ATOPIC DERMATITIS IN A YEAR-OLD CHILD

The case
A one-and-a-half-year-old male child was brought to the physician with complaints of an itchy, scaly, red rash over his cheeks, elbows, knees, and elbows. The lesions were present since the age of 4 months. The itching was intense enough to make the child irritable and scratchy. The lesions waxed and waned but never disappeared completely. Lesions first appeared on the face but within weeks spreaded to other parts of the body. Over the past few weeks, the itching exsudation had spread to the entire body with no particular triggering factor.

There was a family history of similar condition in the family but the child’s father had itchy asthma and frequently suffered from allergic rhinitis.

On examination
The toddler was very restless, crying and uncomfortable, continuously scratching. He was elderly, with a pulse rate of 102/mi and respiratory rate of 22/min. His weight and height were normal for his age. On local examination, erythematous, scaly excoriated lesions were present involving most of the body area. At places there were vesicles, and the scalp had thick scales. The skin on the ventral surface of his elbows and knees and dorsum of his hands and feet had become thickened.

Diagnosis
Atopic dermatitis

Treatment
The child was prescribed topical corticosteroids along with a moisturizer and an anti-allergic agent, and the symptoms gradually improved. However, they skin got aggravated; therefore, a trial of topical 0.03% tacrolimus ointment was suggested. The child responded favorably to the treatment, with decrease in itching and healing of lesions. Three months after starting this treatment, he was almost symptom-free and doing well.

Discussion
Atopic dermatitis (AD) is an itchy chronically relapsing eczematous condition. There is no definitive test to detect AD but the diagnostic criteria proposed by Hanifin and Rajka may be helpful.

Atopic dermatitis is a disease more prevalent in developed and industrialized countries, including India, due to rapid urbanization and industrialization. Immigrants from developing countries migrated to these countries in the last several years. However, their long-term use may lead to side-effects, such as skin atrophy, and hypopigmentation. Tacrolimus is a topical immunomodulator that has demonstrated efficacy in the treatment of atopic dermatitis. It is a moderate to high-potency topical corticosteroid that has demonstrated efficacy in the treatment of atopic dermatitis. However, there are concerns regarding its safety and efficacy in the treatment of atopic dermatitis.

Tacrolimus is a macrolide, produced by Streptomyces tsukubaensis, a fungus found in Japan. Its penetration into the skin barrier is much greater than that of corticosteroids. Tacrolimus is not metabolized locally in the skin, and it is minimally absorbed. After topical application, just 0.1% of the drug appears in the blood. These levels are either undetectable or subtherapeutic.

Tacrolimus exerts its effects on a broad spectrum of inflammatory mediators and processes involved in the pathogenesis of atopic dermatitis. The drug shows good penetration ability and does not seem to cause atrophic changes in the skin. Several double-blind, controlled studies have established the safety and efficacy of this drug in treating atopic dermatitis. Children may particularly benefit from tacrolimus as a suitable alternative to chronic corticosteroid therapy.

Systemic and topical glucocorticosteroids have dominated the anti-inflammatory treatment of eczematous skin diseases, like atopic dermatitis and allergic contact dermatitis for the last several years. However, their long-term use may lead to side-effects, such as skin atrophy, and hypopigmentation. Tacrolimus has been found to be effective for alternative non-steroidal anti-inflammatory agents with a superior risk/benefit ratio. The discovery of topical immunomodulators has filled this need.

Topical immunomodulators are applied to the skin, and modify the immune response locally by either upregulation or downregulation (immunostimulation or immunosuppression). They have been tried in a variety of dermatoses in which cutaneous immunology is altered. They can be either non-steroidal or non-asimal. This article will discuss the non-steroidal immunomodulatory agents, particularly tacrolimus.

Table 1: Classification of non-steroidal topical immunomodulators

McKenzie et al. (2005) have showed good percutaneous penetration and does not seem to cause atrophic changes in the skin. Several double-blind, controlled studies have established the safety and efficacy of this drug in treating atopic dermatitis. Children may particularly benefit from tacrolimus as a suitable alternative to chronic corticosteroid therapy.

 Tacrolimus belongs to the macrolide class, along with pimecrolimus, steroids and cyclosporins. It is a powerful suppressor of the immune system and was initially used to prevent allograft rejection after organ transplantation. Later, the therapeutic efficacy of tacrolimus, both topical as well as systemic, was demonstrated in the treatment of inflammatory skin diseases, such as atopic dermatitis, allergic contact dermatitis, erosive mucosal tissue planus and pemphigoid. Tacrolimus exerts its effects on a broad spectrum of inflammatory mediators and processes involved in the pathogenesis of atopic dermatitis. The drug shows good penetration ability and does not seem to cause atrophic changes in the skin. Several double-blind, controlled studies have established the safety and efficacy of this drug in treating atopic dermatitis. Children may particularly benefit from tacrolimus as a suitable alternative to chronic corticosteroid therapy.

Tacrolimus is a systemic immunomodulator that has demonstrated efficacy in the treatment of atopic dermatitis. It is a moderate to high-potency topical corticosteroid that has demonstrated efficacy in the treatment of atopic dermatitis. However, there are concerns regarding its safety and efficacy in the treatment of atopic dermatitis.

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<td><strong>Corticosteroids</strong></td>
</tr>
<tr>
<td><strong>Antihistamine</strong></td>
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<tr>
<td><strong>Continue routine treatment</strong></td>
</tr>
<tr>
<td><strong>Corticosteroid</strong></td>
</tr>
<tr>
<td><strong>Symptoms do not improve</strong></td>
</tr>
<tr>
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**References**
Eyelash extensions—causing more harm than good

Use of artificial eyelash extensions is growing among modern women desiring to enhance their attractiveness quotient. Technological advances have made full eyelash transplants possible. However, such procedures may be thought of with problems, such as discomfort, irritation and various allergic reactions attributable to the accumulation of dirt and bacteria in the lashes. Lash loss, trichoptilosis and related conditions may also occur due to the tension produced by artificial eyelashes. It would, therefore, be advisable to consult a dermatologist about the potential risks before going for an eyelash extension procedure.

Conclusion

The drug’s onset of action is usually slow. The therapeutic effects of azathioprine often take several months (3–6 months) to become apparent after initiation of therapy, and similarly the effects of dose reduction or cessation of therapy may also be delayed, possibly due to persistence of active drug metabolites. The patient must undergo regular blood tests throughout the treatment period.

Clinical evidence of azathioprine’s efficacy

There is a limited range of treatments for severe atopic dermatitis. Oral administration of azathioprine has shown good results in this condition. In fact, when topical treatment fails, systemic immunosuppression is recommended with azathioprine being one such immunosuppressant.

With growing understanding of the pathways involved in atopic dermatitis, clinicians have been able to use this drug more safely. Maret and colleagues observed that when adjusted to TNPTh activity, azathioprine is a safe drug for the treatment of children with severe atopic dermatitis.

The safety and efficacy of azathioprine as systemic monotherapy for moderate-to-severe atopic dermatitis was evaluated by Maggi et al., who recruited patients with active disease despite optimum topical therapy, and randomized them to receive either azathioprine (142) mg or placebo (212) mg for 12 weeks. At week 12, there was a greater improvement in mean disease activity with azathioprine than with placebo (Figure 3).

In addition, there were significant improvements in pruritus, area of involvement, global assessment, and quality of life. Azathioprine was generally well tolerated.

Oral azathioprine—The systemic immunomodulator

Azathioprine is a thiosemicarbazone product that acts by blocking purine synthesis, and has been shown to be effective for many inflammatory dermatological conditions, such as atopic dermatitis, bullous pemphigoid, pсорiasis vulgaris, cutaneous polyarteritis nodosa, psoriasis gangerminum, cutaneous lupus erythematosus and vasculitis.

With proper laboratory monitoring, azathioprine is a relatively safe medication. However, since azathioprine is metabolized by thiopurine methyltransferase (TPMT), deficiency of this enzyme should be ruled out before using oral azathioprine for immunosuppression.

According to the British Association of Dermatologists’ Guidelines for the Safe Use of Azathioprine, a deficiency of this enzyme should be ruled out before using oral azathioprine for immunosuppression.

A randomized, double-blind study was conducted on 16 patients with chronic plaque-type psoriasis to assess the effects of azathioprine, betamethasone, and alphaprep dermabration. A total of 15 patients completed the study. The average duration of treatment was 12 months. The effects of azathioprine on psoriasis were compared with betamethasone alone and with betamethasone and alphaprep dermabration.

In a similar study by Berth-Jones et al., oral azathioprine caused the Six Area, 75% Improvement, and Psoriasis Area and Severity Index (PASI) to improve by 50% within 1 year of treatment. The drug’s onset of action is usually slow. The therapeutic effects of azathioprine often take several months (3–6 months) to become apparent after initiation of therapy, and similarly the effects of dose reduction or cessation of therapy may also be delayed, possibly due to persistence of active drug metabolites. The patient must undergo regular blood tests throughout the treatment period.

The dose should be adjusted within these limits according to the response and during treatment.

The authors advised monitoring of the full blood count and liver enzymes before stage III or IV disease. Hence, the chances of developing NPM increase if one already has stage III and IV disease developed at least one new primary melanoma after their initial diagnosis. It was also observed that this risk was increased in males with stage III disease.

Additional information is available at http://youcure.me/en/news/eyelash-extensions-may-cause-more-harm-than-good. Eye lash extensions can be associated with complications such as skin infections, allergic reactions attributable to the metals and other materials, or the use of heavy metals, carcinogens and other potentially harmful agents that may cause loss of lashes. Loss of eyelash may also occur due to the tension produced by artificial eyelashes. It would, therefore, be advisable to consult a dermatologist about the potential risks before going for an eyelash extension procedure.

Stage III, IV melanoma poses a threat for new primary melanomas

It is known that treatment of metastatic melanoma with BRAF inhibitors may result in new primary melanomas. For example, patients with stage III melanoma who are at risk of developing NPMs may be at risk of developing NPMs. A study by Berth-Jones et al. discovered that patients with stage III melanoma who were treated with BRAF inhibitors, are at risk of developing NPMs. The authors advised monitoring of the full blood count and liver enzymes.

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With proper laboratory monitoring, azathioprine is a relatively safe medication. However, since azathioprine is metabolized by thiopurine-methyltransferase (TPMT), a deficiency of this enzyme should be ruled out before using oral azathioprine for immunosuppression.

According to the British Association of Dermatologists’ Guidelines for the Safe and Effective Prescribing of Azathioprine 2015, azathioprine should be started with a dose of 1–3 mg/kg/day. The dose should be adjusted according to TPMT levels. Table 1 shows the suggested TPMT-based maintenance dose ranges for the treatment of dermatological conditions.

The dose should be adjusted within these limits according to the response and hematological tolerance, and should be reduced for maintenance therapy following clinical response. Doses at the lower end of the range are recommended for patients with renal or hepatic impairment or the elderly. In the initial 4 weeks of therapy, lower doses should be used as to minimize side-effects, such as nausea.

Table 2: Suggested doses of azathioprine in skin conditions according to TPMT levels

<table>
<thead>
<tr>
<th>Condition</th>
<th>Azathioprine Maintenance Dose</th>
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<tr>
<td>Absent</td>
<td>Azathioprine is not recommended</td>
</tr>
<tr>
<td>Inter.</td>
<td>1-1.5 (mg/kg/day)</td>
</tr>
<tr>
<td>Normal</td>
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The safety and efficacy of azathioprine as systemic monotherapy for moderate-to-severe atopic dermatitis was evaluated by Meggit et al., who recruited patients with active disease despite optimum topical therapy, and randomized them to receive either azathioprine (1mg/2) or placebo (2mL) for 12 weeks. At week 12, there was a greater improvement in mean disease activity with azathioprine than with placebo (Figure 3).

In addition, there were significant improvements in pruritus, area of involvement, global assessment, and quality of life. Azathioprine was generally well-tolerated.

Eyelash extensions-causing more harm than good

Use of artificial eyelash extensions is growing among modern women desiring to enhance their attractiveness quotient. Technological advances have made over 400 eyelash transplantable possible. However, such procedures may be thought of problems, such as discolouration, irritation and various allergic reactions attributable to the introduction of dust and bacteria to the lashes materials or the use of heavy metals, carcinogens and other potentially dangerous chemical agents in making these lashes. Loss of eyelash may also occur due to the tension produced by artificial eyelashes. It would, therefore, be sensible to consult a dermatologist about the potential risks before going for an eyelash extension procedure.

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Hence, the chances of developing NPM increase if one already has stage III and stage IV disease. The risk was also increased in patients with a prior history of skin cancer. The study found that 5% of patients with stage III disease and 1% of those with stage IV disease developed at least one new primary melanoma after their initial diagnosis of melanoma.

Stated III, IV melanoma poses a threat for new primary melanomas

It is known that treatment of metastatic melanoma with BRAF inhibitors may be associated with development of new primary melanomas (NPMs) in some patients. A new study has discovered that patients with stage III or IV melanomas, even if not treated with BRAF inhibitors, are at risk of developing NPM.

The study, which evaluated 4215 patients with stage III melanomas and 3,150 patients with stage IV melanomas, found that 5% of patients with stage III disease and 3% of those with stage IV disease developed at least one new primary melanoma after their initial diagnosis. It was also observed that this risk was increased in males with stage III and stage IV disease. The risk was also increased in patients with a prior history of multiple primary melanomas. The incidence rates were lower than those reported in patients on BRAF inhibitors.

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Atopic dermatitis (AD) is an itchy, chronically relapsing eczematous condition. It is more common in developed countries than in developing countries, with an estimated prevalence ranging from 1% to 30% in children, and 1% to 10% in adults. The disease is seen most frequently in infancy, with a peak in the first 2 years of life, and may persist into adulthood. 

Treatment of Atopic Dermatitis

Corticosteroids
- Low- to mild-potency topical corticosteroids: initial treatment for mild to moderate AD
- Higher potency topical corticosteroids: for severe AD

Antihistamine
- Antihistamine as needed for itching

Topical Immunomodulators
- Topical tacrolimus: approved for treatment of moderate-to-severe AD
- Topical pimecrolimus: approved for treatment of mild-to-moderate AD

Systemic Therapy
- Systemic corticosteroids: for severe, acute cases
- Immunosuppressants: for severe, refractory cases

Figure 1: Treatment of atopic dermatitis

Topical corticosteroids, though well-tolerated, are associated with side-effects if used in large quantities over a wide area due to their potent anti-inflammatory activity. The primary side-effects of topical corticosteroids include skin atrophy, telangiectasia, striae, and skin thinning.Tacrolimus exerts its effects on a broad spectrum of inflammatory mediators and processes involved in the pathogenesis of atopic dermatitis. The drug shows good percutaneous penetration and does not seem to cause atrophic changes in the skin. Several double-blind, controlled studies have established the safety and efficacy of this agent in treating atopic dermatitis. Children may particularly benefit from tacrolimus as a suitable alternative to chronic corticosteroid therapy, either topically or systemically.

Tacrolimus belongs to the macrodilute class, along with pimecrolimus, sirolimus, and cyclosporine. It is a powerful suppressor of the immune system and was initially used to prevent allograft rejection after organ transplantation. Later, the therapeutic efficacy of tacrolimus, both topical as well as systemic, was demonstrated in the treatment of inflammatory skin diseases, such as atopic dermatitis, allergic contact dermatitis, erosive mucosal lesions, and psoriasis vulgaris. Tacrolimus exerts its effects on a broad spectrum of inflammatory mediators and processes involved in the pathogenesis of atopic dermatitis. The drug shows good percutaneous penetration and does not seem to cause atrophic changes in the skin. Several double-blind, controlled studies have established the safety and efficacy of this agent in treating atopic dermatitis. Children may particularly benefit from tacrolimus as a suitable alternative to chronic corticosteroid therapy, either topically or systemically.

Clinical evidence of topical tacrolimus' efficacy in atopic dermatitis

The safety and efficacy of 0.1% tacrolimus ointment for long-term treatment of atopic dermatitis was evaluated by Refael et al, in an open-label, noncomparative study. Researchers recruited 316 adult patients with moderate to severe atopic dermatitis who were treated with 0.1% tacrolimus ointment, which was applied twice daily on all affected skin areas. The treatment did not cause any marked changes in the laboratory values. The drug was only remotely associated with an increased mean Escova Area and Severity Index score with each subsequent week/month of treatment (Figure). Table 1 presents the classification of nonsteroidal topical immunomodulators.

Table 1: Classification of nonsteroidal topical immunomodulators

| Macroantibiotics | Immunostimulators | Antihistamines | Antifungal | Vaccines
|------------------|-------------------|---------------|------------|---------|
| Tacrolimus | Immunostimulators | Antihistamines | Antifungal | Vaccines

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Mean modified Eczema Area and Severity Index score 10 5 20 30 40 50 60 20

Week 1 5 10 15 20 25 30 35 40 45 50

Day 1 5 10 15 20 25 30 35 40 45 50

Statistical significance was seen at various stages of treatment with topical tacrolimus.

There was also marked or excellent improvement or clearance of disease at these time points.

**References**