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Staphylococcus Haemolyticus Infection caused by Topical Tacrolimus use in a Patient with Atopic Cheilitis

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Abstract

Atopic dermatitis is a chronic relapsable inflammatory skin disease, and strongly associated with skin barrier dysfunction and susceptibility to infections. Atopic cheilitis is common in cases of atopic dermatitis. Topical tacrolimus is first-line treatment for the atopic dermatitis but it may cause many side effects after a long-time management. Now we describe a case of Staphylococcus haemolyticus infection in a patient with atopic cheilitis. Clinicians should be aware of this rare complication particularly in the special area of skin

Key words: Atopic dermatitis, Atopic cheilitis, Tacrolimus, Skin barrier dysfunction, Infection

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Introduction

Atopic dermatitis (AD) is a chronic relapsable inflammatory skin disease, characterized by pruritus, dry skin, susceptibility to infections, increased penetration of environmental allergen, with a prevalence ranging from 15 to 30% in children and 2 to 10% in adults[1]. The lesions frequently develop on the scalp and face. The mucocutaneous junction of the lips is a specialized region of transition between the skin and the outer surface of the lips. It is covered by a non-keratinised epithelium, which make it the most sensitive region for AD. The lip involvement is common in cases of AD, which is also described as atopic cheilitis (AC). AC is considered as one of the minor criteria for diagnosing AD according to Hanifin-Ruska criteria[2], and it may appear as an isolated condition, or as part of AD.

Treatment measures for AD basically consist of drug therapy, consisting of emollients and topical anti-inflammatory drug[3]. The main goal of therapy is to improve skin barrier function, reduce inflammation and prevent flares. Currently, topical corticosteroids (TCS) and tacrolimus ointment (TAC-O) were recommended as the first-line treatment for AD[4]. However, here we described a case of severe perioral staphylococcus haemolyticus infection caused by long-term TAC-O use in a patient with AC.

Case report

A 24-year-old man presented to the Department of Oral Medicine with the chief complaint of dry lips with scaling for several years. When the weather was dry, the symptoms turned worse, pruritus, fissures and erythema appeared, which developed on the periorbital area some time as well. His skin was always dry and easy to develop rhagades. His father and grandfather suffered atopic dermatitis for decades. Physical examination revealed swelling and scales on his lips. There were no obvious symptoms on skin. The total serum IgE level and peripheral blood eoshinophil counts were normal. As a result, diagnosis of AC was made, and 0.1% TAC-O (twice a day) was applied. Improvement of the lips dryness and scaling was observed initially, so he used TAC-O intermittently for several months without further consultation. After six months the lesion had gradually become refractory to this treatment, when he stopped the ointment for one week, the condition relapsed, and small-red eczema appeared on the lips, the lesion had been slowly enlarging as well as becoming painful, exudative and itchy.

The patient returned to the hospital, examination revealed erythema, cracks and swelling of lips and perioral skin with a little exudation (Figure 1). To eliminate the possibility of allergic reaction, blood cell count, skin patch test and total serum IgE test were carried out. The results were all within normal range. Then bacterial culture of swabbed sample from the lesion performed and yielded many staphylococcus haemolyticus colonies after 24 hours incubation, which was resistant to penicillin and clindamycin but susceptible to teicoplanin, cefepime, minocycline, gentamycin and cefoperazone. After one week's administration of cefepime, the patient's clinical symptoms improved(Figure 2), the emollient consisting of hyaluronan was suggested for long term applying.

Figure 1. Examination revealed erythema, cracks and swelling of lips and perioral skin with a little exudation.

Figure 2: After one week's administration of cefepime.

Discussion

Tacrolimus is calcineurin inhibitors (CNIs), which belongs to a group of immunosuppressive agents that block T-cell activation through the inhibition of the calcium/calmodulin-dependent phosphatase calcineurin, and has long been used in organ transplantation. The topical form of tacrolimus is mainly indicated for the treatment of inflammatory skin disease, especially AD. Studies showed that tacrolimus can reduce the activity of T lymphocytes and inhibit their cytokines releasing. In addition, tacrolimus has direct effects on keratinocytes and reduces the number of IL-8 cytokine receptors on the keratinocytes, hences reducing inflammation, so tacrolimus ointment (TAC-O) is recommended as first-line treatments with topical corticosteroids for AD[5].

Despite of the efficacy of TAC-O in treatment of AD, there are lingering concerns about the safety of this immunosuppressive agent. In 2003 and 2006, the Japanese and the US Food and Drug Administration (FDA) respectively updated the labeling for TAC-O, highlighting a possible risk of lymphoma and skin cancer[6]. By now, TAC-O had been reported several side effects after long-time management of AD, such as cytotoxicity in renal proximal tubular epithelial cells[7], pulmonary epithelial cells[8], and insulin-secreting b cells[9].

Impaired epidermal permeability barrier function is one of the most important pathogenic factors for AD. Defective skin barrier reduces inflammatory thresholds to irritants and enhances allergen sensitization, leading to allergic responses. Animal study demonstrated that TAC-O induces negative effects on the skin barrier including permeability and antimicrobial functions by inhibiting lipid synthesis, suppressing expression of IL-1α and antimicrobial peptides[10], therefore TAC-O possesses the potential to aggravate the manifestation of AD already at increased risk for cutaneous infections. The lip vermilion is the transition area between skin and mucosa, without the sebaceous and sweat glands as a protective hydro-lipid layer, where the drug absorption rate is high[11], so the negative effects on the lip vermilion maybe further amplified, which lie behind the aggravation of the clinical manifestation and staphylococcus haemolyticus infection in this patient.

Conclusion

Preventing AD flares requires long-term management, TAC-O using, especially in the special area such as lip vermilion, must be particularly considered and reassessed. It may not be the first recommended choice for the treatment of AC, or there should be strict time control, apt concentration of TAC-O used for refractory long-standing AC.

Conflicts of interest

There are no conflicts of interest.

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