



## Atopic Dermatitis: A Case Study of Therapy for a Difficultly Curable Condition

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### Abstract

*This study reviews the use of therapy for a difficultly curable condition in patient. A similar rash came back at age 12, was diagnosed as atopic eczema, and has not disappeared. Erupted, crusty, erythematous, eczematous, lichenified, maculopapular, and smooth vesicular eruptions are present on the face, neck, flexor aspects of both arms and legs, hands, and chest. It is believed that topical corticosteroids penetrate into the stratum corneum by passive diffusion, which varies greatly, depending on the part of the body on which the preparation is used. Allergic sensitization can occur within 2 weeks of therapy, but it may be difficult to diagnose because corticosteroids can modify allergic reactions.*

## Introduction

Atopic dermatitis (DA), also known as eczema, is a chronic inflammatory condition of the skin characterized by pruritus, erythema, and scaly skin (Koda-kimble, 2012). The etiology of AD is still not known with certainty, and from several journals its pathogenesis involves many factors. One theory that is widely used to explain the pathogenesis of AD is the immunological theory in which 75% of patients with AD have a history of other atopic diseases in their family or in themselves. In addition, several immunological parameters can be expressed in AD, such as an increase in serum IgE levels in 60-80% of cases. The presence of specific IgE against various aeroallergens and blood eosinophilia and the presence of IgE molecules on the surface of epidermal Langerhans cells make patients with AD more susceptible to bacterial and viral infections (Takeuchi et al., 2003).

The pathophysiology and pathogenesis of atopic dermatitis (AD) is a combination of a complex series of interactions between genetic susceptibility causing defective or imperfect epidermal barriers, abnormalities in the immune system, and an enhanced immune response to allergens and microbial antigens. Dysfunction of the epidermal barrier (skin barrier) is a major pathogenic factor in the development of AD. In AD patients can be found mutations or defects of the FLG gene that will encode Protein (pro)-filaggrin which is an important protein in the epidermal barrier. The genetic defect of FLG (Filaggrin gene) will disrupt the epidermis and cause contact between immune cells in the dermis with antigens from the external environment. This process will lead to intense itching, scratching, and inflammation.

The scratching process can cause irritation and inflammation of the epidermal skin barrier, which is described as an itchract cycle. Damage to the skin barrier causes migration of activated antigen-presenting cells into the lymph nodes and migration from naive T cells to T helper 2 (Th2) cells. Increased Th2 cytokines together with Tumor Necrosis Factor  $\alpha$  (TNF- $\alpha$ ) and IFN- $\gamma$  cause further damage to the skin barrier by inducing apoptosis of keratinocytes, impairing

tight junction function and increasing Th2 response by increasing the expression of thymic stromal lymphopoietin (TSLP) from cells epithelial. Apart from the genetic factors that cause the above process, in AD there can be innate immune response defects which make DA patients more susceptible to viral and bacterial infections. In the early phase, the T cell response was dominated by Th2, but then there was a shift in dominance to a Th1 response which resulted in the release of pro-inflammatory cytokines and chemokines, namely interleukins (IL) 4, IL 5, and TNF which stimulated IgE production and a systemic inflammatory response. This series of events will cause signs and symptoms of AD such as pruritus.

## **Pharmacological therapy**

### ***Corticosteroids***

Topical is the main choice for reducing inflammation in patients with AD. the use of topical steroids, which is a substance that works and is anti-inflammatory is the basis of therapy for the treatment of eczematous lesions. However, its use will depend on the location and condition of the skin lesions and is safe to use so that Patients should be instructed carefully to avoid potential side effects, especially strong potency should be avoided from the face, genitalia, and intertrigo areas and in general mild potency preparations are recommended in this area. Therefore, the use of topical steroids is emphasized only on AD lesions only. Whereas the skin that is not involved is emollient enough to avoid dry skin and inflammatory processes (Siddappa, 2003; Stamatas et al, 2013).

### ***Topical immunomodulator***

Topical calcineurin inhibitors such as tacrolimus and pimecrolimus, can be used for the treatment of AD. In contrast to corticosteroids, these drugs can be used for long-term treatment, can be used on all parts of the body for a long period without side effects such as those caused by the use of corticosteroids. These drugs cause inhibition calcineurin, which is the initiation of T cell activation. Through inhibition of T, it can reduce inflammation in AD (Malm et al, 2015).

### ***Tar Preparations***

Tar preparations can reduce itching and inflammation of the skin. This product has been used in combination with topical corticosteroids, in addition to lowering the strength so that corticosteroids can be used effectively, in addition to additional therapy with ultraviolet light therapy. Patients can be instructed to use products at bedtime and wash them in the morning. In addition, folliculitis and photosensitivity during use have also been reported (Murphy, 2004; Laing et al, 2006).

## **Supportive Therapy**

### ***Antihistamines***

Antihistamines As a sedative with a side effect of pruritus caused by contact dermatitis can be relieved by the use of sedative oral antihistamines such as diphenhydramine or hydroxyzine. Many oral antihistamines can cause hypotension, dizziness, blurred vision, and confusion. Diphenhydramine and hydroxyzine can be safely administered to children older than 2 years and adults.

### ***Topical Doxepin***

Topical Doxepin can be used to reduce symptoms of itching with an onset of 48 hours after administration. The occurrence of drowsiness is still a problem in its use for therapy (Salinsky et al, 1996)

### ***Antibiotics***

Several antibiotics that can be used for AD therapy include the aminoglycosid group such as gentamicin and bacitracin. Macrolide groups such as erythromycin, clindamycin, and other antibiotics such as 2-5% chlortetracycline or fusidic acid. The use of antibiotics in AD is an additional therapy in case of bacterial infection (Coates & Hu, 2007)

### **Therapy for conditions that are difficult to cure**

#### ***Wet Dressing with Occlusion***

A wet dress or wet body wrap placed directly on the skin is effective in reducing itching, especially at night. Wet body wraps used in conjunction with topical corticosteroids can be used for acute or chronic flares, lichenified lesions and skin acerations. A warm compress is applied to the skin for 20 minutes. 4-6 times a day can help in drying the bleeding lesions (Malm et al, 2015)

#### ***Phototherapy***

Phototherapy is effective for intractable or recalcitrant AD therapy. This therapy may consist of ultraviolet A (UV-A), ultraviolet B (UV-B) or a combination Psoralen plus UV-A (severe psoralen DA) photochemotherapy

#### ***Systemic immunosuppressant***

If aggressive topical therapy and phototherapy fail to control symptoms of AD, systemic immunosuppressant agents can be used as another alternative. Given that AD is a T-cell mediated disease with involvement of Langerhans cells, eosinophils, and mast cells, immunosuppressants can be used in severe medicine. alone because of its detrimental effects, the use of systemic immunosuppressants is rare (Malm et al, 2015)

#### ***Systemic corticosteroids***

Systemic corticosteroids can also be considered as a last resort if they affect the mucosa and in the adult type with severe exacerbations and unsuccessfully topically, but are rarely used in infants and children because of their side effects and rebound reactions when use is discontinued. in a short and tapering time.

#### ***Azathioprine***

A purine analogue is another systemic immunosuppressant that can help in severe cases of AD. Its main disadvantage, compared to cyclosporine, is a long onset of 4-6 weeks. Although many side effects such as myelosuppression, hepatotoxicity and gastrointestinal disturbances, azathioprine can help in the treatment of heavy AD (Malm et al, 2015)

### **Cases**

P.K., a 17 year old boy, came to the dermatology clinic with 30% of his body covered with pruritic rash, eczema. There is extensive involvement of the popliteal and cubital fossa bilaterally. There is evidence of excoriation with cosmetic defects in the antecubital fossa, around the neck, and on the forehead. Family History: both mother and aunt have asthma. One sister (L.K.), age 15, suffers from seasonal allergic rhinitis and atopic eczema. Father and younger brother, age 11, did not appear to have atopic manifestations. Past Medical History: Rash was first noted 1 month after birth. The scalp, face, and neck are the only areas affected, and the rash persists of varying severity up to 2 years of age, when spontaneously resolves.

A similar rash came back at age 12, was diagnosed as atopic eczema, and has not disappeared since then. P.K. developed seasonal allergic rhinitis at age 6 years and had occasional asthma

attacks (last attack, age 15). She's having a hard time following nondrug recommendations for eczema. She has used an over the counter topical hydrocortisone cream to cool flares for years. He reports on variable courses; clears up in summer and during periods of less stress, and gets worse during winter and periods of stress. Physical Examination: P.K. is a well-nourished, well-developed, adolescent male with no abnormal physical findings other than obvious allergy relief, pale nasal mucosa, and Dennie's lines noted near the eye, plus extensive skin lesions. Erupted, crusty, erythematous, eczematous, lichenified, maculopapular, and smooth vesicular eruptions are present on the face, neck, flexor aspects of both arms and legs, hands, and chest. There is some evidence of secondary bacterial infection of the cubital fossa and of the left leg.

### **Identify the presentation history, symptoms, and signs characteristic of eczema**

Atopic dermatitis, a form of eczema, can be acute or sub-acute, but there can be chronic chronic inflammation of the epidermis and dermis. Dermatitis infection in infants can lead to worse development than other medical conditions (eg, allergic rhinitis or asthma).

About 80% of patients with atopic dermatitis have a type I hypersensitivity reaction (IgE mediated) which occurs as a result of the release of vasoactive substances from both mast cells and basophils that have been sensitized by antigen-antigen interactions. In infants and young children, dermatitis often occurs on the surface of the scalp, face, and extensors. In older children and adults, it tends to localize to the flexural areas, especially the cubital and popliteal fossae and the neck. Additionally, the rash can affect the hands and feet.

Pruritus is a characteristic feature of atopic dermatitis. The constant scratching causes a vicious cycle of itching, with some accidentally involving the liquidation of the skin. Atopic dermatitis has been described as "an itchy rash, not an itchy rash." In other words, the itching precedes the rash. Wool, detergent, soap, room temperature change, reliable and / or physical pressure according to pressure. Patients tend to have dry skin (xerosis). This is due to reduced water-binding capacity and higher transdermal water losses.

P.K's family and medical history is a classic disease for atopic dermatitis. Family history is important for asthma, allergic rhinitis, and atopic dermatitis. She had an outbreak initially at 1 month of age and later developed seasonal allergic rhinitis and asthma. Examination of his skin revealed findings of acute and chronic atopic eczema, with a characteristic location and description of the lesion (Kimbel Code 9, 2009).

### **What biopharmaceutical considerations are relevant for selecting topical corticosteroids for P.K?**

It is believed that topical corticosteroids penetrate into the stratum corneum by passive diffusion, which varies greatly, depending on the part of the body on which the preparation is used. When a standard hydrocortisone preparation is applied to different parts of a person, absorption will be 0.14% on the plantar surface of the foot, 1% on the forearm, 4% on the scalp, 7% on the forehead, 13% on the forehead, and 36. % on the scrotum. Due to the high penetration in the groin, axilla and face, topical, non-low chlorine preparations such as 0.5% to 1% hydrocortisone should be used as ointments.

For P.K, 1% hydrocortisone cream should be used on the face and other parts of the higher penetration rate because of possible responsibility for complications. When equal amounts of corticosteroids are incorporated into ointments, gels, creams, and lotions, gel preparations and ointments are generally more active than creams and lotions. However, with the increasing use of optimized vehicles, that rule is not as true as in the past. The addition of certain substances increases penetration and potency. Increasing the corticosteroid concentration in a preparation also increases its potency, but not linearly. Because P.K. After completing the special

examination, cream should be used initially, to facilitate drying. However, patients often express preferences (e.g., cream or gel), and this should be considered (Kimbel Code, 2009).

P.K's sister, L.K., who also has atopic eczema, started using a new topical corticosteroid preparation (halcinonide) 10 days ago. He has complained of a burning sensation that lasts for 1 hour after each application of this product. He stopped using the product 2 days ago because of this.

### **Is it possible that she is allergic to medications containing corticosteroids?**

Allergic sensitization can occur within 2 weeks of therapy, but it may be difficult to diagnose because corticosteroids can modify allergic reactions. One should suspect an allergic reaction if the lesion changes appearance after starting therapy, if healing did not occur during an unexpected period at an earlier time, or the fifth condition improves and gets worse. Most of the response to an allergic reaction (dryness, itching, burning, or irritation) to topical corticosteroids was more in patients at higher risk than in patients at higher risk. To react to basic vehicles rather than active corticosteroid ingredients.

### **Case Settlement**

Based on suffered by a dermatology patient with 30% of his body covered with pruritic rash, eczema. Where has a Past Medical history: The rash was first noted 1 month after birth. The scalp, face, and neck are the only areas affected, and the rash persists of varying severity up to 2 years of age, when spontaneously resolves. A similar rash came back at age 12, was diagnosed as atopic eczema, and has not disappeared since then.

P.K. developed seasonal allergic rhinitis at age 6 years and occasional asthma attacks (last attack, age 15). Patients had difficulty following non-drug recommendations for eczema. Patients have used over-the-counter topical hydrocortisone creams to cool flares for years.

Based on a history of atopic dermatitis where the cause of atopic dermatitis suffered is due to genetic factors, where the risk of atopic dermatitis can increase if there is a family history of other atopic diseases such as fever or asthma, as is known in this case the family, namely PK mother and aunt suffering from asthma. One sister (LK), age 15, suffered from seasonal allergic rhinitis and atopic eczema so there was a 2 to three times greater risk.

In addition, there were complaints of L.K patients: suffering from seasonal allergic rhinitis and atopic eczema. Using a new topical corticosteroid (halcinonide) 10 days ago. One hour after using this product she felt her skin burn.

### **Conclusion**

Appropriate drugs for use in P.K patients are required to use the Topical Calcineurin Inhibitors class of drugs which is a second-line therapy after topical corticosteroids (in the form of pimecrolimus cream) which works by inhibiting the activation of T-cells and Mast cells blocking the production of pro-inflammatory cytokines and inflammatory mediators. One of the advantages of this preparation that is different from other agents is that it can be used on all parts of the body.

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