rate of growth, treatment history, local examination of the lesion -number (single / multiple), site, size, type of lesion- whitish patch, submucous fibrosis (SMF), ulceration, growth, etc.

After the clinical examination, the patients were subjected to scrape cytology. The patient was instructed to rinse his/her oral cavity thoroughly with plain tap water prior to collection of specimen. The lesion was scraped with the help of a flat tongue metal spatula. The specimen collected was then uniformly smeared onto clean and dry glass slides then quickly dipped in a Coplin jar containing 95% ethanol in order to fix the smear and stained with H&E and papanicolau stain.

Results :

A total of 528 cases were included in the present study. 130 cases were subjected to biopsy confirmation. The age of patients ranged from 11 to 80 years. Total number of female patients in our study was 199 and male out numbers female with a M:F ratio of 1.65:1. (Table 1) Maximum number of patients were addicted to Gutka (32.57%) followed by paan with tobacco leaf (20.83%). No female patients showed smoking habit. Mean duration of addiction to Gutka was 19.6 years (table 2).

The patients were presenting various clinical presentations of oral lesions like ulcerative lesions in the buccal mucosa, gum and alveolo-buccal complex, oral submucous fibrosis(OSMF), erythroplakia, leukoplakia, lichen planus, ulcerative lesion in the palate, growth in the oral cavity.

Majority of the patients presented with ulcerative lesion in the buccal mucosa, gum and alveoli (table 3) .Out Of 302 patients clinically diagnosed as ulcerative lesion 5 were diagnosed as squamous cell carcinoma(SCC) (fig 1a b)(table 4) .

In our study dysplastic lesions were most commonly seen in fifth decade but it usually started in third decade. SCC started in 4th decade and maximum number of cases were seen in 6th decade.(table 5). Out of 45 cases clinically diagnosed as leukoplakia; 34 cases were diagnosed cytologically as leucoplakia (fig 2a).

Five cases of leukoplakia subjected to biopsy and diagnosed as leukoplakia without dysplasia,(fig 2b). SCC was most common lesion among 130 cases subjected to biopsy(table 6).3 cases were diagnosed as verrucous carcinoma (fig 3) which was not detected in cytology but advised to do histopathological study as the patients presented with exophytic growth in the oral cavity.SCC was most commonly encountered in alveolao-buccal complex (48.75%), followed by tongue (30.48%), floor of mouth (15.8%),hard palate (3.65%) and lip in 1.21% of cases.In our study we found 100% correlation of histology and cytology in cases of SCC(table 6).

Discussion:

Carcinoma of oral cavity is the most common neoplasm of the

head and neck region; among these commonest is SCC.¹⁰In our study the age of presentation ranged from 11 to 80 years with M:F ratio 1.65:1. Maximum number of patients were seen in 5th and 6th decades . Our study correlates with the study of Bhandari A et al .They also found male preponderance and maximum number of patients in fifth and sixth decade in their study. In the study of R Agarwal et al, they found peak incidence of benign lesions in 4th decade where as in our study the peak incidence of benign lesions in 5th decade though many of them it started in second decade¹¹. Maximum number of cases with malignant lesions were seen in 4th to 7th decades which correlates with the study of Modi D et al.⁷. In present study alveolo-buccal complex is the commonest site (48.75%) of involvement of SCC followed by tongue (30.48%). Andreas Jovanovic et al found tobacco associated SCC in the retromolar area followed by floor of the mouth¹² .In the study of Mehrotra R et al and study of M Babshtet et al they also found buccal mucosa as the commonest site of involvement of SCC^{13,14} .

Out of 130 biopsy specimens from oral lesions, we found verrucous carcinoma in 3 cases (2.30%). The patients with verrucous carcinoma presented as exophytic growth in the oral cavity but it was difficult to diagnose as carcinoma from cytology . The lesions were clinically suspected as malignant lesions and confirmed in histology. Dr Lauren Ackerman who first described the entity; used to express this fact by stating :

" If a lesion looks cytologically like carcinoma ,it is not a verrucous carcinoma"¹⁵. Verrucous carcinoma is an uncommon variant of squamous cell carcinoma. This form of cancer is often seen in those who chew tobacco or use snuff orally, so much so that it is sometimes referred as snuff dipper's cancer¹⁶.Verrucous carcinoma is a warty squamous cell carcinoma characterized by a predominantly exophytic overgrowth of keratinizing epithelium.¹⁷ The microscopic diagnosis of verrucous carcinoma may be difficult because of its well differentiated character. A superficial biopsy will show only hyperkeratosis, acanthosis and benign appearing papillomatosis. Section of an adequate biopsy shows swollen and voluminous retepegs that extends into deeper tissue, where their pattern becomes complex.¹⁸

According to various studies the prevalence of oral submucous fibrosis(OSMF) in India varies between .03% to 3.2% with a malignant transformation rate of 7.6%¹⁹.In our study, prevalence of OSMF was 5.87% which correlates with the study of Sasmitha Panda et al²⁰.In our study we found sensitivity of scrape cytology was 97.27%,specificity 95% and positive predictive value 99%.Bharti Jha et al found 91.5% sensitivity and 100% specificity in their study²¹.

Conclusion : It had been observed that scrape cytology is well accepted by the public at large. From the foregoing observation it may be concluded that scrape cytology still stands a useful screening test for patients with oral lesions.Early diagnosis by scrape cytology if done widely among people will result in effective treatment and prevention of complication.

Table : 1 Age & sex distribution (n=528) (Percentage distribution of tobacco related oral lesion in male & female according to age)

Age group	No. of cases	Male(%)	Female(%)
11-20	8 (1.51%)	7 (1.32%)	1 (0.189%)
21-30	52 (9.84%)	32 (6.06%)	20 (3.78%)
31-40	100 (18.93%)	62 (11.74%)	38 (7.19%)
41-50	154 (29.16%)	104 (19.69%)	50 (9.46%)
51-60	128 (24.24%)	72 (13.63%)	56 (10.60%)
61-70	66 (12.5%)	40 (7.57%)	26 (4.92%)
71 - 80	20 (3.78%)	12 (2.27%)	8 (1.51%)

Table : 2 Tobacco Habits In Patients With Oral Lesion, Average Amt./day & Mean Duration Of Addiction

Item	Male(%)	Female(%)	Total(%)	Avg amount /day	Mean duration (years)
Paan with Tobacco	59 (17.93%)	51 (25.62%)	110 (20.83%)	15	25.65
Zarda Pan	51 (15.50%)	27 (13.56%)	78 (14.77%)	18	22.24
Gutkha	95 (28.87%)	77 (38.69%)	172 (32.57%)	20	19.6
Khaini	28 (8.51%)	40 (20.10%)	68 (12.87%)	8gm	20.75
Bidi	36 (10.94%)	-	36 (6.81%)	1pkt	28.2
Cigarette	21 (6.38%)	-	21 (3.97%)	2pkt	22.3
Mixed (Smoking & Smokeless)	43 (13.06%)	-	43 (18.14%)	1pkt/15	25.2

Table :3 Clinical presentation

Types of lesion	Frequency	Percentage(%)
Ulcer buccal mucosa ,gum, alveoli	302	57.19%
Growth Oral cavity, Clinically Suspicious Lesions	92	17.42%
SMF	31	5.87%
Erythroplakia	14	2.65%
Leukoplakia	45	8.52%
Lichenplanus	26	4.92%
Ulcer Palate	18	3.40%

Table :4 Spectrum of tobacco related oral lesions in different age group

Age group	Benign matured squamous cells only(%)	Inflammatory (%)	Leukoplakia(%)	Dysplasia (%)	SCC(%)
11-20	3 (0.56%)	5 (0.94%)	-	-	-
21-30	10 (1.89%)	31 (5.87%)	7 (1.32%)	4 (0.75%)	-
31-40	15 (2.84%)	61 (11.55%)	10 (1.89%)	8 (1.51%)	6 (1.13%)
41-50	19 (3.59%)	94 (17.80%)	9 (1.70%)	11 (2.08%)	21 (3.97%)
51-60	20 (3.78%)	71 (13.44%)	4 (0.75%)	8 (1.51%)	25 (4.73%)
61-70	4 (0.75%)	35 (6.62%)	3 (0.56%)	6 (1.13%)	18 (3.40%)
71-80	-	4 (0.75%)	1 (0.18%)	3 (0.56%)	12 (2.27%)

Table : 5 Histopathological diagnosis

Types	Frequency	Percentage(%)
Well Differentiated SCC	68	52.30%
Moderately Differentiate SCC	11	8.46%
Poorly Differentiate SCC	3	2.30%
Verrucous Carcinoma	3	2.30%
Leuplakia	5	3.84%
Dysplasia	25	19.23%
Non-specific inflammatory lesion	15	11.53%

Table : 6 Correlation between cytology and histology

Types of lesion diagnosed in cytology	No.	Comparable diagnosis in HP study	Difference in diagnosis	% of Positivity
Inflammatory	16	14	2	87.5%
Leukoplakia	06	5	1	83.33%

Dysplasia	26	25	1	96.15%
SCC	82	82	-	100%

Figure1 a Cytosmear of squamous cells carcinoma showing cohesive fragment highly malignant squamous cells (x200, PAP)

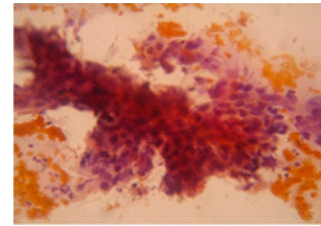


Figure 1 b HP section of invasive well differentiated SCC showing parakeratotic pearl (x100, H&E)

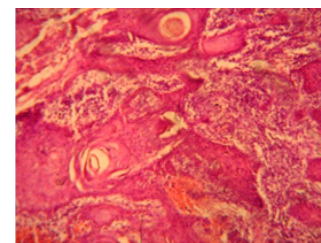


Figure 2 a Cytosmear of leukoplakia showing nucleated and anucleated squames (x200, PAP)

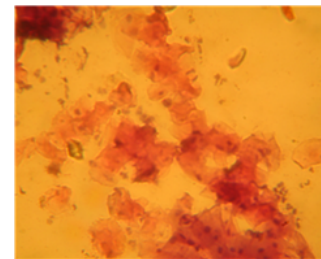


Figure 2 b HP section of leukoplakia without dysplasia showing hyperkeratosis, Parakeratosis irregular acanthosis and a band of inflammatory cells in dermoepidermal junction. (x100, H&E)

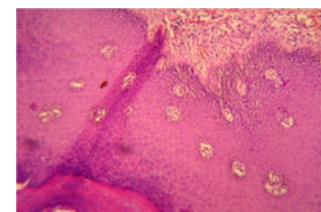
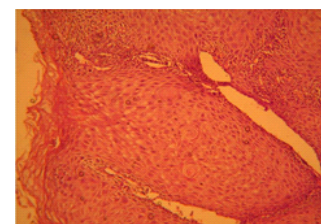


Figure 3 H HP section of verrucous carcinoma showing swollen and voluminous rete pegs extend in to deeper tissue. (x100, H&E)



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