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Case Report

Recurrent aphthous stomatitis treated with fucoidan

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ABSTRACT

Recurrent aphthous stomatitis (RAS) is a rather widespread oral ulcerative condition with an unclear etiology. The clinical characteristics of RAS have been defined and therapies include anesthetic gel, oral anti-inflammatory drugs, Vitamin B12 supplements and corticosteroid ointment used on the lips. However, these approaches have not been rigorously evaluated. Persistent and painful RAS was successfully treated with 4% Power Fucoidan Cream™ (PFC, Daiichi-Sangyo, Osaka, Japan) in two women. RAS was remarkably improved by PFC. Further clinical trials are needed to confirm the value and safety of topical PFC for treating RAS.

Keywords: Aphthous stomatitis, cream, fucoidan

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is a condition characterized by the eruption of painful ulcers varying between <1 mm and >1 cm on the mucous membranes of the mouth. The causes of RAS are multifactorial; thus, treatment needs to be based upon the cause. The treatment objectives are rapid pain management and suppression of the inflammatory response.

Corticosteroid ointment can reduce inflammation associated with RAS. Although corticosteroid ointment sometimes elicits side effects such as damaging of mucous membranes, changes in taste sensation, and secondary oral candidiasis.

Fucoidan is a sulfated fucose-rich polysaccharide that was isolated from brown algae by Kylin in 1918. Studies of the bioactivity and therapeutic value of fucoidan have recently found that this compound has antiviral, antibacterial, anticoagulant, and anti-tumoral bioactivities.[1,2]

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Siddhanta and Murthy[3] found that fucoidan had antitumor and anti-inflammatory effects. Aisa *et al.*[4] reported that fucoidan exerted anticancer effects against human lymphoma HS-Sultan cells. These findings indicate that fucoidan may become important as an anti-viral medication and as therapy against various types of cancer. Power Fucoidan Cream™ (PFC, Daiichi-Sangyo, Osaka, Japan) isolated from *Nemacystus decipiens*[5] has been prepared as a cream consisting of 4% fucoidan in a base comprising stearic acid glyceryl, lectin, adenosine triphosphate, sodium alginate, and other components that enhance permeability [Figure 1].

Although the medical uses of fucoidan have been investigated from the viewpoints of cosmetics or bioactive agents, only a few studies have focused on oral diseases. Thus, we used PFC to treat the 39- and 27-year-old women with symptomatic RAS that caused pain upon eating and speaking and was refractory to various medications. The outcome of

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topical PFC application was remarkable. This is the first report of treating symptomatic RAS with PFC.

CASE REPORTS

Case 1

A 39-year-old Japanese woman presented with painful RAS had less than 1 cm diameter, single, round, regular margins, and gray base ulcer on the surface of the lower lip that had persisted for 2 months [Figure 2a and b]. In spite of this, her lifestyle was quite normal, a nonsmoker, and had no systemic diseases, she was unresponsive to corticosteroid ointment (triamcinolone acetonide) and nonsteroidal anti-inflammatory drugs (NSAIDs). We prescribed PFC twice daily for 1 week, which significantly improved the RAS [Figure 2c] without side effects and recurrence over 3 months of follow-up [Figure 2d].

Figure 1: Power fucoidan cream™

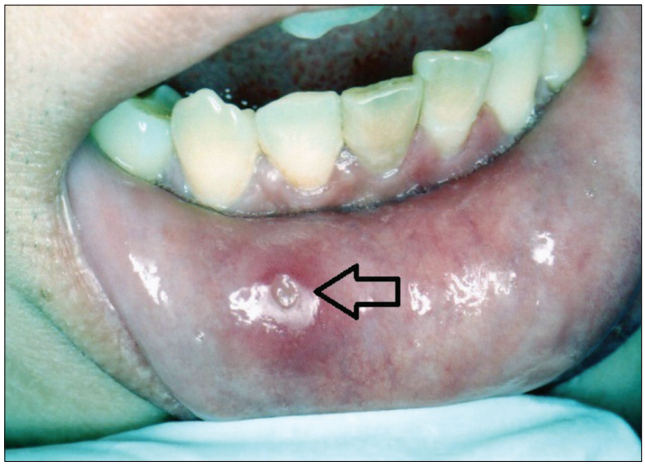

Figure 2a: Before power fucoidan cream™ therapy

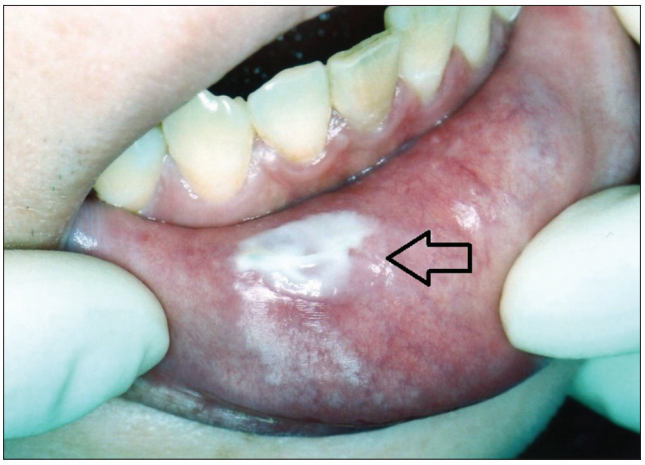

Figure 2b: During power fucoidan cream™ therapy

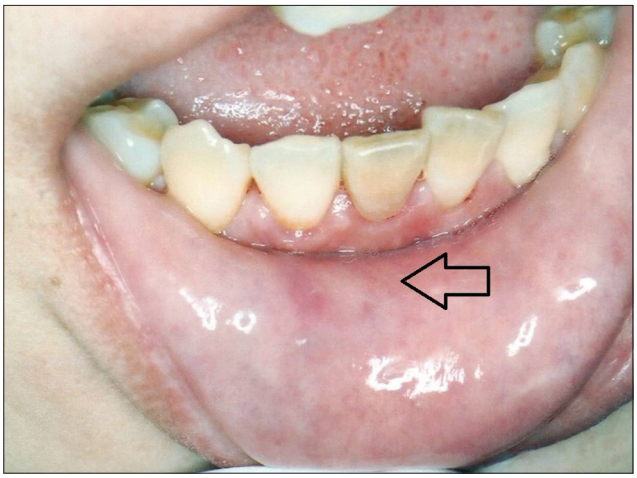

Figure 2c: One week after treatment

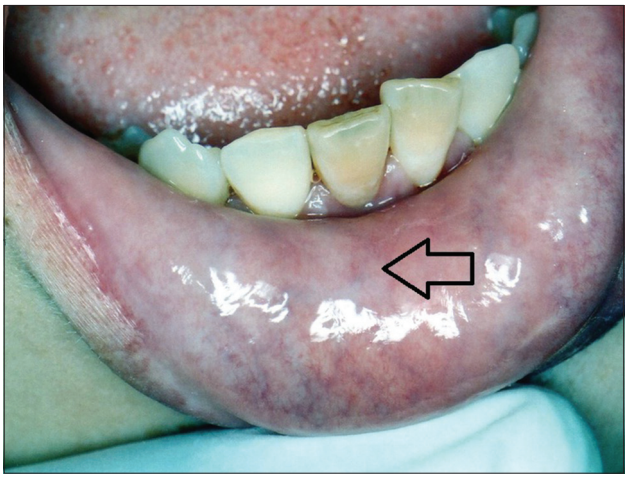

Figure 2d: Three months later

Case 2

A 27-year-old Japanese woman presented with painful RAS had less than 3 mm diameter, single, round, regular margins, and gray base ulcer that had persisted for 3 months on the commissura labiorum [Figure 3a and b]. In spite of this, her lifestyle was quite normal, RAS had appeared intermittently over the past 5 years and had caused pain in the lips and tongue, as well as the buccal and alveolar mucosa. These symptoms were unresponsive to corticosteroid (triamcinolone acetonide) ointment,

anesthetic gel (lidocaine 2% viscous solution), vitamin B12 supplements, and NSAIDs. However, the symptoms significantly improved after applying PFC twice daily for 1 week [Figure 3c]. The patient remained free of side effects [Figure 3b] and recurrence over 3 months of follow-up [Figure 3d].

Investigation and follow up

Patients were confirmed to meet the following criteria: (1) receive initial interview, that is, medical history of general diseases, (2) investigation for aphthous, such as size, sites, type, symptoms, and medication history, (3) consultation of how to use PFC, (4) follow-up, that is, inspection and interview was performed once every month for 3 months.

Application of topical Power fucoidan cream™

Areas of RAS were blotted dry, and then a small amount of PFC was applied with own finger and kept for 5 min. Patients must then refrain from eating or drinking for 30 min.

DISCUSSION

RAS is one of the most widespread oral mucous inflammatory diseases with a reported prevalence in the USA of about 20%.[6] However, little is known about the status of this condition in Japan. Messadi and Younai[7] developed a practical guide for the management of recurrent aphthous ulceration, including local and systemic therapies, and suggested that immune mechanisms might play important roles in the etiology of recurrent apthous ulcers. Furthermore, they identified several nonimmunological factors that are associated with RAS. However, evidence supporting the causative roles of these factors is scarce. Although both patients in the present study described having extreme

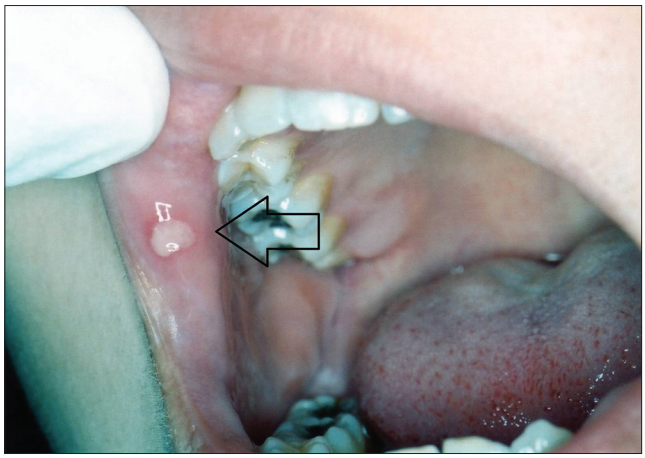

Figure 3a: Before power fucoidan cream™ therapy

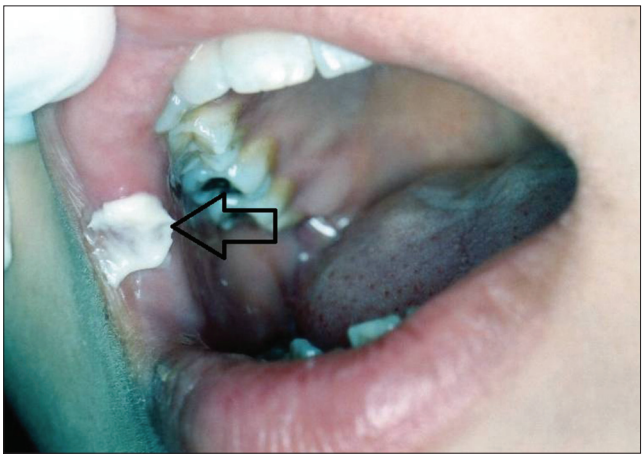

Figure 3b: During power fucoidan cream™ therapy

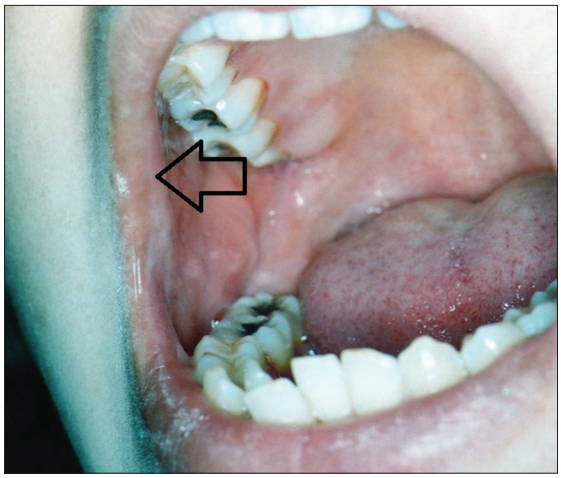

Figure 3c: One week after therapy

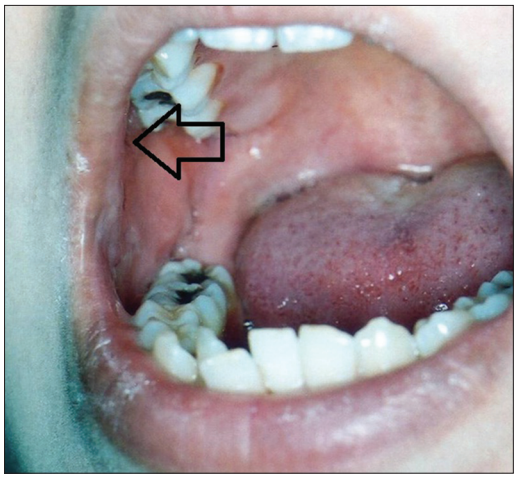

Figure 3d: Three months later

pain, symptomatic treatments were not rigorously evaluated. Various therapies have been attempted, including corticosteroid ointment, NSAID tablets, anesthetic gels, and vitamin B12 supplements, but they were ineffective.

Considering the histological characterization of RAS and the most recent relevant therapy, we decided to apply a fucoidan cream (PFC). After 1 week, the ulcers improved without side effects and no exacerbation was found during a follow-up period of 3 months. Thus, fucoidan was more effective than any other commercial medication.

Our patients did not develop side effects after using PFC, topical application caused no stinging at application sites and healed under 1 week. Conventional medicines require an average of at least 1 week to elicit an effect; in comparison, PFC has the advantage of being fast acting, taking an average of under 5 days for symptomatic relief to become obvious. Both patients demonstrated that regression of the lesion occurred after 3 days with analgestic and healing effects with regard to RAS by the treatment of PFC. Fucoidan results in early tissue remodeling and repair processes that might depend on antiinflammatory properties together with enzyme-like activity.[8] Such activity inhibits various enzymes including matrix metalloproteases, hyaluronidases, and elastases.[9] A clinical study has also indicated that PFC helps to ameliorate skin aging.[10]

The results of PFC therapy in only two patients are difficult to interpret because the observed responses might have simply reflected the natural course of the disease rather than the effect of the medication. Although the mechanism has not yet been fully elucidated, we believe that the fucoidan cream exerted a real therapeutic effect because the previously persistent lesions did not recur. The clinical activity, value, and safety of topical fucoidan cream as a treatment for RAS remain to be determined in clinical trials.

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