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Review Article

Plasma Cell Stomatitis Associated With Khat (*Catha Edulis*): A Brief Review

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ABSTRACT

Plasma cell stomatitis (PCS), an uncommon condition, is characterized by massive and dense infiltration of plasma cells into the connective tissue. The etiology of PCS is unclear, but this condition is believed to be an immunological reaction to certain allergens present in chewing gum, flavoring mint, dentifrices and cinnamon flavoring products. Recently, plasma cell stomatitis has also been reported among habitual khat chewers. Khat, a psychostimulant herb, is cultivated and habitually chewed by millions of people in East Africa and the Arabian Peninsula as well as by immigrants in the west. This article aims to briefly review the current literature of the association of PCS with Khat use and to highlight the treatment approaches for such cases. A review of the literature using PUBMED and Google Scholar revealed ten cases of PCS linked to khat use, most of which were identified in Yemen, where khat chewing is highly prevalent. Interestingly, however, two of the ten cases were also reported in western countries; one was about Somali immigrant in the Denmark and the other was a Yemeni immigrant in the US. Treatment of Khat related-PCS includes cessation of the habit and oral hygiene prophylaxis. The rise of global immigration may potentially increase the incidence of PCS and other khat-related oral lesions worldwide. Therefore, recognition of this habit and its implications on oral health should be emphasized.

Keywords: Plasma cell stomatitis, Khat use, association.

INTRODUCTION

Plasma cell stomatitis/mucositis (PCS) is a rare benign condition characterized by prominent plasma cell infiltrate of the underlying lamina propria without evidence of malignancy, tuberculosis or candidal infection. [(1,2)] This rare condition is of unclear etiology and has been reported in the literature under various names such as oral plasma cell mucositis, [(3)] plasma cell gingivitis, [(4-7)] allergic gingivostomatitis,[(8)] atypical gingivostomatitis, [(9)] idiopathic gingivostomatitis, [(10)] and gingival plasmacytosis. [(11)] This condition is of chronic nature, and presents clinically as marked mucosal erosions and erythema, especially on the gingiva with or without ulceration. The lesions are usually

asymptomatic; however, patients may complain of pruritus, pain, burning sensation, discomfort, or in case of laryngeal involvement, dysphagia and/or hoarseness. [2,3] Histopathological, PCS is recognized mainly by a dense band like plasmacytic infiltrate in the connective tissue. [1]

The exact etiology of PCS is still unknown; it has been associated with many allergens such as chewing gum, mint, and toothpaste. [5,12,13] Recently, plasma cell mucositis has also been reported among habitual khat chewers. [3,14,15] Khat, also known as qat, Kat, and Miraa (Figure 1), is an evergreen plant (Catha edulis) that belongs to the Celastraceae family. [16] It is cultivated predominantly in East Africa and the Arabian Peninsula, where millions of local people habitually chew its fresh leaves and twigs for their stimulating amphetamine-like effects. [16,17] Many people from the region's diaspora communities living in Europe, USA, and Australia also chew Khat regularly. Khat is usually chewed at social gathering (the so-called Khat session) that lasts for several hours per day; khat chewing is mainly a male predominant habit, although the number of women indulging this habit is on the rise. Typically, this habit involves inserting and chewing a quantity of fresh khat leaves, forming bolus that is held in the buccal sulcus against the cheek on one side of the mouth while swallowing its juice. [18] Long-term khat chewing has many detrimental general health effects including cardiovascular disorders, cytotoxic effects on liver and kidneys, respiratory problems, mental illnesses and gastrointestinal disorders. [16] Oral conditions reportedly associated with khat chewing include, but not limited to, keratotic white lesions, hairy tongue, Xerostomia and periodontal diseases. [18-21] Moreover, recent studies have reported PCS in association with khat use. [3,14,15]

This habit is spreading beyond its original home in Yemen and Africa. Indeed the prevalence of khat use is raising globally due to the worldwide immigration from East Africa and the Middle East countries. In Europe and North America, khat is sold in restaurants and grocery stores to East African and Middle Eastern. [16] In this article, we briefly review the current literature regarding the association of PCS with Khat use, and also highlight the treatment approaches for such cases.

MATERIALS AND METHODS

The literature review was conducted using Medical Literature Analysis and Retrieval System Online (MEDLINE) database and the search engine PubMed. Moreover, Google Scholar was also used to search for any relevant publications. We used a combination of the following keywords: khat and plasma cell stomatitis; Khat and plasma cell mucositis; khat and plasma cell gingivitis; Qat and plasma cell gingivitis; Qat and plasma cell mucositis; Qat and plasma cell stomatitis.

Table 1: Summary of the 10 PCS cases reported in the literature

Reference	Age	Country*	symptoms	Location of lesions	Treatment
Marker and Krogdahl [15]	30	UK	Swelling	Gingiva, mucobuccal sulcus, cheek	Discontinuation of khat use
Rawal et al. [14]	40	USA	Pain, swelling, bleeding upon brushing and eating	Gingiva, buccal mucosa	Discontinuation of khat use, analgesics, Oral prophylaxis
Al-Akhali et al. [3]	32	Yemen	Pain, difficulty in swallowing, hoarseness	Gingiva, palate, tongue, larynx	Discontinuation of khat use
	20	Yemen	pain	Gingiva, palate	Discontinuation of khat use
	24	Yemen	Pain, swelling	Gingiva, lip	Discontinuation of khat use
	33	Yemen	Soreness, swelling	Gingiva, lips	Discontinuation of khat use
	24	Yemen	none	Gingiva, cheek	Discontinuation of khat use
	23	Yemen	pain	gingiva	Discontinuation of khat use
	29	Yemen	Pain and swelling	gingiva, lip, tongue, palate	Discontinuation of khat use
	22	Yemen	Pain, hoarseness and swallowing difficulty	Gingiva, tongue, buccal mucosa, lip, larynx	Discontinuation of khat use

*The country where the PMS cases were reported

The search revealed 10 cases of plasma cell stomatitis/gingivitis (PCS) associated with khat use, reported in 3 studies (Table 1). Of these, one patient was a Somali immigrant in the Denmark, one Yemeni immigrant in the USA, and the other 8 cases were reported in Yemen.

Figure 1: Khat leaves

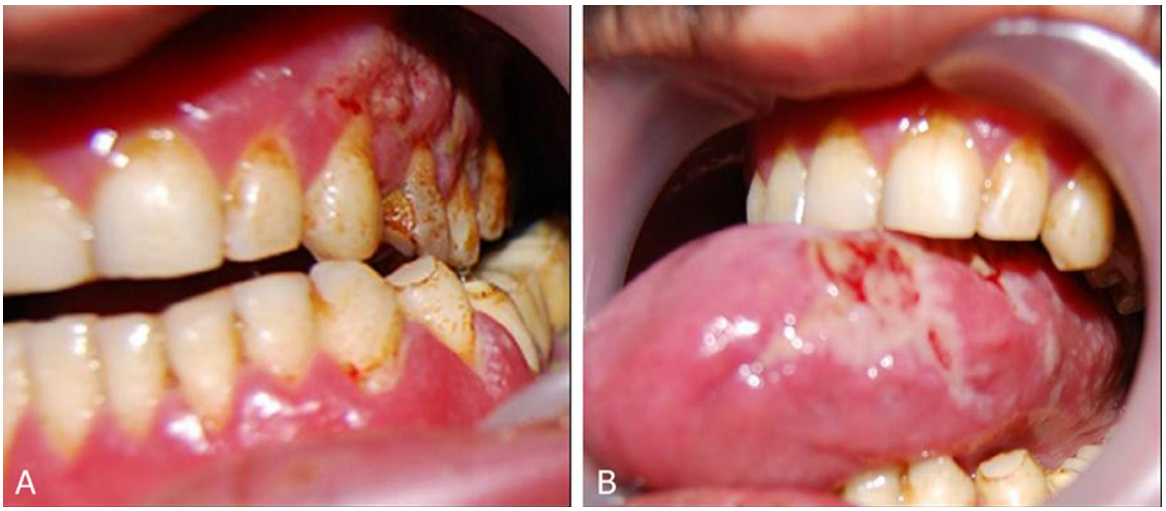

Figure 2: Plasma cell gingivitis affecting gingiva and tongue. A: Edematous and erythematous gingiva with some erosions. (B) Slight swelling and fibrin-covered ulceration on the lateral side of the tongue. This figure is adapted from Al-Akhali et al. (3)

DISCUSSION

PCS, an uncommon condition, is benign plasma cell proliferative disorder of the upper aerodigestive tract. Although the etiology of PCS is still unknown, some authors propose that the prominent presence of plasma cells suggests an allergic reaction that is associated with certain components in toothpastes, mint pastel and food stuff. [4,12,13] Nevertheless, in some cases no agent could be identified and thus considered idiopathic. Interestingly, some recent reports have also linked PCS to Khat leaves. [3,14,15]

A summary of the 10 khat-related PCG cases reported in the literature is presented in Table 1. The age of patients was in the range of 20-40 years, with an average age of 30 years. All patients were young males. Among the reported cases, one was a Yemeni immigrant in USA and the other was a Somali immigrant in the Denmark. All remaining cases reported young adults in Yemen. All of these patients were long-term regular khat chewers, who reported having the daily habit for several years. In 2002, Marker and Krogdahl [15] reported the first case of Khat -related PCS in a Somali immigrant in the Denmark. The 30-year old male patient was referred to department of oral and Maxillofacial surgery by his dental surgeon for gingivitis-like changes in the buccal gingiva that was refractory to the conventional periodontal treatment. The authors reported that lesions were mainly located on the left side of the mouth, mainly on mandibular gingiva and buccal mucosa at the site of khat placement. The gingiva was described as intensely erythematous and swollen with the presence of fibrin clot. The sulcus and the buccal

mucosa in the same side were also similarly affected. The histological analysis showed infiltration of polyclonal plasma cells. Based on the history of habitual khat chewing as well as histopathological and clinical findings, the authors concluded that the final diagnosis was PCS with allergic reaction. [15]

The second case reported a Yemeni immigrant in the USA. The 40-year old male presented with the complaint of pain, swelling and extreme redness of the left buccal gingiva. The clinical features and histopathological findings were identical to the above mentioned case. Likewise, the patient admitted that he always placed the khat in the left buccal mucosa. Therefore, authors of this case also made a final diagnosis of PCS. [14]

In 2014 Al-Khali and colleagues [3] reported the largest series of khat-related PCS. The authors reported 8 cases of PCS among Yemeni young adults who presented with different complaints to department of periodontology, Sana'a University. Similar to the previous two cases, Al-Akhali et al. reported the typical features of edematous and erythematous gingiva with velvety surface accompanied with the involvement of the adjacent buccal mucosa at the site of khat chewing. Interestingly, however, the involvement of other parts of the mouth such as the tongue, palate, lips was evident in most of these cases (Figure 2). Moreover, hoarseness, a sign of laryngeal involvement that has rarely been reported in the literature, was noted in two cases. [3]

Some authors have categorized PCS into three subgroups: 1) caused by allergen, 2) neoplastic, 3) unknown cause. [13,22] As the changes and symptoms had developed after prolonged use of khat, PCS cases discussed in this review seems to fall in the first group. This is compatible to PMS caused by herbal toothpaste or other allergens. As noted above, all of the 10 patients were regular khat chewers, who consumed khat for long time; and none of patients reported using any allergen known to be related to PCS. Some of the reported PMS cases (cases associated with herbal toothpaste and other allergens) were observed mostly in the anterior gingiva, more frequently on the maxilla. By contrast, in khat-related PCS, the changes were more prominent on the facial posterior gingiva involving the mucobuccal sulcus and the adjacent buccal mucosa and to lesser extent, some parts of tongue, palate and lip. This can be explained by the direct contact with the allergen (Khat), which is usually placed on the mucobuccal sulcus, usually unilaterally, where it is held for several hours in direct contact with the gingiva and buccal mucosa. Moreover, in the above mentioned cases, the cessation of khat chewing brought about remission or significant improvement within days. This indicates clearly that the erythema of the gingiva and other parts of the mucosa was mainly associated with khat use. It has been reported in the literature that PCS has slight male predominance of 1.2-1. [2] Interestingly, however, all khat-related PMS cases were reported among males. This can be explained by the fact that khat habit is a predominantly men habit, rather than a gender-related lesion. Moreover, compared to females, Khat is more frequently consumed and for longer hours among males. [18]

Khat chewing is associated with several oral and dental adverse effects. It has been associated with white keratotic lesions, mucosal pigmentation, hairy tongue, poor oral hygiene, teeth discoloration and Xerostomia. [17,18,23,24] Several studies have evaluated the association between khat use and gingival and periodontal diseases; most studies found a positive association [20,21,25] while a few did not. [26] Khat contains several various chemical constituents including psychoactive substances cathinone and cathine, alkaloids, carbohydrates, tannic acid, and other substances. [16] It is assumed that tannic acid is responsible for induced stomatitis among some of khat chewers.

In addition to history taking as well as clinical and histological findings, the

diagnosis of PCS requires hematological analyses to exclude leukemia. Further serological investigations are also needed to exclude similarly - appearing connective tissue disorder like lupus erythematous. Other possible clinical differential diagnosis of PCS includes lichen planus, mucous membrane Pemphigoid, pemphigus, plaque-induced gingivitis, erythroplasia, sarcoidosis and Wegner's granulomatosis [(2)] Histopathological findings (plasma cell infiltrate) should be differentiated from other more serious disorders such as plasmacytoma and multiple myeloma. [(2,5)]

Management of PCS in general is aimed to alleviate related symptoms. PCS is a benign condition with fairly well prognosis, and progression to more serious conditions such as plasma cell neoplasm or lymphoma has never been reported in the literature. Generally, removal of the offending allergen i.e. cessation of khat chewing habit in case of khat-related PCS results in improvement of the case with possible complete resolution. Furthermore, removal of other local aggravating factors such as plaque and calculus is also crucial. Topical anti-inflammatory medications such as corticosteroids can be used in severe cases to accelerate healing.

CONCLUSIONS

There is an association between Khat chewing and PCS. Given the fact that khat chewing habit is increasing worldwide with global immigration from countries of high use (East Africa and the Middle East), it is becoming more likely that khat-related oral lesions including PCS will be seen throughout the world. It is therefore imperative that general dental practitioners, periodontists and oral medicine specialists, especially those in the new world should be aware of this habit and its association with PCS and other oral complications.

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