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Dermatology

ATOPIC DERMATITIS – AN OVERVIEW

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ABSTRACT Atopic dermatitis is a chronic relapsing inflammatory skin disorder with a complex pathogenesis involving genetic susceptibility, immunologic and epidermal barrier dysfunction, and environmental factors. Pruritus is a primary symptom; skin lesions range from mild erythema to severe lichenification to erythroderma. Diagnosis is by history and examination. Treatments include counseling on appropriate skin care, avoidance of triggers, and topical corticosteroids and immunosuppressants. Control of pruritus and superinfections is also important. Severe cases may require systemic immunosuppressive treatment. Childhood atopic dermatitis frequently resolves or lessens significantly by adulthood.

KEYWORDS :

DEFINITION

The term atopic dermatitis describes an inherited, chronic, relapsing pruritic skin condition of xerosis and inflammation, associated with numerous pharmacologic and immunologic abnormalities including a tendency to overproduce specific IgE (reagins) in response to common environmental antigens.

Genetic Predisposition

There is a strong family history of associated atopic diseases in families of patients with AD. In a study of AD patients there was a 58 percent family history of atopic diseases, whereas in the control group the incidence was 32 per cent.[1] If one parent has an atopic diathesis, there is a 60 percent chance of the child being atopic, and the figure increases to 80 percent if both parents are affected. [2]. In non-atopic families the likelihood of having an atopic child is 19 percent [3]. The mode of inheritance is not entirely clear, but appears to be polygenic

History and Physical Examination

AD is usually the first manifestation of atopic disease and presents in 85 percent of cases during the first year of life, usually around 3 months of age, and in 38 percent of cases even earlier.[4] In 95 percent of cases, the disease develops by 5 years of age[5]

Hill and Sulzberger characterized three distinct clinical phases of AD, in which both the site and the morphology of the lesions change with age. These phases may overlap or be separated by a period of remission. The sites of predilection have been confirmed by studies [6], the infantile phase occurs up to 2 years of age; the childhood phase from age 2 to puberty; and the adult phase from puberty onward.

The characteristic and most important symptom and the major cause of morbidity in AD is pruritus, which may be unbearable and often interferes with normal sleep patterns. Infants will often claw at their skin and rub themselves against hard objects. Some physicians believe that there is no primary lesion of AD, and that the major clinical picture is the result of scratching. Jacquet is quoted as saying that AD is " an itch that rashes " as opposed to a rash that itches. [7] However, one frequently sees erythematous eruption may in infants before the " itch-scratch " mechanism develops, which is usually at 3 months of age. This is also the time that parents become aware of the disease, although many of the features may be present much earlier.

The eruption in infancy characteristically starts on the cheeks and scalp, but often involves the lateral aspects of the extensors of the lower legs [8]. Other areas are also involved although the diaper area is often spared. The lesions are usually symmetric, ill-defined, erythematous plaques with areas of crusting. Generalized xerosis including dry hair and scalp is a major feature and is most helpful in establishing the diagnosis.

In the childhood phase, the flexural areas are the sites of predilection. The antecubital and popliteal areas are most commonly affected, with the neck, flexures of the wrists and ankles, and the buttock-thigh crease also commonly involved. These areas are particularly prone to sweating. This contrasts with the infancy phase where the extensors are mainly affected. The lesions are pruritic, ill-defined, erythematous, scaly patches, often studded with crusts and excoriations. This is the time lichenification first manifests.

Associated Findings

- Ichthyosis vulgaris mainly affecting the lower legs occurs in 20 percent to 37 percent of patients with AD[9]
- Keratosis pilaris is a condition that is seen on the extensor aspect of the upper arms, back and anterior thighs of patients with AD. In young children these findings are also often seen on the lateral aspects of the cheeks and are often mistaken for childhood acne.
- Pityriasis alba is found in both normal children and those with AD. It is identified by hypopigmented patches on the cheeks, particularly toward the end of summer when the rest of the face is tanned.
- The Dennie -Morgan fold is a double line found under the lower eyelid of patients with AD and may be present at birth or soon thereafter.
- Eye findings include keratoconjunctivitis, which may occur in painful form known as vernal conjunctivits. Pruritus and photophobia were the most common findings in over 200 patients studied by Gelmetti. Cataracts, which may be anterior or posterior subcapsular, have been described in more severe cases in up to 13 per cent of patients. Keratoconus does not occur before adolescence and was not seen in the study by Gelmetti.[10]

Three other conditions are alleged to be variations of AD but may also occur independently of the disease: dyshidrotic eczema, nummular dermatitis, and juvenile plantar dermatosis.

Dyshidrotic eczema consists of vesicles on the palms and soles, and is associated with hyperhidrosis in many cases. The lesions consist of small, pruritic, multiloculated vesicles along the side of the fingers and toes and on the palms and soles, resembling " **sago grain vesicles**". These rupture leaving crusts and scaling with erythema. This condition is difficult to distinguish from an Id reaction or a fungal infection, but the latter tends to be unilateral.

Nummular dermatitis is so named because of its coin-shaped configuration. Well-demarcated, scaly lesions with variable erythema identify it. It occurs more frequently in older people, often affecting the lower legs and is thought to be a result of xerosis. In children nummular exudative lesions occur with AD, although they are also seen in children with no other stigmata of the disease; they are fairly resistant to standard treatment and may be recurrent.

Juvenile plantar dermatitis (JPD) is seen before puberty and presents with scaling, cracking, and painful fissuring on both feet. The big toe and heel are often involved. The problem seems to be much worse when wearing rubber soles, sneakers, and plastic boots and is often worse in the winter when these occlusive footwear and nylon socks are worn. Now that sneakers are worn both in summer and winter, the condition often persists in the summer months. It is frequently worse in atopics.[11]

(See Figures 1 to 10)

Diagnostic Clinical Features in Atopic Dermatitis

Essential features
Pruritus Dermatitis (eczema)—acute, subacute, or chronic, with • Typical age-specific patterns† • Chronic or relapsing history
Important features

Early age of onset
Personal or family history of atopic disease
IgE reactivity
Xerosis
Associated features (help to suggest the diagnosis)
White dermatographism
Keratosis pilaris
Pityriasis alba

Complications of Atopic Dermatitis

Children with AD have a tendency to develop viral and bacterial skin infections. The causes of the viral infections are usually limited to herpes simplex and vaccinia and are known as eczema herpeticum and eczema vaccinatum, or as Kaposi's varicelliform eruption.

Other viral infections, verrucae [12] and mollusca contagiosa [13] have been thought to be more common in AD.

Patients with AD have significant ***S.aureus*** colonization on their skin. Aly found ***S.aureus*** colonization in 93 per cent of involved skin and in 76 percent of uninvolved skin.[14] In contrast, ***Staphylococcus*** colonizes only 20 percent of involved skin in psoriatic patients and less than 10 per cent on the skin in the normal population. It has been questioned whether ***S.aureus*** may initiate the whole eczematous process.

Laboratory diagnosis

For a long time, absolute eosinophil counts, and serum IgE levels were useful laboratory markers of atopy. This is no longer tenable, though.

More recent biomarkers include serum thymus and activation-regulated chemokine (TARC), cutaneous T-cell-attracting chemokine (CTACK) and squamous cell carcinoma A (SSCA).

Many studies have been conducted to validate these biomarkers. [15]

Differential Diagnosis

The differential diagnosis of AD includes other eczematous disorders: scabies, seborrheic dermatitis, contact dermatitis and psoriasis.

AD may be so severe that the whole body becomes erythrodermic. It is important to distinguish this from other causes of erythroderma. These include epidermolytic hyperkeratosis, Netherton syndrome, psoriasis, pityriasis rubra pilaris, nutritional deficiencies, and most important, drug eruptions. Other diseases that manifest eczematous lesions include the following: -

1. Acrodermatitis enteropathica
2. Agammmaglobulinemia
3. Ahistidinemia
4. Ataxia telangiectasia
5. Gluten-sensitive enteropathy
6. Hartnup's disease
7. Histiocytosis-X
8. Hurler syndrome
9. Leiner's disease
10. Phenylketonuria
11. Prolidase deficiency
12. Wiskott-Aldrich syndrome

Prognosis and Course of the Disease

AD is a disease of exacerbations and remissions. Most patients tend to improve with age. Data from follow-up surveys show variable results owing to their completely different patient sampling. In general, the more severe and long lasting the AD, the more likely it is that the disease will persist on to adult life. One follow-up study showed persistence during adult life in approximately 70 per cent of patients with severe AD and 60 per cent with milder disease [16].

Asthma develops in many patients with AD.[17]. AD tends to develop somewhat earlier than asthma, but there are still many cases of asthma that develop in the first year of life.

Allergic rhinitis develops in 25 per cent of AD patients[18].

Management

General Measures

The most important aspect of the treatment is to establish an honest, trusting relationship with the parents, explaining the nature of the disease, particularly stressing that treatment is aimed at good control of the pruritus and eczematous lesions, but that cure is not possible. A distraught, guilt-ridden mother with a sleepless child who is unable to stop scratching needs calm assurance.

Specific measures

Topical Treatment: - At present until the basic defect is recognized and can be rectified, the mainstay of management is to treat the inflammation, dryness and itch. The inflammation is best treated with corticosteroid ointments. Potent corticosteroids should never be used on the face where hydrocortisone 1 per cent ointment three times a day is very effective. This should be used until improvement occurs and then withdrawn. The ointment base acts as an emollient for the dry skin, but a cream may be substituted in very humid weather and if troublesome folliculitus occurs.

In the majority of children with AD there is no deleterious effect from the use of topical corticosteroids. Rarely serum cortisol levels may be depressed but return to normal as soon as the inflammation is under control, which is often less than a week. Growth delay is a much more difficult problem to assess as the disease itself may impair growth.

The xerosis is treated with emollients rather than corticosteroids. Numerous emollients are available, some containing urea. Parents should be warned only to apply urea products when the skin is moist, because burning and irritation may otherwise occur. Urea-containing products are usually too strong to use on the face. These compounds are difficult to mix and should be heated prior to incorporation into the vehicle. The dryness is best treated with a bathing regimen using agents such as nonperfumed bath oils or oilated oatmeal powder to soothe the skin. Bathing should take only 5 minutes as dehydration of the skin may occur if continued longer. Long showers are contraindicated because of their drying effect. In this age it is no longer acceptable for children not to bathe, and if oilating agents are used, hydration of the skin instead of dehydration results. After bathing, the child should be dried lightly so that an oily film is left on the skin. The dry but noninflamed areas of skin are covered with a lubricating ointment such as Vaseline or 10 per cent urea while damp, and after corticosteroids are applied to the inflamed areas. Soaps may be eliminated completely as the oils contain cleansing agents, or mild nonperfumed soap may be used.

Antihistamines, such as hydroxyzine hydrochloride [19] in an appropriate dosage may alleviate the incessant itch and allow the patient some peaceful hours of sleep. The combination of H1 and H2 antihistamines does not appear to be more useful. [20] Recently, less sedating antihistamines have been used, but proof of their specific usefulness over traditional antihistamines and placebo has not been shown

Many physicians find oral antibiotics useful in treating recalcitrant lesions. Dhar et.al.[21] found a reduction in colony count and clinical improvement in patients treated with oral erythromycin and cloxacilin. Antibiotics are of obvious value in infected lesions and in preventing secondary infection in widespread Kaposi's varicelliform eruption.

Systemic corticosteroids have been found to control particularly severe exacerbations, but in view of the multiple side effects and an unwanted rebound flare when they are discontinued, they are rarely indicated. In the occasional case where they are used as a last resort, a 2-week tapering dose should be used. Prednisolone is given as 1 mg /kg/day for 4 days. 0.75 mg/kg/day for 4 days, 0.5mg/kg/day for 4 days, after which the medication is stopped. It should be stressed that continued use of systemic corticosteroids is unwarranted and dangerous.

As our understanding of the pathogenesis of the disease increases, newer agents are being used with variable success.

UV Light

It has been known for many years that lesions improve in the summer months. There are now numerous studies defining the benefits from exposure to both UVA and B. [22]

Cyclosporine - In recent years oral cyclosporine have been used in the treatment of AD. Vanjoost et.al noted a clinical improvement in seven adult patients with severe disease by using oral cyclosporine.[23]. After discontinuing the drug, the lesions returned.

Chinese Herbs - Sheehan and Atherton administered Chinese herbs to 37 children with widespread AD and found a good response over placebo, with few side effects except in palatability. Another blinded,

crossover study in adults showed improvement in erythema, itch and sleeplessness. The decoction consists of 10 different herbs although they are variously formulated depending on the individual patient. The major side effect has been the unpalatability of the medication.[24] The mechanism by which these herbs produce improvement is not known.

Other therapies

Topical tacrolimus and pimecrolimus are calcineurin inhibitors. They are T-cell inhibitors and can be used for mild to moderate atopic dermatitis or when corticosteroid adverse effects are a concern. Tacrolimus ointment or pimecrolimus cream is applied 2 times a day. Burning or stinging after application is usually transient and abates after a few days. Flushing is less common.[25,26]

Crisaborole 2% ointment is a topical phosphodiesterase-4 inhibitor. It can be used for mild to moderate atopic dermatitis in patients 2 years of age or older. Crisaborole is applied to areas of eczema 2 times a day. It cannot be used on mucous membranes. Burning or stinging after application is the most common adverse effect.[27,28]

Dupilumab is a fully human monoclonal IgG4 antibody that blocks the signaling of IL-4 and IL-13, both proinflammatory Th2 cytokines, in atopic dermatitis. It is given subcutaneously as a 600-mg loading dose, followed by 300 mg every 2 weeks; for patients weighing < 60 kg, a 400-mg loading dose is followed by 200 mg every other week.[29] Dupilumab is available for the treatment of moderate to severe atopic dermatitis in patients 6 years and older and is recommended for patients whose disease is not adequately controlled with other treatments. Several more targeted systemic immunosuppressants (biologics) are in development for atopic dermatitis.

Antistaphylococcal antibiotics, both topical (e.g., mupirocin, fusidic acid, ozenoxacin) and oral, are used to treat bacterial skin superinfections, such as impetigo, folliculitis, or furunculosis. *Staphylococcus aureus* is the most common bacterium causing skin infections in patients with atopic dermatitis and is often resistant to methicillin (methicillin-resistant *S. aureus* [MRSA]).[30] Doxycycline or trimethoprim/sulfamethoxazole is a good initial choice of systemic antibiotic because MRSA is most often sensitive to these drugs. However, bacterial cultures with resistance testing are recommended before starting systemic antibiotics because resistance cannot be predicted. Nasal mupirocin is recommended for patients who are nasal carriers of *Staphylococcus aureus*, a potential source of recurrent impetiginization.

Key Points

- Atopic dermatitis is common, particularly in developed nations, affecting up to 20% of children and 10% of adults
- A genetically determined skin barrier defect predisposes to inflammation with skin irritants and thus atopic dermatitis
- Common triggers include excessive washing and bathing
- Common findings vary with age and include pruritus and scaly erythematous patches and plaques and lichenification in the antecubital and popliteal fossae and on the eyelids, neck, and wrists
- Superinfections (particularly *S. aureus* infections and eczema herpeticum) are common
- Atopic dermatitis frequently resolves or lessens significantly by adulthood
- First-line treatments include moisturizers, topical corticosteroids, and antihistamines as needed for pruritus
- For disease unresponsive to topical therapy, consider phototherapy or systemic immunosuppressants

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