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Review Article

Atopic eczema

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The prevalence and incidence of atopic eczema , a chronic inflammatory condition of the skin is increasing worldwide. New research has shed more light on the etiology and pathogenesis of the disease and also new drugs for treatment have been recently been introduced.

One of the most common childhood skin disease atopic eczema is an acute or chronic intensely pruritic inflammatory conditions of the skin. The age of onset is generally in the first year of life in 60% of patients. (1). There are mainly two types of atopic eczema, extrinsic atopic eczema which is IgE mediated and is aggravated by external factors. It accounts for 70-80% of patients; and the intrinsic atopic eczema without IgE sensitization affects 20 to 30% of patients. (2) .The prevalence rate of the disease has been increasing recently especially in the urban areas. (3)

Epidemiology

The lifetime prevalence of atopic eczema in children is 10-20%, and a prevalence of 1-3% in adults. (3). In Europe and America, the disease has increased by two to three folds over the last three decades. An intriguing factor is the higher prevalence in developed countries and urban areas versus developing countries and rural areas. It is more common in the higher socio-economic class than in the lower class. (4)

Atopic eczema is often associated with a personal or family history of atopic eczema, asthma, and allergic rhinitis. In one series 60% of adults with atomic eczema had children with the same disease. (5)

Some eliciting factors in extrinsic atopic eczema are foods like eggs, milk, peanuts, fish, soybeans and wheat. Inhalants, especially dust mites and exotoxins of Staphylococcus aurous can induce eczema in predisposed individuals. Skin dehydration by frequent bathing, skin infections, winter season and woolen clothing in contact with skin and emotional stress are known to be exacerbating factors.

Lifestyle and environmental factors play a role in the expression of atopic dermatitis. (6) Small family, higher income and education, Western lifestyle and increased use of antibiotics are considered risk factors in developing atopic eczema (7). These findings have been supported by studies, which show that T-helper (Th) type 1 immune responses are responsible for fighting infections. T-helper (Th) type 2 immune responses are responsible for producing allergies. Since Th 1 immune responses deter the development of type 2 T helper cells, decreased childhood infections and thereby decreased type 1 immune signals may possibly predispose children to more allergies like atopic eczema. (8)

Clinical Diagnosis

The most essential features are: (9)
Marked pruritis,
Facial and extensor eczema in infants and children
Flexural eczema in adults.
Chronic or relapsing dermatitis.

Frequently associated features:
Personal or family history of atopic disease
Dry skin (Xerosis)
Frequent skin infections
Non specific hand dermatitis
Early age of onset

Other features:
Icthyosis, kertosis pilaris, pityriasis alba
Nipple eczema.
Anterior subcapsular cataracta, keratoconus
Facial erythema or pallor
Orbital darkening, Dannie- Morgan infraorbital folds
Acute skin lesions: Seen in infants and children as ill defined erythematous patches papules and plaques. Lesions may or may not be scaly; Skin appears 'puffy' and edematous. Erosions are moist and crusted .excoriations from scratching are common. Secondary skin infections like impetigo and follicular pustules are common.
Chronic skin lesions: Lichenification resulting from repeated scratching or rubbing, Follicular lichenification is more common in brown skin persons.

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The distribution of the skin rash is generally flexures, front and sides of the neck, eyelids, forehead, face, wrists, and dorsa of the feet and hands. It may be generalized in severe disease.

Presentation according to age:

Infants : The lesions are especially present on the face sparing the peri-oral area as red scaly exudative lesions with crusts and fissures. The lesions are more prominent on the extensor aspect of limbs.

Childhood and adults: The lesions are papular, lichenified plaques, erosions and crusts especially on the antecubital and popliteal fossae. Non specific hand dermatitis is also commonly seen in adult atopic dermatitis.

Differential diagnosis of Atopic Dermatitis:

Chronic Dermatosis: Seborrhoic dermatitis, Contact dermatitis, Nummular eczema, Psoriasis, Icthyosis.

Infections and infestation: Scabies, HIV-associated dermatitis, dermatophytosis

Malignant disease: Cutaneous T-cell lymphoma, Letterer-Siwe disease.

Immunological disorders: Dermatitis herpetiformis, Pemphigus foliaceous, Graft versus host disease.

Immunodeficiency: Wiskott-Aldrich syndrome, Hyper IgE syndrome, HIV infection.

Metabolic disorders: Zinc deficiency, Phenylketonuria

Pathogenesis

Great progress in understanding the disease has been made recently. In nearly all patients there is peripheral eosinophilia and raised serum IgE concentrations. And nearly 80% of children with atopic eczema have allergic rhinitis or asthma suggesting that sensitisation occurs through the skin. (10) The mononuclear cells in peripheral blood of patients have a decreased capacity to produce gamma interferon, which is inversely related to serum IgE levels. In atopic dermatitis the skin contains an increased number of IgE-bearing Langerhans cells. These cells contribute to the capture and internalisation of allergens and presenting them to naïve T-cells. Interleukin 16, a chemoattractant for CD4 T cells is present more in atopic dermatitis.

Course and Prognosis:

In more than 40% of patients with atopic eczema, spontaneous, more or less complete remission occurs during childhood. In many patients the disease persists in a less severe form. About 30 –50% of patients develop asthma and or hay fever. Adult onset atopic dermatitis runs a severe course.

Management

Successful treatment requires a careful attention to: skin care, removal of triggering or aggravating factors and topical anti-inflammatory treatment.

Skin care

The skin of patients with atopic dermatitis is very dry with increased trans- epidermal water loss due to reduced ceramide in the skin. (11). Irritants such as soaps or detergents, chemicals, alcohol and astringents and woolen clothing in contact with skin can aggravate atopic eczema. Soaps with moisturizing content and neutral pH like Dove soap and glycerine soaps are preferred .Xerosis or very dry skin causes microfissures to develop in the skin through which pathogens, allergens and chemicals can enter. The skin should be lubricated by generous application of emollients or oil on a daily basis. Emollients reduce itching and the need for topical steroids. Ordinary soaps should generally be avoided except on intertrigenous parts.

Removal of triggering factors

Skin prick tests and history can help identify allergens to be avoided. Avoidance of foods implicated in allergy tests results in clinical improvement. Most children outgrow their food hypersensitivity in a few years of life. House dust mite avoidance results in marked improvement in sensitized patients. This can be done by using dust mite proof encasings on pillows, mattresses; washing bedding in hot water weekly; removal of bedroom carpeting; and decreasing indoor humidity. (12)

Topical anti-inflammatory agents

Glucocorticoids- Topical steroids are the mainstay of atopic dermatitis treatment. They are used to control exacerbations of the disease and once control is achieved maintenance therapy with twice-weekly application of topical fluticasone to regions that have healed but are prone to develop eczema can be used. (13) Side effects from topical steroids are directly related to its potency, quantity and duration of use. Hence very high potency steroid s like clobetasol propionate and betamethasone dipropionate should be used for short periods only and are not to be used on the face or body folds. Systemic glucocorticoids should rarely be used in atopic dermatitis.

Tacrolimus Topical tacrolimus, a calcineurin inhibitor, is safe and highly effective in the treatment of atopic dermatitis.. Tacrolimus inhibits activation of several cells involved in atopic dermatitis, such as T cells, mast cells, Langerhan`s cells and keratinocytes. Trials with 0.03% and 0.1% tacrolimus

ointment have shown relief of pruritus in 3 days. Local burning sensation is the only common adverse effect. Long term studies (14) with tacrolimus ointment applied on 100% body surface have shown no major side effects. Unlike topical steroids tacrolimus ointment does not cause atrophy of the skin and has been used safely for facial and eyelid eczema. A 0.03% tacrolimus ointment has been approved for short-term and long term use in children 2-15 years of age with moderate to severe atopic eczema: and 0.03% and 0.1% for adults.

Pimecrolimus This drug has the same mechanism of action as tacrolimus and they inhibit production of Th1 and Th2 cytokines, and inhibit release of mediators from mast cells and basophils.1% pimecrolimus is effective and safe in adults and children with atopic dermatitis. (15). When used as maintenance therapy, topical pimecrolimus reduces relapse of the disease and use of topical steroids.

The development and use of tacrolimus and pimecrolimus for atopic dermatitis is a recent major development in the treatment of patients with atopic dermatitis. These drugs can be used when patients do not respond well to topical steroids and treatment of face and neck dermatitis where fear of steroid induced skin atrophy is to be considered. It can also be used for maintenance therapy. These drugs are expensive and currently are not available in the local pharmacies.

Coal Tar preparations: These were in use before topical steroids. They have some anti- pruritic and anti- inflammatory effects. Their use is however is mainly confined to chronic lesions. They must not be used in the body folds and on the face and neck, as it can cause acute irritation. Main side effects are folliculitis and photosenstivity. Coal tars are potential carcinogens, though its risks are extremely minimal in clinical use.

Management of skin infections

The skin of patients with atopic dermatitis is highly colonised or infected with *Staphylococcus aureus*. And most patients are sensitised to its exotoxins. Topical mupirocin or fusidic acid is useful in mild to moderate localised infection. In extensive superinfection, a course of systemic antibiotics such as erythromycin, cloxacillin or cephalosporins may be used.

Patients are prone to develop viral skin infections such as warts and molllusca contagiosa. Herpes simplex can present as eczema herpeticum and can be serious. The presence of punched-out erosions, vesicles, pustules that do not respond to antibiotics should be considered to be herpes simplex. Acyclovir 400mg five times a day for five days can be given.

Fungal infections are also more commonly seen in patients with atopic dermatitis and are an aggravating factor. Antibodies against *Malassezia furfur* is commonly seen especially in those with head and neck eczema. The symptoms are often relieved after treatment with antifungal agents.

Phototherapy--- Natural sunlight is often helpful in atopic dermatitis. But very hot sun and high humidity should be avoided, as it can provoke pruritus and sweating. Broad-band ultraviolet A and B and narrow-band ultraviolet B are useful adjuncts in the treatment (16). Photochemotherapy with psoralen and ultraviolet A (PUVA) should be reserved for patients with severe and extensive disease. PUVA therapy can cause skin redness, pain, pruritus and pigmentation short term and premature skin aging and skin cancers long term.

Systemic Treatment

Antihistamines----Antihistamines act by blocking the H1 receptors on dermal mast cells. They are more useful in patients having atopic dermatitis along with urticaria. As pruritus is worse at night, sedating antihistamines like hydroxyzine, diphenhydramine are useful when given at bed-time. Non sedating H1 specific antihistamines like cetirizine and fexofenadine can be given at day-time. Treatment with topical antihistamine and calamine lotions are useless and can cause sensitisation.

Systemic glucocorticoids------Its use should be discouraged as it is followed by a severe rebound flare on stopping the drug. Serious long term side effects with prolonged use make it an unacceptable drug in treating atopic dermatitis. .It may be given in a short tapering dose to control a severe flare along with topical treatment in patients who also have bronchial asthma.

Gamma interferon -It inhibits Th2 cell function, resulting in clinical improvement. (17). Side effects like fever, headaches and flu like symptoms limit its use.

Ciclosporin It is a strong immunosuppressive drug that acts mainly by suppressing T cells. Patients who do not respond to the conventional treatment can be given this drug on a short-term basis. (18) But patients often relapse on stopping the treatment. Ciclosporin can raise serum creatinine levels, impair the kidneys and raise the blood pressure

Chinese herbal therapy Results of several studies have shown clear evidence of benefit from treatment with Chinese herbal therapy. (19)

Psychological Counseling Patients often respond to frustrations, and stressful events by increased pruritus and scratching. Stress can cause immunological changes in such patients. (20) Psychological counseling should be considered in such patients. Relaxation, behavior modification can be helpful in-patients with habitual scratching.

Future research

Research is needed to identify the genes leading to atopic dermatitis and a better understanding of the immunoregulatory mechanism underlying the disease. Research into new ways to prevent relapse, and development of highly effective, safe and cost-effective drugs to control the disease is needed.

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