Oral changes associated with kolanut use: a report of 2 cases

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Introduction. Contact stomatitis (CS) is an inflammatory reaction of the oral mucosa induced by contact with an irritant, such as menthol and cinnamon compounds. We are reporting 2 cases of CS related to the use of kolanut, a caffeine-containing nut of evergreen trees.

Case Description. Case 1 was a 22-year-old man with history of chewing kolanut for the past 10 years; he presented with a grayish-white, velvety, leukoplakia-like plaque with ill-defined borders in the mandibular anterior facial vestibule and extending to the lower labial mucosa. The patient had never consumed tobacco products or alcohol before. Histopathologic analysis revealed hyperparakeratosis with otherwise normal epithelium. The patient continued kolanut consumption with persistent oral changes. Case 2 was a 29-year-old man with history of chewing kolanut for the past 2 years; he presented with extensive, diffuse, white, leukoplakia-like plaques on the anterior maxillary and all mandibular gingiva and vestibule, with epithelial desquamation and erosive patches. The patient reported smoking 30 cigarettes per day for the last 11 year. Following cessation of kolanut use, the leukoplakia-like lesion resolved with persistent erythema.

Conclusions. This is the first report of histopathologic characterization of CS associated with the use of kolanut, which is believed to be reactive in nature with unknown premalignant potential. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130:e5–e9)

Contact stomatitis (CS) is an inflammatory reaction of the oral mucosa induced by contact with an irritant or allergen.[1] Several agents, such as food and toothpastes additives, cinnamon flavoring agents, dental alloys, composite and amalgam restorations, have been reported to be associated with CS.[2-4] Moreover, smokeless tobacco is a known CS irritant with premalignant potential in the oral mucosa.[5] This includes, but is not limited to, chewing tobacco, dry and moist snuff, gutka, betel quid with tobacco, snus, toombac, and iqmik, and tobacco lozenges.[6] The clinical features of CS include whitish or erythematous plaques, vesiculation and/or ulceration associated with pain, burning sensation, and itching, or it is often asymptomatic at the contact site.[5] Histologically, CS may present as variable forms of hyperkeratosis, depending on the type of irritant, epithelial hyperplasia, intracellular edema, and/or infiltration of inflammatory cells.[1,5] For management, removal of the offending agent will likely result in resolution of CS. In selected cases, topical corticosteroid may be indicated to expedite the healing process.[5]

Kolanut is the seed kernel of a large African tree grown commercially around the world, particularly in Nigeria, Sri Lanka, Indonesia, and Brazil and other parts of South America. It can be divided into several types based on the number of cotyledons, with *Cola acuminate* (oji Igbo) and *Cola nitida* (goro) being the most popular among users (Figure 1). Historically, consumption of kolanut has been a popular habit in African communities, where it is served in ceremonies and social and ritual events. In addition, it is used by laborers, students, and long-distant drivers to help cope with hunger and fatigue and to suppress sleep craving.[7] Kolanut users usually tend to chew it and then pack it in the buccal vestibule to slowly release its juices for maximum effect. Until now, the short- and long-term effects of kolanut on the oral cavity remain unknown.

We are reporting the cases of 2 patients who had a history of kolanut consumption and developed unique mucosal CS. To our knowledge, this is the first report to include histopathologic characterization of oral changes associated with kolanut chewing.

CASE DESCRIPTION

Case 1

A 22-year-old man attended the dental clinic at the King Abdulaziz University - Faculty of Dentistry (KAUFD), King Abdulaziz University (Jeddah, Saudi Arabia), for dental evaluation. The patient had no significant medical history and denied taking any medication or having any known allergies. In addition, he had no significant family history and had never smoked or consumed any tobacco products or alcohol before. Upon further history taking, the patient reported chewing on *C. nitida* (goro) five times per day for the past 10 years. No significant findings were noted on extraoral examination. However, intraoral examination was significant for a grayish-white, velvety, folded, leukoplakia-like plaque with ill-defined borders (2 × 3 cm)

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Received for publication Mar 7, 2020; returned for revision Mar 28, 2020; accepted for publication Apr 4, 2020.

2212-4403/$-see front matter
https://doi.org/10.1016/j.oooo.2020.04.004

Fig. 1. *Cola nitida* (goro) fruit with 2 cotyledons, ready to use.

and extending from the mandibular buccal attached gingiva of the anterior teeth into the vestibule and lower labial mucosa where *C. nitida* was typically packed (Figure 2). To confirm the diagnosis, a 4-mm punch biopsy specimen was obtained from the center of the plaque lesion and sent for histopathologic analysis, which showed hyperparakeratosis without dysplastic changes within the epithelium. The connective tissue was fibrovascular, with no inflammation or hyalinization (Figure 3). The case was managed with patient education and advice to discontinue consumption of *C. nitida* until further data on its effect on the oral mucosa could be obtained. The patient was followed up for 1 year, during which time, the patient continued to use *C. nitida*, and the associated oral changes persisted.

Case 2

A 29-year-old man attended the dental clinic at the KAUFD, King Abdulaziz University (Jeddah, Saudi Arabia) for dental evaluation. The patient had no significant medical history and denied taking any medication or having any known allergies. In addition, he had no significant family history. However, he had been smoking 30 cigarettes per day for the last 11 years. In addition, he reported having consumed different smokeless tobacco products but quitting the habit 10 years ago. He also had been chewing on *C. nitida* for the past 2 years once daily. Extraoral examination was insignificant. Intraoral examination was significant for extensive, diffuse, white, leukoplakia-like plaques of the anterior maxillary and all mandibular gingiva and vestibule, with epithelial desquamation and erosive patches (Figure 4). The patient declined obtaining a biopsy for further investigation. The case was managed with patient education and advice to discontinue consumption of *C. nitida*, similar to case 1. Three months after the consultation visit, the leukoplakia-like lesion had resolved completely after cessation of *C. nitida* use, but the erythema persisted (Figure 5).

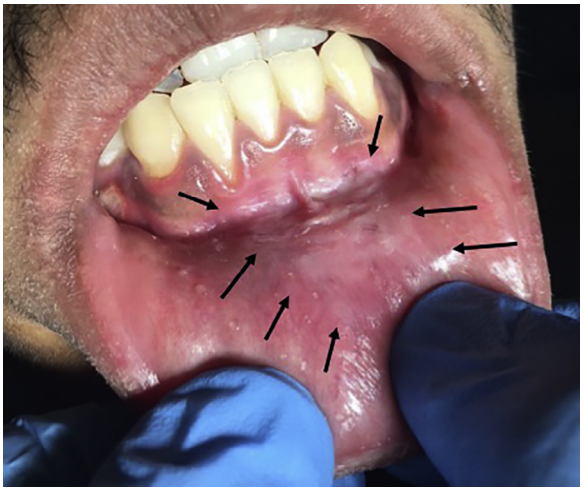

Fig. 2. A grayish-white, velvety, folded, leukoplakia-like plaque with ill-defined borders (2 × 3 cm) extending from the mandibular buccal attached gingiva of anterior teeth into the vestibule and extending to the lower labial mucosa of Case 1 *(black arrows)*.

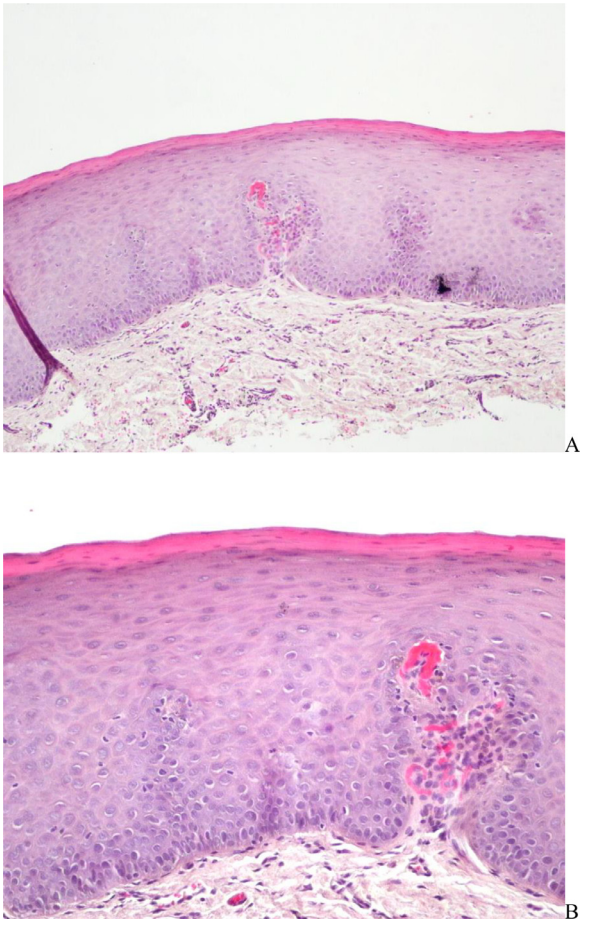

Fig. 3. Histopathologic characterization of case 1 demonstrating hyperkeratosis and mild basal cell hyperplasia (hematoxylin-eosin stain, original magnification ×10 [A] and ×20 [B]).

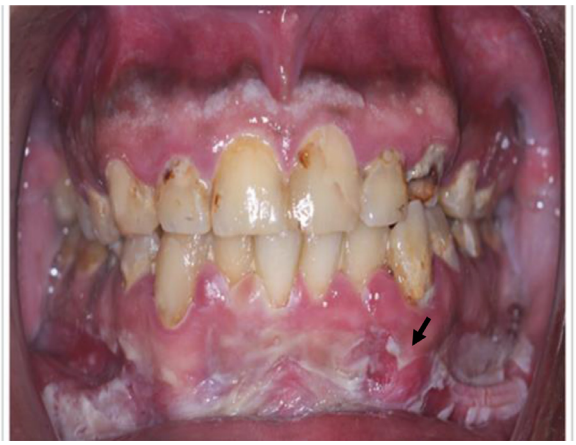

Fig. 4. Clinical presentation of case 2 demonstrating hyperkeratotic changes of the anterior maxillary buccal gingiva and all of the mandibular buccal vestibule, with epithelial desquamation and erosive patches *(black arrow)*.

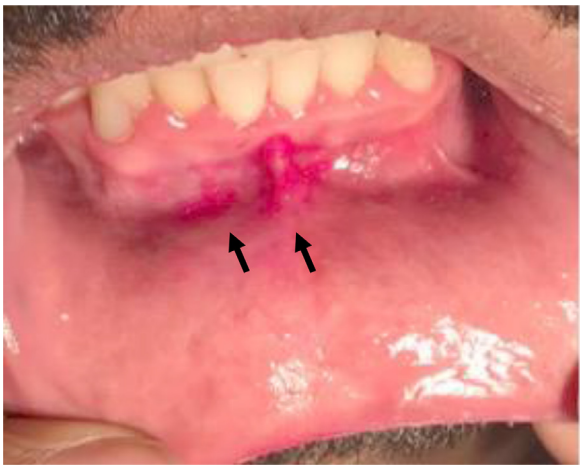

Fig. 5. Three-month follow-up time point for case 2 after kolanut cessation, demonstrating resolution of the white leukoplakia-like plaque but persistence of erythema of the lower labial mucosa *(black arrows)*.

DISCUSSION

Kolanut is a bitter-flavored fruit containing caffeine, theobromine, tannins, phenolics, phlobaphene, kola red, betaine, protein, starch, fat, thiamine, riboflavin, and niacin. Historically, kolanut was used by Asante army soldiers in the nineteenth century as a stimulant and to provide additional "strength" during battle.[8] In addition, kolanut extracts have been used in a herbal preparation for management for mental and physical fatigue.[9,10] This particular effect has been associated, for the most part, with kolanut's caffeine contents.[11,12] However, other contents have been suggested to play a role in boosting this effect on the human body. Theobromine, a compound in kolanut, belongs to the xanthine family and functions through inhibition of phosphodiesterase and increasing intracellular cyclic adenosine monophosphate levels. Similar to caffeine, theobromine is believed to stimulate the human nervous system and skeletal muscle.[13,14]

Other effects reported with kolanuts use include modification of body fat metabolism. A 6-month randomized, double-blinded, placebo-controlled trial examined the influence of herbal Ma Huang and kolanut on 167 patients and reported significant reduction in weight, fat, and low density lipoprotein (LDL) among participants.[15] Moreover, methanol extracted from kolanut was reported to have anti-inflammatory and analgesic effects through a cholinergic pathway.[16] In addition, in a study on rats, exposing the gastrointestinal muscles to kolanut methanol demonstrated antispasmolytic and antidiarrheal effects.[17] However, increased gastric secretions and irritation of surrounding tissues were reported as secondary adverse events.[18] Because of its potential benefits, the U.S. Food and Drug Administration has approved kolanut extract to be used as a safe and inactive ingredient in commercial foods and supplements.[19,20] As a result, public interest in kolanut has been on the rise, and it is marketed in different formulations, as supplement pills and as a flavoring agent in such items as hard and soft candies, alcoholic and nonalcoholic beverages, gelatin, and baked goods.[21,22]

Even with kolanut extract being safely used in the food industry with no reported adverse events, its topical effect on the oral mucosa is not fully understood. Both patients in the current report had a history of chewing kolanut and presented with asymptomatic, white keratotic plaques in the buccal vestibule, where kolanut used to be packed regularly. On the basis of the clinical presentation, these changes were consistent with CS in both cases. Similar hyperkeratotic changes have been reported previously by Odukoya et al., who believed that kolanut promotes keratinization of the palatal mucosa, as confirmed by cytology, mimicking the effect of tobacco-induced keratosis.[23] In general, patients with CS may present with localized pain, burning sensation, and itching or are often asymptomatic, as in the current cases. As of today, the specific component in kolanut contributing to mucosal irritation remains unclear. In addition, mechanical irritation of the oral mucosa by kolanut may have played a role in inducing the late hyperkeratotic effects. To our knowledge, this is the first report of CS-like mucosal lesions associated with kolanut consumption.

As part of the oral lesions workup, an incisional biopsy specimen was obtained from case 1. Histopathologic analysis showed epithelium with hyperparakeratosis, slight basal cell hyperplasia, and no inflammation in the connective tissue. To characterize kolanut mucosal changes, the histopathologic features were compared with those of other CS cases reported in the

literature. For instance, CS related to toothpaste use typically would show acanthosis, intracellular edema of the stratum spinosum, and hyperparakeratosis, with parts detached from the epithelium.[5] Furthermore, smokeless tobacco use generally demonstrates parakeratosis or orthokeratosis, with chevron-like wavy keratosis and acanthosis and little or no inflammation in the connective tissue.[5] The current case demonstrated a similar increase in keratinization potential and likely reactive basal cell changes without acanthosis or intracellular edema, which may justify categorizing kolanut changes under CS-like lesions.

Unlike smokeless tobacco, the malignant transformation potential of the oral lesions associated with kolanut use is not clear yet. As one of the kolanut contents, tannic acid has potential carcinogenic effects in the setting of chronic dietary consumption. It is a phenolic compound present in a large quantity in kolanut and has been reported to stimulate production of reactive oxygen intermediates and inflammatory gene expression.[24,25] In a retrospective study of patients with primary head and neck cancer in Nigeria, 34 of the 143 included patients reported a history of tobacco smoking, tobacco chewing, and alcohol use, in addition to kolanut chewing. The study outcome demonstrated kolanut use as the main risk factor associated with the development of squamous cell carcinoma (13 of 34; 38.2%), followed by tobacco use (11 of 34; 32.3%), and alcohol consumption (10 of 34; 29.4%).[26] A retrospective study in Maiduguri, Nigeria, reported 43 cases of intraoral carcinomas among all patients with head and neck carcinomas. Of all patients, 4 patients reported a history of chronic kolanut use.[27] In the current reported cases, no malignant transformation was noted for the whole follow-up duration.

CONCLUSIONS

Kolanut use is a common cultural practice among several communities around the world. Here, we have reported for the first time 2 cases with oral CS-like changes associated with *C. nitida* use, a subtype of kolanut. As of today, it is reasonable to believe that these changes are benign in nature, based on histopathologic analysis. However, the pathogenesis, long-term prognosis, and risk for malignant transformation of this entity has yet to be investigated. Longer follow-up of a larger group of patients is warranted to better understand any potential adverse effects of kolanut use and prognosis of oral changes.

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