

Bromelain improved long-term erythema multiforme attacks induced by herpes simplex infection: A case report

Herpes simpleks enfeksiyonunun tetiklediği uzun süren eritema multiforme atakları bromelain tedavisi ile düzeldi: Bir olgu sunumu

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ABSTRACT

Erythema multiforme is an immune-mediated skin disorder characterized by erythematous target-like macules, papules and plaques commonly located over distal extremities as well as mucosal involvement. It is mostly induced by herpes simplex infections and various medications. Recurrences of herpes simplex infections result in new erythema multiforme lesions in immunologically susceptible people. Therefore, suppressing herpes reactivations also suppresses erythema multiforme attacks. Antiviral medications such as acyclovir, valacyclovir and famciclovir have limited capacity to prevent such recurrences due to their inadequate efficiency after continuous use. Those patients usually seek an absolute remedy to prevent recurrences. Bromelain is a well-known herbal supplement containing proteolytic enzymes produced from pineapple plant. It has been used in many clinical conditions including sinusitis, sports injuries and neoplastic diseases for years with a great safety profile. Herein, we present a young female patient with long-term erythema multiforme attacks induced by herpes simplex infections. She became free of disease after using oral bromelain 500 mg twice a day for one year.

Keywords: Bromelain, Erythema multiforme, Herpes infection

ÖZ

Eritema multiforme, genellikle ekstremitelerde yerleşen, eritemli, hedef benzeri maküller, papüller ve plaklar ile mukozal tutulumla karakterize immün kökenli bir cilt hastalığıdır. Etiyolojide sıklıkla ilaçlar ve herpes enfeksiyonları vardır. Herpes simpleks enfeksiyonlarının tekrarı, immünojenik açıdan duyarlı kişilerde yeni eritema multiforme lezyonlarına neden olur. Bu nedenle, herpes reaktivasyonlarını baskılamak, eritema multiforme ataklarını da baskılar. Asiklovir, valasiklovir ve famsiklovir gibi antiviral ilaçlar sürekli kullanım sonrası yetersiz etkileri nedeniyle, nükslerin önlenmesi için sınırlı kapasiteye sahiptir. Hastalar nüksleri önlemek için genellikle kesin bir tedavi arar. Bromelain, ananas bitkisinden üretilen ve proteolitik enzimler içeren iyi bilinen herbal bir üründür. Mükemmel güvenlik profili ile yıllardır sinüzit, spor yaralanmaları ve neoplastik hastalıklar gibi birçok hastalıkta kullanılmaktadır. Burada, herpes simpleks enfeksiyonlarının neden olduğu uzun süredir eritema multiforme atakları yaşayan genç bir bayan hastayı sunuyoruz. Bir yıl boyunca oral yolla 1 gram bromelain kullanan hastada herpes ve eritema multiforme atakları tamamen kayboldu.

Anahtar kelimeler : Bromelain, Eritema multiforme, Herpes enfeksiyonu

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INTRODUCTION

Erythema multiforme (EM) is an immune-mediated skin condition manifested by erythematous target-like maculopapular lesions, sometimes accompanying with mucosal erosions involving mouth and genitalia. Most EM cases are caused by infections or medications, particularly herpes simplex infections [1]. EM follows herpes infection in immunologically susceptible people. Herpes simplex infection especially involving face usually runs in a chronic intermittent course. Every herpes infection results in an EM episode. So, the treatment of herpes infection reactivations also prevents EM attacks in those patients. Acyclovir, valacyclovir and famciclovir have been used to treat herpes virus infections for certain time in various dosages depending on acute or chronic forms [2]. Suppressing herpes simplex reactivations by antiviral drugs can also prevent herpes associated erythema multiforme episodes. However, despite long term antiviral treatments such as six or more months, the disease comes back when the treatment discontinued.

Bromelain is a well-known herbal supplement used in many clinical conditions such as sinusitis, soft tissue injuries, some types of cancers etc due to its antiinflammatory, anticancer, immunomodulatory and antithrombotic properties. Its actions have been proved in several studies [3]. Bromelain could have possible effect on herpes simplex and erythema multiforme through its antiinflammatory and immunomodulatory actions. Bromelain inhibits bradykinin synthesis at the site of inflammation. In vitro studies have shown that bromelain is effective on immune cells including T-cells, macrophages and natural killer cells as its modulation effect on superficial adhesion [4].

It is hypothesized in the presented case that bromelain-induced immunomodulation may have suppressing effect on herpes simplex virus reactivation.

CASE REPORT

34 yr female patient had been followed for recurrent EM episodes induced by herpes labialis infection at our dermatology department for five years. She had oral erosions, multiple erythematous target-like papules and plaques located hands [Fig

1], forearms and distal lower extremities in every attack numbering five or more episodes a year, each one lasting weeks. Valacyclovir 500 mg a day was effective in suppressing herpes infection at early years with a use of six months, but herpes and following EM attack rapidly occurred just after discontinuation of medication. Ongoing courses of valacyclovir resulted in loss of efficiency in time.



Fig 1. Multiple erythematous target-like papules and plaques located over hands

Bromelain use was planned hoping to enhance immune response due to its immunomodulatory action which was already proven clinically at previous studies. The patient was otherwise healthy apart from herpes induced erythema multiforme episodes, including cardiac and hematological disorders. She had also not any bleeding history. So there was no contraindication for bromelain use. Informed consent was obtained from the patient before treatment.

After beginning oral bromelain 500 mg twice a day, frequency and severity of episodes gradually decreased within months and completely resolved at the end of one year. There was no side effect during and after treatment. No sign of bleeding, gastric intolerance, and blood pressure changes were noted. Hematological and biochemical searches were found to be normal. She is free of attacks at third year after discontinuation of bromelain.

DISCUSSION

Bromelain, a herbal supplement, showed a considerable efficacy in a patient suffering from longstanding erythema multiforme attacks induced by recurrent herpes simplex infections occurred over her face. In this patient, who did not respond well to classical treatment, including oral antivirals,

over a 5-year period, a striking response could be attributed to bromelain although a spontaneous recovery is not completely ignored. This drug has well-known antimicrobial, anticancer, immunomodulatory, and other actions to be able to fight such viral infections observed in this presented patient.

Erythema multiforme is an immune-mediated cutaneous disorder. Infections and medications are the most common causes of EM and the most frequently implicated infectious agent causing clinical disease is the herpes simplex virus [5]. While majority of cases follow a benign course and improve with relatively safe medications, recurrent episodes give significant morbidity to the patients. Thus, prevention of herpes simplex reactivations is highly important. Using oral antiviral drugs acyclovir and valacyclovir for four to six months or more in daily basis can provide a remission by preventing herpes simplex attacks ,however the condition reappears after the treatment stops. In clinical practice, those patients often expect a complete remission from this uncomfortable ailment. Nevertheless, currently, there is no proven treatment to satisfy the patients.

In a recent study,it was shown that immunoenhancing natural medicine together with valacyclovir could help in controlling herpes associated erythema multiforme [6].Bromelain is a promising agent in the treatment of many immune-mediated diseases including romatoid arthritis, inflammatory bowel diseases, ankylosing spondilitis in addition to malignancies, infections and soft tissue injuries with great safety profile.Bromelain has been used safely even in children under 11 years old [7].

We thought to use oral bromelain treatment expecting its immunomodulatory action since the patient could not take a satisfactory outcome from previous treatments.As we hoped, bromelain worked in our case eliminating herpes and erythema multiforme attacks within a year.

Improvement observed in our patient after bromelain treatment may be a chance or a true action of bromelain which we did not know the exact mechanism. Bromelain can possibly regulate the immune function of the patient to fight against herpes virus recurrences. It is impossible to pose that bromelain is effective in the treatment of herpes simplex induced EM attacks with a single patient,

however it is also worth to present such patient having several attacks for years ,and then saving her from distressing condition with a relatively safe drug, bromelain.

As a limitation, we were not be able to perform a serological validation test for diagnosing herpes simplex infection in the patient.

Consequently, there is a need for further extensive studies establishing the exact role of bromelain in those immune-mediated disorders.

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