CASE SERIES

Malignant transformation of oral submucous fibrosis
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Abstract
Several studies have demonstrated an independent association of deleterious oral habits such as smoking, betel quid chewing, and chewing tobacco with the occurrence of oral cancer. The potentially malignant conditions such as oral submucous fibrosis (OSF), leukoplakia, erythroplakia associated with smoking, and smokeless tobacco, have a greater prevalence in our country. OSF has high cancer turnover potentiality and if detected early can be prevented and treated successfully. Pindborg et al. demonstrated a malignant transformation rate of 4.5%. From the same area and patient group, 66 patients with OSMF were followed up for a period of 17 years by Murti et al., who recorded a malignant transformation rate of 7.6%. With a longer follow-up of the same group, the malignant transformation rates could increase further. Hereby, we are presenting a case series of patients on gutkha habit who reported to our department with OSF, the most common premalignant condition along with presence of a suspicious mass which on histopathologic examination diagnosed as oral squamous cell carcinoma.

Keywords:
Gutkha, malignancy, oral submucous fibrosis, oral squamous cell carcinoma, tobacco

Introduction
Oral cancer is ranked as the sixth most common cancer worldwide that shows varied geographic occurrence and is one of the leading causes of cancers in India and south-east Asia.[1] Oral squamous cell carcinoma (OSCC) is the most common malignant epithelial neoplasm affecting the oral mucosa.[2] The incidence of OSCC differs widely in various parts of the world and ranges from 2 to 10 per 1,00,000 in a year. In the Indian subcontinent, oral cancer is mainly due to chew tobacco (paan masala, gutkha, gudakhu, khaini, and many other tobacco made products).[3] The World Health Organization predicts that tobacco deaths in India may exceed 1.5 million annually by 2020.[4] Oral cancer progress through the transformation of tobacco exposed normal oral mucosa to potentially malignant lesions which ultimately changes to carcinoma. Oral submucous fibrosis (OSF) is now globally accepted as an Indian disease.[5] It has one of the highest rates of malignant transformation amongst potentially malignant oral lesions and conditions, therefore, a cause of concern for oral health care professionals. However, its incidence of malignant transformation is as 7.6% with a follow-up of 17 years.[5]

Hereby, we are presenting a case series of patients on gutkha habit who reported to our department with OSF, the most common premalignant condition along with presence of a suspicious mass which on histopathologic examination diagnosed as OSCC.

Case Reports
Case report of patients is noted in Table 1.

Discussion
Chewing of areca nut is an ancient custom in India, several parts of south-east Asia, south Pacific islands, and Taiwan. This practice is followed from several 1000 years and has become a part of the tradition and culture. There are archives for the presence of areca nut dated back from 1st century BC in ancient Greek, Sanskrit, and Chinese literature. Enormous references to areca nut palm in the Sanskrit manuscripts and its usage has been mentioned as food, medicine for social, and religious ceremonies.[6]

OSF, is the most common seen in people of south Asian countries or in south Asian immigrants in other parts of the world.[5] In the south and south-east Asia (India, Bangladesh, Pakistan, and Sri Lanka), the malignant disease of the oral cavity constitutes the most important group of malignancies. WHO experts warned that oral malignancy may become an epidemic

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Table 1: Case Reports

<table>
<thead>
<tr>
<th>Serial number</th>
<th>Case number</th>
<th>Chief complaint</th>
<th>Habit associated</th>
<th>Mouth opening</th>
<th>Lesion description</th>
<th>Hematologic findings</th>
<th>Histopathological reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40/M</td>
<td>Reduced mouth opening and pain in left cheek region since 2 months</td>
<td>Gutkha 6-7 packets daily since 20 years</td>
<td>1.2 cm</td>
<td>Firm, irregular mass, severely tender on palpation with no induration (Figure 1 and b)</td>
<td>No abnormalities detected</td>
<td>Carcinoma of left buccal mucosa</td>
</tr>
<tr>
<td>2</td>
<td>40/M</td>
<td>Severe pain in the right lower back teeth region since 1 month</td>
<td>Gutkha 5-6 packets/day since 10 years</td>
<td>2 cm</td>
<td>Exophytic growth seen on the right edentulous vestibular region in relation to 46, firm and severely tender on palpation (Figure 2 and b)</td>
<td>No abnormalities detected</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>3</td>
<td>52/M</td>
<td>Gradual reduction in mouth opening</td>
<td>Pan and gutkha 7-8 packets daily since 30 years</td>
<td>2.4 cm</td>
<td>Solitary, irregular, whitish plaque seen on the right lateral border of tongue, measuring 1 cm × 1 cm in size which was non tender and firm on palpation (Figure 3 a and b)</td>
<td>No abnormalities detected</td>
<td>Carcinoma of lateral border of tongue</td>
</tr>
<tr>
<td>4</td>
<td>30/M</td>
<td>Pain in right lower back teeth region since 4 days</td>
<td>Gutkha 3-5 packets daily since 7 years</td>
<td>1.2 cm</td>
<td>Exophytic growth was present on right posterior vestibular region</td>
<td>No abnormalities detected</td>
<td>Carcinoma of right buccal mucosa</td>
</tr>
<tr>
<td>5</td>
<td>52/M</td>
<td>Pain and reduced mouth opening since 1 month</td>
<td>Gutkha, betel nut and slaked lime together 5-7 times daily since 20 years</td>
<td>2.2 cm</td>
<td>A well-defined ulceroproliferative growth seen on right buccal mucosa in the right retromolar region, measuring approximately 3 cm×2 cm in size. On palpation, growth was firm, tender and indurated (Figure 4 and b)</td>
<td>No abnormalities detected</td>
<td>Squamous cell carcinoma of right buccal mucosa</td>
</tr>
<tr>
<td>6</td>
<td>30/M</td>
<td>Pain in the right cheek region since 3 months</td>
<td>Pan and gutkha 4-5 times/day since 5 years associated with habit of regular alcohol</td>
<td>1.7 cm</td>
<td>Diffuse erythematous, plaque seen on retromolar region of right buccal mucosa with interspersed white patches over it (Figure 5 and b)</td>
<td>No abnormalities detected</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>7</td>
<td>35/M</td>
<td>Reduced mouth opening since 1 month which is gradually worsening with time</td>
<td>Pan, gutkha chewing 10-12 packets/day since 20 years</td>
<td>0.4 cm</td>
<td>Clinically lesion was not appreciable due to reduced mouth opening. CT scan revealed a nodular uniformly radiolucent mass on right buccal mucosa (Figure 6 and b)</td>
<td>No abnormalities detected</td>
<td>Squamous cell carcinoma of right buccal mucosa</td>
</tr>
</tbody>
</table>

CT: Computed tomography

in south-east Asia unless the current trends of chewing areca nut and tobacco have been slowed down or reversed (WHO, 1984; 1992).\textsuperscript{[8]} Available data from Punjab and Uttar Pradesh consider OSMF as a poorly understood and unsatisfactorily treated disease. 390 subjects with consumption of commercially available areca nut showed severe grading of OSMF in Indore. In Patna, Bihar 157 OSMF patients were studied of which the youngest reported case of 11 years old is an alarming situation. Afroz et al. in Aligarh in 2006, a study on 58 patients of OSMF showed unsatisfactory response and considering their malignant potential, prohibition of the use of Gutkha, paan masala should be considered.\textsuperscript{[9,10]} A prevalence study on OSMF reported from Rajasthan, Hyderabad, and Delhi indicated an extensive use of smokeless tobacco.\textsuperscript{[9,11]}

In India, National Cancer Registry Program was launched in 1982 by Indian Council of Medical Research to provide true information on cancer prevalence and incidence. A total of 3.3% of the population is covered by these registries. Data from population based registries indicate that “oral cavity” is the leading site for malignancy in males and third commonest site in females. In India, more number of persons suffering from oral cavity malignancies than malignancies of other parts of the body.\textsuperscript{[8]}

Reddy and Gupta in 2004 had done a study in the North-East region of India with the age group ranging from 13 to 15 which showed tobacco or betel quid chewers vary from 2.7% in Himachal Pradesh to 63% in Nagaland.\textsuperscript{[12,13]} Prevalence surveys from India, Pakistan, and Nepal over a couple of decades have reported the use of these products between 20% and 40% among adolescents and adults. A recent study, in Pakistan, among the adolescents and adults of a Karachi squatter settlement, reported that 40% of the population was using at least one chewable...
product everyday of betel, areca, and tobacco.\textsuperscript{[13]}

In the study of Mazahir \textit{et al.}, use of tobacco and its associated products was more common among males because it is socially more acceptable for males than females. Similar results were obtained in another study in which 193 subjects (75.4\%) were male in a group of 256 subjects who consume tobacco and its associated products.\textsuperscript{[14]} In many parts of India such as Bihar, Madhya Pradesh, Gujarat, and Maharashtra especially the younger generation, there is a marked increase in occurrence of OSMF was observed more due to availability of areca nut products in different multicolored attractive pouches.\textsuperscript{[12,15]}

Social security is influenced by socioeconomic status in terms of accessibility, affordability, acceptability and actual utilization of oral, and general health. Prasad developed a classification (scale) to measure socioeconomic status, which is based on per capita monthly income. It has been extensively used in the Indian scenario.\textsuperscript{[16]} Parental education also has an affect over the development of noxious oral habits. It has been seen that higher parental education prevents the development of noxious habits in their offspring. Illiteracy or lower education status encourages the development of noxious habits. The incidence of OSMF was high in low socioeconomic status.\textsuperscript{[13,14]}

The possible reasons proposed for the increased prevalence of OSMF and its malignant transformation in India:\textsuperscript{[17]}

\textbf{Figure 1:} (a and b) Reduced mouth opening of case 1 patient; firm, irregular mass on left buccal mucosa

\textbf{Figure 2:} (a and b) Reduced mouth opening of case 2 patient; exophytic growth on the right edentulous vestibular region in relation to 46

\textbf{Figure 3:} (a and b) Reduced mouth opening of case 3 patient; solitary, irregular, whitish plaque on the right lateral border of tongue

\textbf{Figure 4:} Exophytic growth was present on right posterior vestibular region in case 5

\textbf{Figure 5:} (a and b) Reduced mouth opening of case 6 patient; ulceroproliferative growth on right buccal mucosa in the right retromolar region

\textbf{Figure 6:} (a and b) Reduced mouth opening of case 7 patient; computed tomography scan revealed a nodular uniformly radiolucent mass on right buccal mucosa
People getting attracted to tobacco or areca nut products may be due to its easy availability, low cost, attractive packaging, and aggressive marketing.

Portrayal of these products as breath fresheners could be another reason of attraction.

In certain remote countries, female smoking is considered as a taboo; hence consumption of chewing tobacco is practiced.

During occasions like marriages, areca nut is distributed as a part of cultural or religious belief, so is not objectionable.

Lack of awareness in the population regarding the disease progression.

The paymaster was the first who postulated the precancerous nature of OSMF, from one-third patients of OSMF with slow growing squamous cell mass in the Tata Memorial Hospital, Bombay. Based on clinical and epidemiological grounds, this precancerous nature was supported by few other authors. The potential of malignant conversion in patients with OSMF ranges from 3% to 6%. Gupta et al. reported malignant transformation in 2.3% of patients with OSMF over a 10 years follow-up study in Ernakulam district, Kerala. Pindborg et al. in the same area over a 15 years follow-up demonstrated a malignant transformation rate of 4.5%. 66 patients with OSMF were followed up again in the same region for 17 years by Murti et al., suggested malignant transformation rate of 7.6%. The Higher rate of malignant transformation can be expected over a longer period of follow-up.[15,18,19] Surveys reveal a 15-20% frequency of oral cancer among all cancers in India. The finding of a high frequency of OSMF among oral cancer patients in India (e.g., 40 among 100 oral cancer patients) has strengthened the postulated link between the two. In recent years, studies in India, China, southeast Asia, and South Africa and on Asian migrants in the UK have shown a clear link between areca nut, gutkha chewing with OSMF. Several case-control studies in India have shown a high risk for OSMF among tobacco chewers. Based on three new cases arising among 10145 persons in an 8 years follow-up, the relative risk of malignant transformation of OSMF was reported to be 397 compared with lesion free controls with tobacco habits. Ekanayaka and Tilakaratne in 2013 have stated that in Pakistan, the malignant transformation rate was reported to be 19 times higher in patients with OSMF.[20,21]

Suggestions to help curb the OSMF epidemic in India:[17]

1. In rural and urban areas public awareness through mass media such as television, radio, flash mob, street plays, and door-to-door campaigns to depict the hazards of these harmful products.
2. Oral screening for the population should be done on a large scale for detecting early oral lesions.
3. Appeal on the ban of these products should be strictly taken into considerations by Government authorities.

Conclusion

It can be hypothesized that as OSMF is a symptomatic condition, the patient can recognize the disease process at an early stage.

Hence, proper counseling and education of the patient regarding the devastating effects may help or reduce the incidence of malignant transformation of OSMF.

References
