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Esophageal changes in oral submucous fibrosis using fiber-optic endoscopy

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Abstract

Aim: The aim of this study was to determine the extent of esophageal involvement and the association between the clinical and functional stages of oral submucous fibrosis and esophageal changes in oral submucous fibrosis patients.

Methods: Thirty of 35 biopsied patients with proven oral submucous fibrosis, and 20 patients with no evidence of disease, underwent upper gastrointestinal endoscopy. Biopsies were taken from upper third, middle third, and lower third of the esophagus and sent for histopathological evaluation. The esophageal changes in the clinical and functional stages were studied both endoscopically and histopathologically.

Results: We found that most patients had blanching in clinical stage 2, functional stage B, and functional stage C. In most patients, blanching was found in the upper third of the esophagus, followed by the middle third and lower third. Fibrosis in the middle third of the esophagus was found in most patients.

Conclusion: The present study concludes that oral submucous fibrosis is not only confined to the oral cavity, but also extends to the esophagus. We found that there is an inverse relationship between the opening of the mouth and esophageal involvement.

Introduction

Oral submucous fibrosis (OSMF) is an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Occasionally it is preceded and/or associated with vesicle formation, and is always associated with a juxta-epithelial inflammatory reaction, followed by progressive hyalinization of the lamina propria. The later subepithelial and submucosal myofibrosis leads to the stiffness of the oral mucosa and deeper tissues with progressive limitation in the opening of the mouth and protrusion of the tongue, thus causing difficulty in eating, swallowing, and phonation.[1] OSMF is predominantly a disease of the oral cavity, although involvement of the esophagus has occasionally been reported. Fibrosis is known to extend into the pharynx via the faucial pillars and down to the pyriform fossa.[2] Betel nut or tobacco that is chewed or kept in the mouth will go down the esophagus, leading to irritation of the esophageal mucosa, which is similar to that of the oral cavity.[3] This led us to think that other systems, especially the gastrointestinal tract, might be involved in this disease. Thus, this study was set up to determine the extent of esophageal involvement and the association between the clinical and functional stages of OSMF and esophageal changes in OSMF patients.

Materials and methods

The study group consisted of 35 cases of clinically- and histopathologically-diagnosed OSMF, and 20 cases of normal individuals as the control group. Of the 35 patients, five patients refused repetition of the endoscopy and biopsy procedures, as their esophageal biopsies were

superficial and tissue was inadequate after processing. Thus, only 30 patients were included in the study. All patients previously diagnosed with systemic diseases, such as hypertension, diabetes mellitus, anemic stomatitis, and scleroderma, and other diseases, including radiation fibrosis, were excluded from our study. The patients' personal histories was recorded, including chewing habits, frequency and duration of chewing, and the brand used. Information about the site of the quid, time duration, whether the patient swallows it or spits it out, and if the patient had a burning sensation to spicy food, was obtained. Symptoms, such as a burning sensation, restricted mouth opening, difficulty in swallowing, and speech, and their duration, were noted. The clinical and functional staging of OSMF was done according to Haider *et al.*[4] The clinical photograph of OSMF is shown in Figure 1. Under local anesthesia, incisional biopsy was done from the buccal mucosa where fibrous bands were palpable. Thereafter, all patients underwent upper gastrointestinal endoscopy using an Olympus GIF Type II endoscope (Tokyo, Japan) with a video camera. The lower esophagus (37–42 cm from incisors), mid-esophagus (30–36 cm from incisors), and upper esophagus (20 cm onwards from incisors) were assessed systematically for the presence of blanched areas only. Biopsies were obtained from the upper third, middle third, and lower third of the esophagus using fenestrated cup biopsy forceps. We encountered many difficulties, including inserting the mouthguard in a severely-restricted mouth, for which a small-sized mouthguard was used. Many esophageal biopsies were superficial, and tissue was inadequate after processing, for which repetition of the endoscopy and biopsy procedures was done. Biopsy specimens were fixed in 10% formalin solution and sent for histopathological examination. The hematoxylin–eosin-stained, 5-μm thick sections were evaluated by a histopathologist.

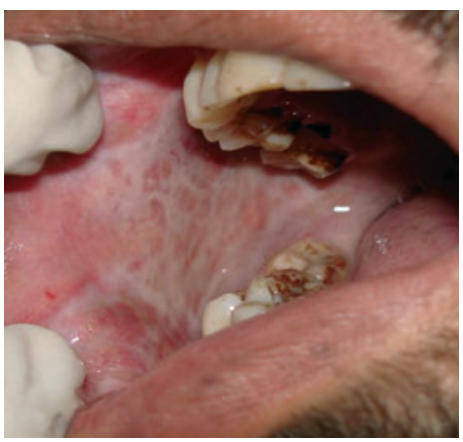

Figure 1. Diffuse blanching involving the buccal mucosa.

The oral histopathological staging of OSMF was done according to Pindborg and Sirsat.[5]

Statistical analysis

The visual esophageal endoscopy changes and esophageal histological changes in the clinical and functional stages were statistically analyzed by chi-squared test and Fisher's exact test.

Results

Controls

The age range of the control group was 17–38 years. The majority of patients were 22–30 years; 17 were male and 3 were female. None of the patients showed any esophageal abnormality upon endoscopy. The esophageal mucosa was normal upon endoscopy in all control patients. Histopathologically, no abnormalities were seen in the esophageal biopsies.

Patients

The 30 OSMF patients were in the age range of 18–46 years. The majority of patients (18 [60%]) were between 21 and 30 years. All 30 (100%) patients were males. Among the 30 patients, 28 (93.3%) had burning sensation to spicy food, 21 (70%) had difficulty in mouth opening, and nine (30%) had difficulty swallowing. All patients chewed either Gutka, betel nut, tobacco, or a combination of some or all of these with or without betel leaf. All patients consumed betel nut in one form or another. Of the 30 patients, six (20%) were smokers. No patients were in clinical stage 1, 19 (63.3%) were in clinical stage 2 with both faucial and buccal bands, and 11 (36.7%) were in clinical stage 3 with faucial bands, buccal bands, and labial bands. Most patients (19 [63.3%]) were in clinical stage 2. Functional staging was done according to the mouth opening. There were 23 (76.7%) patients in stage A with a mouth opening of ≥20 mm, six (20%) in stage B with a mouth opening of 11–19 mm, and one (3.3%) in stage C with a mouth opening ≤10 mm. It was observed that most patients (23 [76.7%]) were in functional stage A. Upon oral histopathological staging, it was found that five (16.7%) patients were in very early stage (stage I), 14 (46.7%) patients were in early stage (stage II), and 11 (36.6%) patients were in moderately-advanced stage (stage III). There were no patients showing advanced stage (stage IV). Among the 30 patients' oral biopsies, only one (3.3%) patient showed dysplastic changes. Upon endoscopy, normal mucosa was seen in 10 (33.3%) of the upper third, 14 (46.7%) of the middle third, and 19 (63.4%) of the lower third of the esophagus of patients.

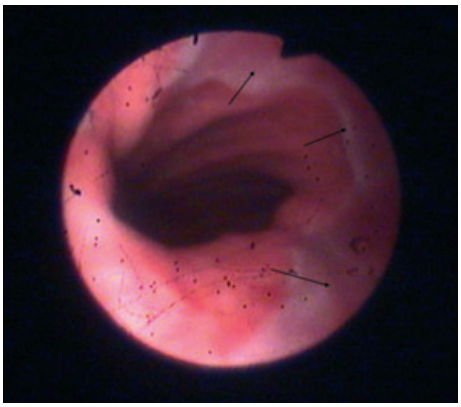

Figure 2. Endoscopic view of the esophagus with diffuse blanching.

Blanching, as shown in the Figure 2, was seen in 19 (63.4%) of the upper third, 16 (53.3%) of the middle third, and nine (30%) of the lower third of the esophagus of patients. It was observed that the upper third of the esophagus showed blanching in most patients (19 [63.4%]). Histopathologically, esophageal biopsies showed a normal epithelium in four (13.3%) of the upper third, three (10%) of the middle third, and seven (23.3%) of the lower third of the esophagus of patients. An edematous epithelium (EE) was seen in nine (30%) of the upper third, 10 (33.3%) of the middle third, and eight (26.7%) of the lower third of the esophagus of patients. A hyperplastic epithelium (HE) was seen in 14 (46.7%) of the upper third, 13 (43.3%) of the middle third, and 12 (40%) of the lower third of the esophagus of patients (see Discussion). EE and mild fibrosis were seen in two (6.7%) of the upper third, three (10%) of the middle third, and two (6.7%) of the lower third of the esophagus of patients. HE and mild fibrosis were seen in one (3.3%) of the upper third, one (3.3%) of the middle third, and one (3.3%) of the lower third of the esophagus of patients.

Visual esophageal endoscopic changes (blanching) in the clinical stages of OMSF

Overall, of the 19 patients with clinical stage 2, three (15.8%) patients had normal mucosa and 16 (84.2%) had visual esophageal endoscopic changes (blanching). Of the 11 patients with clinical stage 3, three (27.3%) patients had normal mucosa and eight (72.7%) patients had visual esophageal endoscopic changes (blanching). Fisher's exact test was applied, and the value of P was 0.38 (>0.05), which was not significant. It was observed that most patients with visual esophageal endoscopic changes were seen in clinical stage 2. In most patients, normal mucosa was found in the lower third of the esophagus, followed by the middle third and upper third in clinical stage 2, and in the lower third and middle third of the esophagus, followed by the upper third in clinical stage 3. In most patients, blanching was found in the upper third of the esophagus, followed by the middle third and lower third in both clinical stages 2 and 3 (Table 1).

Table 1. Visual esophageal endoscopic changes (blanching) in parts of the esophagus in the clinical stages of oral submucous fibrosis

Clinical stage (n = 30)	Part of esophagus	No. cases (%)	
		Normal	Blanching
2 (n = 19)	Upper third	7 (36.7)	12 (63.3)
	Middle third	8 (42.1)	11 (57.9)
	Lower third	13 (62.4)	6 (31.6)
3 (n = 11)	Upper third	3 (27.3)	8 (72.7)
	Middle third	6 (54.5)	5 (45.5)
	Lower third	6 (54.5)	5 (45.5)

Esophageal histological changes in the clinical stages of OMSF

Of the 19 patients with clinical stage 2, one (5.3%) patient had a normal epithelium, 16 (84.2%) patients had only epithelial changes (EE + HE), and two (10.5%) patients had both epithelial and connective tissue changes (EE and mild fibrosis/HE and mild fibrosis). Of the 11 patients with clinical stage 3, no patients had a normal epithelium, eight (72.7%) patients had only epithelial changes (EE + HE), and three (27.3%) patients had both epithelial and connective tissue changes (EE and mild fibrosis/HE and mild fibrosis). Chi-squared test was applied, and the value of P was 0.39 (>0.05), which was not significant. Overall, it was observed that most patients (16 [84.2%]) with only esophageal epithelial changes were seen in clinical stage 2, and most patients (3 [27.3%]) with both esophageal epithelial and connective tissue changes were seen in clinical stage 3. Most fibrosis in patients was found in the middle third of the esophagus, followed by the lower third and upper third (Table 2).

Visual esophageal endoscopic changes (blanching) in the functional stages of OSMF

Of the 23 patients with functional stage A, six (26.1%) had normal mucosa and 17 (73.9%) had visual esophageal endoscopic changes (blanching). In functional stages B and C, all patients had visual esophageal endoscopic changes (blanching), that is, six (100%) and one (100%). Chi-squared test was applied, and the value of P was 0.32 (>0.05), which was not significant. Overall, 100% of patients in functional stages B and C showed visual esophageal endoscopic changes compared to functional stage A. In most patients, normal mucosa was found in

Table 2. Esophageal histological changes in parts of esophagus in the clinical stages of oral submucous fibrosis

Clinical stage (n = 30)	Part of esophagus	No. cases (%)				
		Normal	EE	HE	EE + MF	HE + MF
2 (n = 19)	Upper third	3 (15.7)	4 (21.1)	11 (57.9)	1 (5.3)	0 (0)
	Middle third	2 (10.5)	7 (36.8)	9 (47.4)	1 (5.3)	0 (0)
	Lower third	5 (26.3)	4 (21.1)	9 (47.4)	1 (5.3)	1 (5.3)
3 (n = 11)	Upper third	1 (9.1)	5 (45.5)	3 (27.2)	1 (9.1)	1 (9.1)
	Middle third	1 (9.1)	3 (27.2)	4 (36.4)	2 (18.2)	1 (9.1)
	Lower third	2 (18.2)	4 (36.3)	3 (27.2)	1 (9.1)	1 (9.1)

EE, edematous epithelium; HE, hyperplastic epithelium; MF, mild fibrosis.

Table 3. Visual esophageal endoscopic changes (blanching) in parts of the esophagus in the functional stages of oral submucous fibrosis

Functional stage (n = 30)	Part of esophagus	No. cases (%)	
		Normal	Blanching
A (n = 23)	Upper third	9 (39.2)	14 (60.8)
	Middle third	12 (52.2)	11 (47.8)
	Lower third	15 (65.3)	8 (34.7)
B (n = 6)	Upper third	1 (16.7)	5 (83.3)
	Middle third	2 (33.3)	4 (66.7)
	Lower third	4 (66.7)	2 (33.3)
C (n = 1)	Upper third	0 (0)	1 (100)
	Middle third	0 (0)	1 (100)
	Lower third	0 (0)	1 (100)

the lower third of the esophagus, followed by the middle third and upper third in both functional stages A and B. In most patients, blanching was found in upper third of the esophagus, followed by middle third and lower third in both functional stages A and B (Table 3).

Esophageal histological changes in functional stages of OSMF

Of the 23 patients with functional stage A, one (4.3%) patient had a normal epithelium, 20 (87%) patients had only epithelial changes (EE/HE), and two (8.7%) patients had both epithelial and connective tissue changes (EE and mild fibrosis/HE and mild fibrosis). In functional stage B, of six patients, four (66.7%) had only epithelial changes and two (33.3%) had both epithelial and connective tissue changes. In functional stage C, all patients (1 [100%]) had both epithelial and connective tissue changes. chi-squared test was applied, and the value of P was 0.12 (>0.05), which was not significant. Overall, it was observed that most patients (20 [87%]) with only epithelial changes found in functional stage A, and 100% of patients in functional stage C, showed both epithelial and connective tissue changes. In most patients, fibrosis was found in the middle third of the esophagus, followed by lower third and upper third (Table 4).

Discussion

Oral submucous fibrosis is a common condition among Indian patients who consume betel nut, tobacco, pan masala, and Gutka with or without betel leaf. It has also been seen among Indians living in Kenya, Malaysia, Uganda, South Africa, Fiji, and the UK,[6–10] and cases have been reported from ethnic groups in Taiwan, Nepal, Thailand, Vietnam, and Sri Lanka.[5,11,12] OSMF is predominantly a disease of the oral cavity, and fibrosis is

Table 4. Esophageal histological changes in parts of the esophagus in the functional stages of oral submucous fibrosis

Functional stage (n = 30)	Part of esophagus	No. cases (%)				
		Normal	EE	HE	EE + MF	HE + MF
A (n = 23)	Upper third	3 (13.1)	6 (26.1)	13 (56.5)	1 (4.3)	0 (0)
	Middle third	2 (8.7)	7 (30.4)	12 (52.2)	2 (8.7)	0 (0)
	Lower third	6 (26.1)	5 (21.8)	11 (47.8)	1 (4.3)	0 (0)
B (n = 6)	Upper third	1 (16.6)	3 (50.0)	1 (16.7)	1 (16.7)	0 (0)
	Middle third	1 (16.6)	3 (50.0)	1 (16.7)	1 (16.7)	0 (0)
	Lower third	1 (16.6)	3 (50.0)	1 (47.4)	1 (5.3)	0 (0)
C (n = 1)	Upper third	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)
	Middle third	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)
	Lower third	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)

EE, edematous epithelium; HE, hyperplastic epithelium; MF, mild fibrosis.

known to extend into the pharynx via the faucial pillars and down to the pyriform fossa.[2] Betel nut or tobacco that is chewed or kept in the mouth will go down the esophagus, leading to irritation of the esophageal mucosa, which is similar to that of the oral cavity.[3] Only literature few studies have looked at cases of esophageal involvement.[2,3,13,14] Esophageal involvement was more common in patients who had consumed betel nut, tobacco, pan masala, or Gutka with or without betel leaf for longer periods. In the present study, it was noted that in most patients, blanching was found in the upper third of the esophagus, followed by the middle third and lower third. This would be because of more irritation of the upper esophagus than other parts, as it would come into contact early when Gutka or tobacco or their juice is swallowed. In most of patients, normal mucosa was found in the lower third of the esophagus, followed by the middle third and upper third. This would be because of less irritation of the lower esophagus than other parts, as it would come into contact late when Gutka or tobacco or their juice is swallowed.

Histopathologically, it was interesting to note that all of the patients in the present study showed either a HE or EE in the upper third, middle third, and lower third of the esophagus, which is also a feature of submucous fibrosis. None of the patients showed an atrophic epithelium. A HE could be due to increased mitotic activity and the selection of case and site of biopsy. Although the atrophic epithelium is the hallmark of SMF, it can also show a HE.[15]

We observed that in most patients, visual esophageal endoscopic changes were seen in clinical stage 2 (84.2%) compared to clinical stage 3 (72.7%). This could be attributed to differences in patients' chewing habits of Gutka or tobacco in clinical stages 2 and 3. In most patients, blanching was found in the upper third of the esophagus, followed by the middle third and lower third in both clinical stages 2 and 3. In most patients (84.2%), esophageal epithelial changes were seen only in clinical stage 2, and in most patients (27.3%), both esophageal epithelial and connective tissue changes were seen in clinical stage 3. In 100% of patients, visual esophageal endoscopic changes were found in functional stages B and C compared to functional stage A (73.9%). This indicates that as the mouth opening decreases, the extent of involvement of the esophagus also increases. In most patients (87%), epithelial changes were only found in functional stage A, and in 100% of patients, both epithelial and connective tissue changes were found in functional stage C. This indicates that as the mouth opening decreases, the extent of esophageal fibrosis also increases, so there is an inverse relationship between the opening of the mouth and esophageal fibrosis.

The present study found that there is a relationship between the clinical and functional stages of OSMF with the visual and histological esophageal changes, which will assist in determining the extent and severity of the disease, which in turn helps in its management. We also found that there is an inverse relationship between the opening of the mouth and esophageal fibrosis. Thus, the present study advises the evaluation of esophageal involvement using upper gastrointestinal endoscopy in all OSMF patients who were chronic users of betel quid and Gutka; patients who swallow Betel quid, Gutka, and/or tobacco; OSMF patients with restricted mouth opening; and patients with dysphagia. However, the association between the clinical and functional stages of OSMF and the visual and histological esophageal changes was not statistically significant as our sample size was small. Further studies with large samples and longer time periods are needed to assess the changes in the esophageal mucosa, grade the esophageal involvement, and to determine the malignant potential of esophageal mucosa in OSMF, as it is considered a premalignant condition.[8,16]

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References

1 Rajendran R. Oral submucous fibrosis: etiology, pathogenesis, and future research. *Bulletin of WHO* 1994; **72**: 985–96.

2 Mathew B, Warrier PKR, Zachariah J *et al.* Esophageal changes in oral submucous fibrosis. *J Pathol and Bacterol* 1967; **10**: 349–53.

3 Misra SP, Misra V, Dwivedi M *et al.* Esophageal subepithelial fibrosis: an extension of oral submucosal fibrosis. *Postgrad Med J* 1998; **74**: 733–6.

4 Haider SM, Merchant AT, Fikree FF *et al.* Clinical and functional staging of oral submucous fibrosis. *Brit J Oral Maxillofac Surg* 2000; **38**: 12–5.

5 Pindborg JJ, Sirsat SM. Oral submucous fibrosis. *Oral Surg Oral Med & Oral Pathol* 1966; **22**: 764–79.

6 Kennedy TF, Mc Donald DG. Oral submucous fibrosis. A case report. *Brit Dent J* 1968; **124**: 121–4.

7 Moos KF, Madan DK. Submucous fibrosis. *Brit Dent J* 1968; **125**: 313–7.

8 McGurk M, Craig GT. Oral submucous fibrosis: two cases of malignant transformation in Asian immigrants to the United Kingdom. *Brit J Oral Max Surg* 1984; **22**: 56–64.
9 Foster BA. Oral submucous fibrosis: a cause for concern. *Brit Dent J* 1986; **160**: 378.
10 Canniff JP, Harvey W, Harris M. Oral submucous fibrosis: its pathogenesis and management. *Brit Dent J* 1986; **160**: 429–34.
11 Su JP. Idiopathic scleroderma of the mouth. Report of three cases. *Arch Otolaryngol* 1954; **59**: 331–2.
12 Shiaw YY, Kwan HW. Submucous fibrosis in Taiwan. *Oral Surg* 1979; **47**: 453–7.
13 Balakrishnan V, Narendranathan M, Moni VS. G.I. tract in submucous fibrosis. *J Asso Phys Ind* 1979; **27**: 429–31.
14 Maher R, Ahmed W, Qureshi H *et al.* Esophageal changes in oral submucous fibrosis using fibreoptic endoscopy—a pilot study. *J Pak Med Assoc* 1991; **41**: 312–3.
15 Mani NJ, Singh B. Studies on oral submucous fibrosis, III. Epithelial changes. *Oral Surg* 1976; **41**: 203–14.
16 Pindborg JJ, Murthi PR, Bhonsle RB *et al.* Oral submucous fibrosis as a precancerous condition. *Scand J Dent Res* 1984; **92**: 224–9.

