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Histopathological changes in oral mucosa due to takhzeen al-qat: a study of 70 biopsies

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BACKGROUND: Chewing qat leaves (takhzeen al-qat) is a common habit in East Africa and Yemen. It has been reported to cause different systemic effects. At the oral mucosa, it causes clinical changes that appear as white lesions. The aim of this paper was to study the histopathological changes in the oral mucosa related to takhzeen al-qat.

METHOD: Seventy biopsies were studied. Biopsies were divided into three groups: (G1) Forty biopsies were taken from the oral mucosa of the chewing side. (G2) Twenty biopsies were taken from the oral mucosa of the opposite side and (G3) 10 biopsies were taken from the oral mucosa of non-chewing volunteers. All biopsies were conventionally prepared, paraffin embedded and histopathological protocol was followed for each case to study the histopathological changes.

RESULTS: Acanthosis appeared in 97.5% (GI) and 50% (G2), parakeratosis in 45% (GI) and 0% (G2), orthokeratosis in 25% (GI) and 10% (G2), abnormal rete ridges in 97.5% (GI) and 25% (G2), intracellular edema in 80% (GI) and 65% (G2), inflammatory infiltration in the subjacent connective tissue of 55% (GI) and 5% (G2), increased amount of collagenous fibers in 47.5% (GI) and 0% (G2), and mild epithelial dysplasia in 25% (GI) and 0% (G2). Biopsies taken from G3 showed no histopathological changes except one case with intracellular edema. Differences were statistically significant.

CONCLUSION: Takhzeen al-qat caused histopathological changes in the oral mucosa at the side of chewing; however, these changes were innocuous and without any evidence of malignancy.

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Keywords: epithelial dysplasia; keratosis; oral white lesions; qat

Introduction

Qat belongs to the plant species Catha edulis Forskal of the family Celastraceae, which grows best in East Africa and south Arabia mainly in Yemen (1). Takhzeen al-qat (qat chewing) is a common habit among Yemenis. This habit involves picking tender leaves of qat, inserting them into one side of the mouth, chewing them for a while and storing them in the same side of the mouth. People chew gat to get psycho-stimulation effect in the form of euphoria and excitement because of cathinone contents (2). Tanic acid is another important ingredient of gat responsible for the local negative effects on gastro-intestinal tube (GIT) (3). Takhzeen al-qat showed adverse effects on the cardiovascular (4), genitourinary and reproductive (5, 6), and digestive systems (7-9). El-Gunaid et al. (10) reported no significant histopathological changes associated with regular daily qat chewing in the upper esophagus among Yemeni patients suffering from indigestion, however, mild abnormal growth of gastric mucosal cells (dysplasia) and abnormal intestinal cells (metaplasia) at the lower esophagus were relatively higher in gat chewers than in non-chewers. Another study demonstrated that tannins in gat increase the mucosal thickness of the oropharynx and the esophagus (11). The carcinogenic risk of takhzeen al-qat is not well established. Craddock (12) mentioned in his book on cancer of the esophagus that takhzeen al-qat may be carcinogenic.

A few studies of the effect of takhzeen al-qat on the oral cavity have been published. Stomatitis, pain at the site of chewing, stress and staining of teeth have been observed by some authors (7, 3) in persons who chew qat for a long period. Another clinical, but not histopathological, study reported some degree of keratosis without dysplasia or malignancy among qat chewers in Yemen (13).

In a recent research (14), takhzeen al-qat has also been reported to increase the risk of factors related to oral and para-oral lesions such as gingivitis, periodontal pocketing, gingival recession, tooth mobility and mortality, attrition, buccal and gingival white lesions,

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temporomandibular joint click and pain, mouth dryness and facial asymmetry. The same research also documented that takhzeen al-qat causes benign histopathological changes in the oral mucosa at the site of chewing.

Recently, oral keratotic white lesions were reported in 22.4% of 1528 Yemeni qat chewers (15). The aim of this paper was to study the histopathological changes in the oral mucosa caused by takhzeen al-qat among Yemenis.

Materials and methods

This study was carried out on 70 biopsies taken from the buccal mucosa of Yemeni individuals in the Department of Oral Pathology and Medicine during 2002–2003. Biopsies were divided into the following groups:

Group 1 (G1): forty biopsies taken from the oral mucosa at the chewing side of 40 individuals who chewed qat for at least 3 years. Mean age was 38.53 years (range 22–60, SD 13.13). Of them 35 were males and five females.

Group 2 (G2): twenty biopsies taken from the oral mucosa at the side opposite to the chewing in 20 G1 individuals. Mean age was 36.25 years (range 22–57, SD 11.60). Seventeen were males and three females.

Group 3 (G3): ten biopsies taken from the oral mucosa of 10 non-chewer healthy Yemeni volunteers. Mean age was 38.10 years (range 28–52, SD 8.33). Eight were males and two females.

Clinical information of each case has been collected. Cigarette smoking has been coded. Users of any other social habit such as shamma, tumbol, or mada'a were excluded.

Biopsy taking

Biopsies were taken from white lesions at sites most affected by chewing in G1, while biopsies in G2 were taken from similar oral mucosa at the opposite side. Biopsies of G3 were taken from similar oral mucosa of non-chewers. The process involved removal of a small piece of tissue (about $7 \times 5 \times 4$ mm) under local anesthesia using disposable blades and syringe needles. The injection for local anesthesia was injected far from the site of biopsy to avoid damage to the tissue. All specimens were removed with tissue forceps and immediately placed in a fixative container. The containers were wide-mouthed sterile glass containing 4% formalin and covered tightly with leak-proof caps. Each container was then labeled and sent to the oral histopathology laboratory for further processing.

Laboratory procedure

Each of the biopsies was formalin-fixed and processed according to routine histologic procedures. Hematoxylin and eosin (H&E)-stained sections were evaluated by light microscopy according to a pre-designed clinicopathological protocol that contains the following: orthokeratosis, parakeratosis, acanthosis, abnormal rete ridges, intracellular edema, epithelial dysplasia (absence, mild, moderate and severe), inflammatory cell infiltration in the subjacent connective tissue and the increased amount of collagenous fibers.

Statistical analysis

Data obtained in this study were analyzed using SPSS, PC Statistical Package. Statistical analysis was performed with chi-square test. *P*-value < 0.05 and CI at 95% were considered statistically significant. However, when an expected cell value in chi-square is < 5, Fisher test was used.

Results

Results are displayed in Tables 1 and 2. Our results showed clear histopathological changes in biopsies taken from the oral mucosa at the side of chewing (G1). All biopsies taken from the oral mucosa of non-chewing individuals were normal except one, which showed mild intracellular edema. The histopathological differences between G1 and G2, and between G1 and G3 were statistically significant (P < 0.002).

In relation to smoking, 17 and 11 cases were smokers in G1 and G2, respectively. There were no differences in the histopathological changes between biopsies taken from the oral mucosa of smokers and non-smokers among G1 and G2 (Table 2). These differences were statistically not significant (P > 0.05).

Table 1Histopathological differences between biopsies in groups 1, 2and 3

	G1 (n = 40) (%)	G2 (n = 20) (%)	G3 (n = 10) (%)
Acanthosis	39 (97.5)	10 (50)	0 (0)
Orthokeratosis	10 (25)	2 (10)	0 (0)
Parakeratosis	18 (45)	0 (0)	0 (0)
Abnormal ret ridges	39 (97.5)	5 (25)	0 (0)
Epithelial dysplasia	10 (25)	0 (0)	0 (0)
Intracellular edema	32 (80)	13 (65)	1 (10)
Inflammatory infiltration ^a	22 (55)	1 (5)	0 (0)
Increase amount of collagen fibers	19 (47)	0 (0)	0 (0)

^aThe inflammatory cell infiltration was in the subjacent connective tissue.

Table 2 Histopathological differences between smokers and non-smokers in G1 and G2 $\,$

	G1 (n = 40)		G2 (n = 20)	
	Smoker [n = 17] (%)	Non-smoker [n = 23] (%)	Smoker [n = 11] (%)	Non-smoker [n = 9] (%)
Acanthosis	16 (94)	23 (100)	4 (36)	6 (67)
Orthokeratosis	4 (23.5)	6 (26)	2 (18)	0 (0)
Parakeratosis	9 (25.9)	9 (39)	2 (18)	0 (0)
Abnormal ret ridges	16 (94)	23 (100)	5 (45)	0 (0)
Epithelial dysplasia	5 (29.4)	5 (21.7)	0 (0)	0 (0)
Intracellular edema	15 (88)	17 (74)	6 (54)	7 (78)
Inflammatory infiltration ^a	10 (59)	12 (52)	1 (9)	0 (0)
Increase amount of collagen fibers	8 (47)	11 (47.8)	0 (0)	0 (0)

^aThe inflammatory cell infiltration was in the subjacent connective tissue.

Discussion

To our knowledge, no study has investigated the histopathological changes of the oral mucosa in relation to takhzeen al-qat. The clinical changes caused by takhzeen al-qat at the side of chewing, which have been reported recently (15), encouraged us to study the histopathological changes in the oral mucosa of qat chewers.

The histopathological differences found in this study are in agreement with the clinical differences reported before (15) and with a study carried out on the GIT, which documented that qat contents increase the mucosal thickness of the oropharynx and the esophagus (11). Our results show that white lesions appeared clinically on the oral mucosa of qat chewers might be histopathologically because of the increase in the epithelial thickness with keratosis (Fig. 1) or intracellular edema (Figs 2 and 3).

The mechanism by which takhzeen al-qat induced these histopathological changes might probably be due to the chronic mechanical friction of qat fibers on the oral mucosa. A similar mechanism explaining oral white lesions induced by traumatic focal 'frictional' hyperkeratosis has been reported (16). Chemical components of qat and/or pesticides may also play a role in the etiology of these histopathological changes. Pesticides added to tobacco plants are documented as a cause of similar histopathological changes in the oral mucosa (17).

The explanation of some histopathological changes presented in biopsies taken from the opposite side (G2)

might be due to the chemical irritant action of qat components and/or pesticides added to the plant particularly in persons who chew a large amount of qat where a small quid of qat can easily move to the opposite side. The presence of intracellular edema in both sides is an additional explanation for the chemical etiology (Figs 2 and 3).

Smoking has been documented to develop similar histopathological changes in the oral mucosa (17, 18). However, the histopathological changes in our study were related to takhzeen al-qat and not to smoking as these changes were located on the side of chewing while changes related to smoking may appear anywhere in the oral cavity. Moreover, differences in histopathological changes between chewers smokers and chewers nonsmokers were statistically not significant. On the contrary, when we remove the confounding factor 'smoking' the risk remains.

Epithelial dysplasia (Fig. 4) was detected in 10 biopsies. All were of mild grade and only from the side of chewing G1 (25%, n = 40). However, mild-grade epithelial dysplasia is not considered as a marker of malignant transformation in contrast to moderate and severe grades (19–21). These alterations might from part of the frictional or hyperplastic changes (e.g. acanthosis and abnormal rete ridges). In our opinion takhzeen al-qat is less likely to induce pre-malignant or malignant lesions. Our histopathological finding was in agreement

Figure 2 Microphotograph showing acanthosis, abnormal rete ridges, epithelial dysplasia and intracellular edema in the buccal mucosa at the chewing side (H&E; \times 10).



Figure 1 Magnified microphotograph showing the intracellular edema (H&E; $\times 40).$





Figure 3 Microphotograph showing acanthosis, abnormal rete ridges with thick orthokeratinization in the buccal mucosa at the chewing side (H&E; \times 10).



Figure 4 Magnified microphotograph showing dysplastic epithelium with increase amount of collagenous fibers in the subjacent corium (H&E; $\times 25$).

with previous clinical studies that could not detect any aggressive white lesions caused by takhzeen al-qat (13, 15). Furthermore, the prevalence of oral cancer in Yemen is not as in other parts of the world (22) despite the practice of chewing qat.

In conclusion that takhzeen al-qat showed clear histopathological changes in biopsies taken from the oral mucosa at the side of chewing, and some of these changes may appear on the opposite side with low severity. These changes are secondary to frictional and/ or chemical pathogenesis and show minimal pre-malignant phenomena.

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