



Clinical observation of allergic contact stomatitis treated with Kangfuxin solution as adjuvant: case report

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Background: Allergic contact stomatitis (ACS) is common among people with allergic constitution and who have allergy reaction to specific allergen such as drugs, food, and materials because of immune dysfunction. With the development of materials science, the increasing diversity of cosmetics and food additives has gradually raised the incidence rate of ACS. Now systemic and local therapy are adopted in the therapy of ACS. However, the systemic therapy would drop the drugs' concentration after it reaches the treatment area through the layers of human barriers, while the locally-used drugs such as collutory may not be suitable for patients with skin lesion. Kangfuxin contains a variety of biological extracts which is anti-inflammatory and curative and can produce connective tissues whether it's skin or mucous membrane. It can be used not only in non-oral diseases such as gastric ulcer or gynecological diseases, but also in the treatment of recurrent aphthous ulcer and many kinds of stomatitis and has shown good anti-inflammatory and curative effects. This study aimed to explore the effectiveness of Kangfuxin solution as a local-used adjuvant drug to treat ACS.

Case Description: We present a 22-year-old male with ACS whose complaint at the first visit was severe pain, accompanied by salivation, tongue enlargement, bleeding, tonsil enlargement, and symptoms of difficulty in eating, fatigue, and dizziness. After the physical and laboratory examination, we found no abnormalities other than a history of eating the kiwi fruit, which is a common allergen. Thus, he was diagnosed as ACS. In this case, we provided a pharmacologic therapeutic intervention of chlorpheniramine (one tablet, three times a day) and Kangfuxin solution (gargle for 15 min, three times a day) with advice that no exposure to the allergen. On the third day, the patient felt no significant relief of symptoms, while one week after the first visit, the symptoms had obviously alleviated and most of the red lip erosion disappeared. The patient recovered completely with no discomfort in ten days after the initial visit.

Conclusions: This study investigated the therapeutic effect of Kangfuxin solution combined with chlorpheniramine on ACS.

Keywords: Allergic contact stomatitis (ACS); Kangfuxin solution; oral mucosa diseases; stomatitis; case report

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Introduction

Allergic Contact Stomatitis (ACS) is an inflammatory disease (1). Upon contact with an allergen, such as some drugs, food, or chemical materials, people with allergic constitution may have an allergic reaction (2). This is because the immunity of skin and mucous membranes against foreign matter is too strong to have a Type IV hypersensitivity response and finally leads to ACS (3,4). The clinical features mainly manifest as local damage to the allergen contacted area and include congestion and swelling of the mucous membrane in mild cases and blister/ulcer/erosion accompanied with itch when more severe. Under extreme circumstances the lesion may cause a life-threatening emergency (5,6). With the development of materials science, the increasing diversity of cosmetics and food additives has gradually raised the incidence rate of ACS in these days (7) and the resulting severe pain causes great suffering (8). At present, both systemic and local therapy are adopted in clinical practice (9). The former approach involves identifying and avoiding exposure to the allergen, and using rehydration therapy and anti-allergy drugs. In severe cases, adrenocorticosteroids (10), and anti-inflammatory drugs, such as antibiotics, and gargarism medicine can be used (11). A small quantity of anesthetic drugs may be implemented to relieve the pain of severely ill patients. Systemic anti-allergy drugs such as chlorpheniramine, and local medications such as gargles, including chlorhexidine, can also be used (12). However, the concentration of systemic drugs may decrease by the time they reach the site of action, resulting in a diminished therapeutic effect. When using locally-used drugs like gargles, the therapeutic effect may not be ideal in patients with skin lesions at the same time as stomatitis, because the drugs' composition and concentration may not be applicable to the skin lesion.

Therefore, a milder and more widely applicable drug is needed. As an ethanol extract preparation of *Periplaneta Americana*, Kangfuxin solution contains a variety of biological extracts that can produce connective tissues, and has shown promising anti-inflammatory and curative effect (13). The chemical composition of Kangfuxin solution is complex, including 18 kinds of amino acids, peptides, nucleosides, polyols and other substances. Its main clinical effect is to promote wound healing, especially for mucosal and skin damage caused by trauma, such as burns and scalds. At present, study (14) has shown that this may be related to the effect of Kangfuxin solution on epidermal cell growth factor (EGF) and basic fibroblast growth factor (bFGF), which

can not only promote the formation of fibroblast, but also further promote the formation of granulation tissue and tissue reconstruction. In addition, study (15) has shown that Kangfuxin solution can also eliminate inflammation and edema by promoting the synthesis and expression of local bFGF and TNF- β , and increasing the phagocytosis of NK cells and macrophages to pathogenic substances. In addition, Kangfuxin solution can also reduce the number of CD3⁺, CD4⁺ cells and CD3⁺/CD4⁺ ratio in peripheral blood, and increase the number of CD8⁺ cells, thus improving immune function. These mechanisms and effects make Kangfuxin solution widely used in clinic. It has been widely used in peptic ulcer (16,17), gynecological diseases (18), surgical diseases (19), as well as in the prevention and treatment of various skin and mucosal diseases (20). In the oral field, Kangfuxin solution can be used to treat recurrent aphthous ulcer, herpetic stomatitis and pharyngitis, radioactive stomatitis, lichenous planus, and gingivitis (21). However, it has no anti-allergy effect itself, but can only treat the local clinical symptoms of ACS. Therefore, in this study, we chose the combination of chlorpheniramine, a systemic anti-allergy drug commonly used in clinical practice, and Kangfuxin solution. Chlorpheniramine is an H1 receptor antagonist, which can competitively block the histamine H1 receptor on the target cells of allergic reaction, so that histamine cannot bind to H1 receptor, thus inhibiting the allergic reaction caused by it. Through this case report, we can observe the curative effect of Kangfuxin solution as a local drug in the treatment of ACS, so as to make a supplement and new suggestion to the existing treatment plan. Therefore, this study aims to examine the effectiveness of Kangfuxin solution as adjuvant for the treatment of ACS. We present the following case in accordance with the CARE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-2734/rc>).

Case presentation

A 22-year-old male attended the Chinese PLA General Hospital with food allergic stomatitis due to ingestion of kiwi fruit on January 20th, 2022. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal. The patient reported



Figure 1 The first visit.



Figure 3 One week after treatment commenced.



Figure 2 Day 3 following treatment.



Figure 4 Complete recovery after 10 days.

no history of medical, family, or relevant genetic issues. At the first visit he complained of severe pain accompanied by salivation, tongue enlargement, bleeding, tonsil inflammation, and difficulty in eating, fatigue, and dizziness. A large area of erosion of the lips, partially covered with yellow pseudo-membrane and blood clots was seen (*Figure 1*). The patient reported the onset of symptoms as three days ago after eating some kiwi fruit, a common allergen, and had sought no previous care. The results of physical and laboratory examination were not characteristic of other oral diseases but a history of allergen exposure. Thus he was diagnosed allergic stomatitis based on the allergen exposure history and clinical performance.

The symptoms occurred following the ingestion of kiwi fruit and included those typical of allergic stomatitis such as hyperemia, edema, and mucosal erythema. Several large erosive areas with bleeding and percolation on his upper and lower lips were seen.

As the cause of ACS may not be clear to patients, doctors may miss the best time to deal with the disease, making

the situation worse, and the key to good management is determining the allergen and avoiding exposure to it in the future. The key to diagnose the ACS is the determination of the allergen and the symptoms may be relieved after unexposure to the allergen. Once the allergen is identified and treatment is provided in a timely manner, the prognosis is generally good.

In this case, we provided a pharmacologic therapeutic intervention of chlorpheniramine (one tablet, three times a day) and Kangfuxin solution (gargle for 15 min, three times a day) and advised the patient to avoid contact with allergens, eat a light diet, and take sufficient rest.

On the third day, the patient felt no significant relief of symptoms except a short period of pain relief after gargling (*Figure 2*). One week after the first visit, the symptoms had obviously alleviated and most of the red lip erosion disappeared. There was no pain, and the tongue and tonsils were no longer enlarged (*Figure 3*). Ten days after the initial visit, the patient had recovered completely with no discomfort (*Figure 4*).

We recorded the course of disease by calling the patient every day by telephoning him or using Wechat. During the follow-up time, the patient's intervention adherence was so good that we could observe the full course of the disease. The patient reported no discomfort or adverse or unanticipated events and was satisfied with the treatment.

Discussion

ACS is common among people with allergic constitution (22) and who suffer allergy reactions to specific allergens such as drugs, food, and materials because of their immune dysfunction. Due to the increasing variety of food, makeup, and other materials, the incidence rate of ACS is rising (23). However, its cause can be unclear if patients are not aware of the allergens. In some cases, there is no obvious characteristics in the clinical manifestations and doctors may ignore or misdiagnose the condition (24). In this regard, research into ACS has drawn great interests. Kangfuxin solution can be used in the treatment of recurrent aphthous ulcer and many kinds of stomatitis and has shown good anti-inflammatory and curative effects (25,26). The aim of our study was to observe the effect of Kangfuxin solution in curing ACS.

Medications for ACS can be divided into those acting locally and systemically. The advantages of systemic medication are that it is more convenient to use and can reach many locations that local medication cannot (27). However, there may be adverse drug reactions, and the effectiveness of the treatment will be affected if the drug concentration drops after it reaches the treatment area through the layers of human barriers.

Chlorpheniramine is an H1 receptor antagonist, which can competitively block the histamine H1 receptor on the target cells of allergic reaction, so that histamine cannot bind to H1 receptor, thus inhibiting the allergic reaction caused by it. However, its local anti-inflammatory and pro-repair effect was not obvious due to the human's barriers. Kangfuxin solution can be used to not only eliminate inflammatory edema and fight infection, but to promote necrotic tissue shedding and create conditions for its repair. Besides its anti-inflammatory effect, it can significantly accelerate wound healing by promoting structural and functional recovery and improving immune function. This may be related to improvement in the phagocytosis capacity of macrophages and the activity of lymphocytes and serum lysozymes with the superoxide dismutase (SOD) value rising.

Both chlorpheniramine and Kangfuxin solution were

used together in this case as the systemic anti-allergy effect of the latter alone is not good, and while chlorpheniramine is a commonly used anti-allergy drug, its local damage repair effect is not ideal. The Kangfuxin solution used in this study is a local medication characterized by local administration, and can avoid the first pass elimination of drugs and adverse drug reactions (28). To prevent the erosive effect of saliva from reducing the effective concentration and to ensure the effect, the patient in this case soaked the new solution in cotton and wet applied it to the affected area. The recovery period of food allergic stomatitis is usually about 1 week, although patients with systemic symptoms or severe symptoms may need 15–20 days to fully recover. The patient with severe symptoms in this study was cured in only 10 days, indicating Kangfuxin solution is indeed effective as adjuvant in the treatment of allergic stomatitis.

In addition, Kangfuxin solution is a commonly used drug in the treatment of oral mucosa diseases, which means it can be effective not only in the treatment of ACS but also in other diseases. For those with other mucosal diseases, it can be used to avoid excessive medications and cure two or more concurrent or parallel diseases. As a locally used drug which can promote repair, Kangfuxin solution can also be used in the treatment of severe ACS based on systemic support therapy with hormone drugs, to achieve a better synergistic treatment effect.

However, the results of this study must be considered with caution for several reasons. Firstly, studying more cases could help suppress the random error and reduce the standard deviation of the result. Second, the errors caused by different stages of the course of disease should be eliminated in future studies by further categorizing patients based on the stage of the disease. Further, in this study, to ensure the principle of a single variable, we only compared the efficacy of two drug combinations, and no other local drugs (such as chlorhexidine) were used.

In future experiments, we will compare the efficacy of more local and systemic medication, which will not only further evaluate the effect of Kangfuxin solution but will allow us to find the most effective combination medication plan to treat ACS. In conclusion, this study investigated the therapeutic effect of Kangfuxin solution combined with chlorpheniramine on ACS.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-2734/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-2734/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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