

## ORAL LICHENOID ULCERATIONS ASSOCIATED WITH *KHAT* (*CATHUS EDULIS*)

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إن مضغ القات المعروف بتأثيره المهديء عادة معروفة تاريخياً لدى شعوب شرق أفريقيا والجزء الجنوبي الغربي من شبه الجزيرة العربية، تم كشف حالتين من تقرح مخاطية الفم التالي لمضغ القات، وقد بينت الفحوص النسيجية للخزعات المأخوذة من المريضين تغيرات مجهرية نموذجية للحزاز المنبسط أو للانذفات الحزازية الدوائية. إن القات عبارة عن نبتة لا بدورها، نبتة محلية في أجزاء معينة في شرق أفريقيا والجزء الجنوبي الغربي لشبه الجزيرة العربية. الأوراق اليابسة من النبات هي المفضلة لأنها سهلة المضغ وأكثر فعالية. أثناء عملية المضغ تبقى الأوراق المصغرة في اللعاب والميزاب الحدي (الدلهيزي) حوالي 5 ساعات بينما تبتلع بقاياها، ونقل القات إلى أوروبا والولايات المتحدة.

إن عادة مضغ القات قادت إلى زيادة الاهتمام لمعرفة المواد الفعالة والتأثيرات الدوائية لها. لقد تم في مخبر العقاقير المهدئة التابعة للأمم المتحدة عزل الكاتينون (-) القلي من أوراق القات اليابسة. يتحول الكاتينون (-) إلى الأفيدين الكاذب (+) خلال مرحلة جفاف الأوراق.

لقد استنتج (هاك باك) أن تأثير القات يعود بشكل رئيسي إلى الترابط الشديد لجزيئات مركبات نبات القات. التأثيرات النفسية، القلبية، الهضمية، وإضافة إلى تأثيرات أخرى أصبحت معروفة بشكل واضح. ظهرت بعض إصابات التهابات الفم المزمنة لدى بعض مستعملي القات. والدراسة التالية توضح تأثيرات فموية أخرى لمرضى يعينين بعد الاستعمال الطويل للقات حيث ظهرت تقرحات فموية منتشرة مع بعض مناطق فرط التقرن. النتائج المجهرية للفحوص النسيجية لم تتوافق مع الدلائل التشخيصية للحزاز المنبسط المحددة من قبل (أيزبرغ).

في كلتا الحالتين لم تقتصر الرشاحة الالتهابية على البشرة بل امتدت وذلك بخلاف الحزاز الكلاسيكي. إذ لوحظت جريبات ممتدة في عمق النسيج الضام.

لقد اعتبر التدخين ومعالجة التهاب المفصل شبه الرثوي بالبرودة من العوامل المساعدة للانذفات النسيجية الحزازية علماً بأن واحد من المرضى المشمولين في هذه الدراسة أعطى قصة التهاب مفصل شبه رثوي لكن دون تلقي أية معالجة دوائية.

لقد لاحظ (نيومن جونس) كثرة الإصابات بالحزاز المنبسط من النموذج المسطح في المدخنين وقد أوضح أحد المرضى لدينا أنه كان يدخن لكنه امتنع عن هذه العادة بحوالي عام قبل حدوث الانذفات الحزازية داخل الفم. مع أن الانذفات تعتبر كتأثير جانبي لكثير من الأدوية ولكن لم يؤكد حدوث مثلها مع القات. لقد أثبتت بعض الدراسات حدوث آفات تشبه الحزاز المنبسط في المخاطية الدهليزية لدى الشعوب الهندية التي تمضغ جوزة الطيب. لوحظت أن الآفات المخاطية الفموية مجاورة للميزاب الدهليزي حيث توضع اللقافة (لقافة الطيب). ويتصف ارتكاس النسيج المخاطي في خلايا البشرة القاعدية مرافقاً بارتشاحات خلوية وحيدة النوى في طبقة النسيج الضام السطحية للطبقة المخاطية ولا تزال حتى الآن آلية التخرب هذه مجهولة الأسباب. لقد بينت الدراسات الحديثة حدوث ارتكاسات مناعية خلوية نتيجة للتغيرات في خلايا البشرة المخاطية أو الجلدية.

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إن التغيرات الحاصلة في خلايا البشرة المخاطية أو الجلدية تلعب دور المحرض المناعي حيث تثير ارتكاس مناعي خلوي وسبب هذه التغيرات يعزى إلى أسباب عديدة تغيرات فيزيائية وكيميائية، دوائية أطعمة وحتى بعض الجراثيم. والتغيرات الكيميائية الحيوية للبشرة والعوامل الوراثية يمكن أن تجعل الفرد مؤهلاً لمثل هذه التغيرات المخاطية السابقة الذكر وذلك استجابة للمحرضات المذكورة أعلاه. كثير من المواد الكيميائية اعتبرت كعوامل للتقرحات شبه الحزازية وعلى حسب معلوماتنا فهذا أول بحث يظهر العلاقة بين القات والتقرحات الحزازية للمخاطية الفموية.

The habit of chewing *khat* (*Catha edulis*) for its euphoric effect has been historically limited to east Africa and southwestern Arabian Peninsula. Two cases of severe oral mucosal ulcerations which occurred after chewing *khat* are reported. The histopathological examinations of specimens from both patients revealed microscopic features which were considered as a typical lichen planus or lichenoid drug eruption.

### Introduction

*Khat* (*Catha edulis*), a seedless plant, is indigenous and limited to certain parts of east Africa and the southwestern Arabian Peninsula. The young leaves of the plant are most favored because they are more potent and tender to chew.<sup>1</sup> The masticated leaves are stored in the buccal sulcus for about five hours during each chewing session and the saliva, and leaf extracts are usually swallowed.<sup>2</sup>

Recent improvement in air transportation to these areas has resulted in shipment of the plant to Europe and the United States.<sup>3</sup> The growing habit of chewing *khat* has motivated an interest to further the knowledge on its active ingredients and pharmacological effects. The United Nations narcotics laboratory isolated an alkaloid (-) cathinone from young *khat* leaves. The (-) cathinone is transformed into (+) pseudoephedrine during wilting of the leaves.<sup>3</sup>

Halback<sup>4</sup> reviewed the clinical and pharmacological actions of *khat* and concluded that the effects were mainly due to the sympathomimetic ingredients of the plant. The psychotropic, cardiac, gastric and other<sup>1,3,4</sup> Chronic stomatitis has been observed in some *khat* users.<sup>1,2</sup> This paper reports additional oral findings in two Yemeni nationals after prolonged use of *khat*.

### Case Reports

#### Case 1

A 28-year-old Yemeni national presented to the Oral Medicine Clinic, College of Dentistry, King Saud University, Riyadh in April 1984. His chief complaint was painful intraoral sores which he

had noticed in 1982 when he resumed chewing *khat* during a visit to his home country. He had used *khat* for 10 years prior to moving to Saudi Arabia wherein he stopped the habit. He was a smoker (20 sticks/day) but quit the habit one year before the onset of painful oral ulcers.

Oral examination showed a network of lacy white lines bilaterally on the buccal mucosa. At the center of the lacy network were deep ulcers covered with yellowish pseudomembrane about 1 cm at greatest dimension [Fig. 1]. The dorsum of the tongue showed multiple white round hyperkeratotic patches [Fig. 2]. Similar white patches were observed on the lateral and ventral aspects of the tongue.

Histological examination revealed hyperkeratinized stratified squamous epithelium, which is variably hyperplastic, atrophic and



Figure 1. Clinical photograph of Case 1 showing raised white keratotic lines that surrounds painful ulcers distributed bilaterally on the buccal mucosa.

ulcerated. The epithelium has saw-tooth rete-bridge morphology with liquefaction degeneration of the basal cell layer [Fig. 3]. The underlying connective tissue contained dense chronic



Figure 2. Clinical photograph of Case 1 showing white keratotic patches on the dorsum of the tongue.

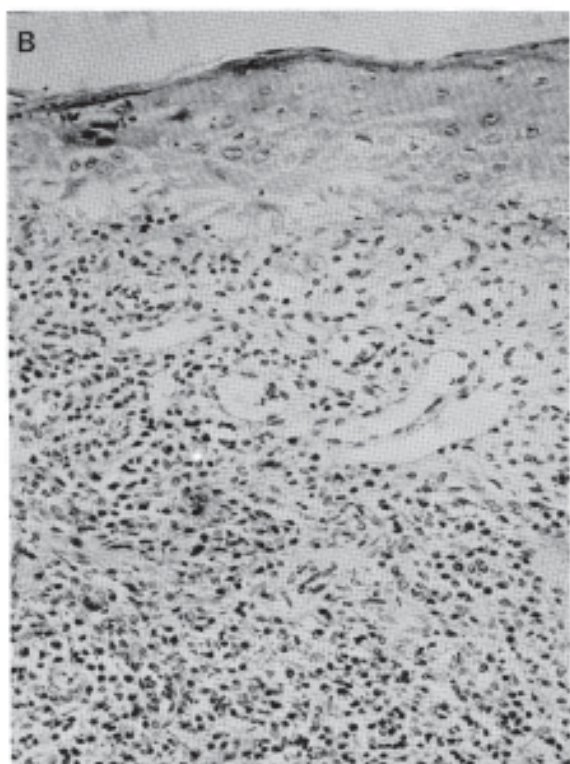


Figure 3. Photomicrograph of the biopsied specimen (Case 1) from Fig. 1 showing atrophic epithelium, early liquefaction degeneration of the basal layer and intense lymphocytic cell infiltrate in the lamina propria. Lymphoid follicle (arrows) is present in the submucosa. (Hematoxylin-eosin stain; original magnifications  $\times 100$ ).

inflammatory cell infiltrate consisting predominantly of lymphocytes. The inflammatory cell infiltrate was rather diffuse and was not closely related to the epithelium. Aggregation of lymphocytes into follicles were observed within the inflammatory cell infiltrate. A mixed inflammatory cell infiltrate, consisting of polymorpho-nuclear leukocytes and lymphocytes, was seen in areas of the connective tissue that lacked epithelium. An eosinophilic band is seen immediately below the epithelium. Histopathological appearance was consistent with lichen planus or a lichenoid drug eruption. The patient was advised to stop smoking and was started on 0.1 % triamcinolone acetamide ointment mixed with equal parts of orabase paste applied topically four times daily.<sup>5</sup> There was remarkable improvement after two weeks of treatment and complete resolution after five weeks.

## Case 2

A 36-year-old male patient from Taiz, Northern Yemen attended the Oral Medicine Clinic at the College of Dentistry, King Saud University with a chief complaint of a burning mouth sensation of 2 weeks duration. The patient gave a history of rheumatoid arthritis, muscle pain and occasional paraesthesia in both arms and legs. He started chewing *khat* since the age often but stopped the habit two weeks before he experienced the burning sensation in the oral cavity. Clinical examination revealed bilateral buccal mucosal ulcerations surrounded by erythematous areas and white keratotic lines. The mucosal ulcerations extended from the commissures of the mouth to the retromolar region [Fig. 4]. White keratotic plaques were seen on the dorsal and ventral aspects of the tongue, the soft palate and floor of the mouth; marginal gingiva was red and edematous. Histological evaluation of the specimen from the buccal mucosa showed relatively atrophic epithelium alternating with areas of complete lack of epithelium. Lymphocytes were evenly distributed with the atrophic epithelium. The epithelial connective tissue interface showed liquefaction degeneration and early vesicle formation. A band-like inflammatory infiltrate consisting predominantly of lymphocytes occupied the whole lamina propria [Fig. 5]. The patient was put on topical 0.1% triamcinolone acetamide in orabase paste applied four to five

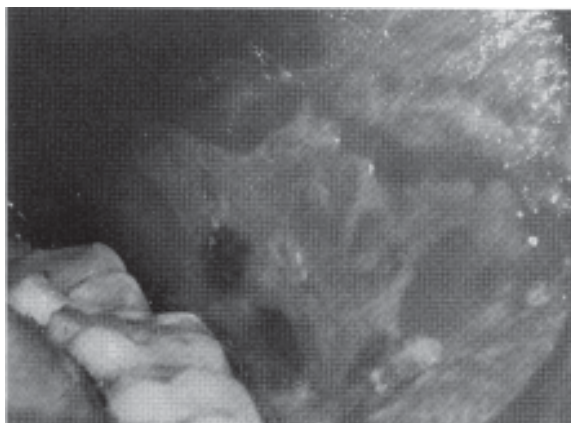


Figure 4, Clinical photograph of Case 2 showing atrophic mucosa with multiple ovoid to round ulcers bilaterally on the buccal mucosa.

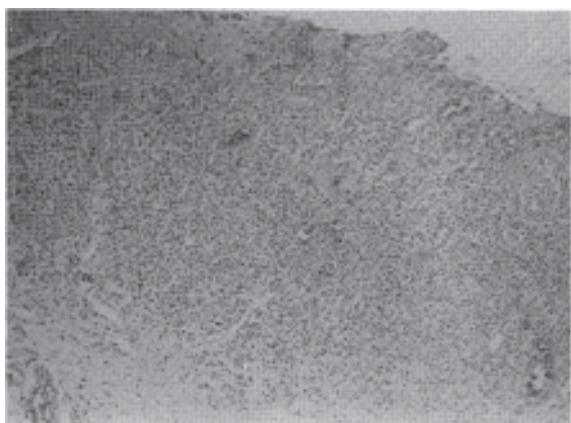


Figure 5. Photomicrograph of the biopsied specimen (Case 2) from Fig. 4 showing atrophic epithelium being replaced by eosinophilic material. Liquefaction degeneration of the basal cells lymphocytic infiltrate in the lamina propria are the main histopathological changes. (Hematoxylin-eosin stain; original magnifications (x40).

times daily. There was considerable improvement after four weeks of treatment, and patient was clear of any symptoms after a one-year follow up.

### Discussion

The active ingredients in *khat* identified to date include (-) cathinone, cathinine, cathidine, edulin and ephedrine.<sup>3</sup> The most important of these active ingredients, (-) cathinone, is present mainly in young leaves but it is rapidly transformed to norpseudoephedrine during wilting of the leaves.

Rapid transformation of the active ingredients might explain the special preference for the young leaves by *khat* users.

Stomatitis, esophagitis and gastritis have been reported as side effects of *khat*.<sup>4</sup> Luqman and Danowski,<sup>2</sup> observed generalized stomatitis among *khat* users, while Halbach<sup>2</sup> reported esophagitis and gastritis in addition to stomatitis. Luqman and Danowski<sup>2</sup> speculated that the concomitant smoking of tobacco, poor diet and vitamin deficiency may probably contribute to chronic irritation of the oral mucosa with subsequent superimposed infection. Hill and Gibson<sup>1</sup> observed low caries rate and inverse relationship between the periodontal pocket depth and the chewing side. They noticed some evidence of temporomandibular joint dysfunction and oral mucosa changes, such as hyperkeratosis and localized stomatitis.

The two cases presented in this report showed ex-tensive oral mucosal ulcerations with areas of hyperkeratosis. Histopathological features did not satisfy the criteria defined by Eisenberg and Krutchoff<sup>6</sup> for diagnosing lichen planus. The inflammatory infiltrate observed in both cases were rather diffused and not closely related to the epithelium as in classical lichen planus. Lymphoid follicle deep in the lamina propria was noticed in one case.

Cigarette smoking<sup>7,8,9</sup> and chrysotherapy for rheumatoid arthritis have been implicated as possible etiological agents of lichenoid tissue reaction.<sup>10,11</sup> Although one of our patients gave a history of rheumatoid arthritis, he did not report the use of any medications. Neumann-jensen *et al*<sup>9</sup> noticed a higher prevalence of plaque type of lichen planus in smokers compared to non-smokers. A history of smoking was given by one of our patients but he quit the habit one year prior to oral lichenoid eruptions.

Lichenoid drug reaction has been reported as a side effect of various drugs<sup>10,12</sup> but never in conjunction with *khat*. Daffary *et al*,<sup>13</sup> reported the occurrence of lichen planus-like lesions in the buccal mucosa of an Indian population that chewed betel nut. The oral mucosal lesions were observed adjacent to the vestibular sulcus where the betel-tobacco was inserted.

The lichenoid tissue reaction is characterized by epithelial basal cell damage that is intimately

associated with a massive infiltration of mononuclear cells in the upper connective tissue of the mucosa.<sup>10,14</sup> The mechanism by which this cell damage occurs is not known. Recent experimental evidence gave support to a localized cell mediated immune response to an induced antigenic alteration in epithelial or epidermal cells of the mucosa or skin with the basal epithelial or epidermal cells perceived as foreign, because of the altered surface antigenicity.

Such alteration may occur in response to many different insults, such as physical trauma, action of chemicals, drugs, foods or microorganisms. The biochemical alterations of the epithelium and genetic factors may render an individual susceptible to such mucosal changes in response to any of the above stimulus. Many chemicals have been implicated in the etiology of lichenoid ulcerations. To our knowledge, this report is the first observation of a possible linkage between *khat* (*Cathus edulis*) and lichenoid ulcerations of the oral mucosa.

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