Natural History and Risk Factors of Infantile Atopic Dermatitis: A Case Report and Literature Review

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Citation : Christopher Paulus Mario , Hung Maggie Stella. Natural History and Risk Factors of Infantile Atopic Dermatitis: A Case Report and Literature Review
Medicinus. 2019 October; 7(7):229 – 235
Keywords : Atopic dermatitis, infant, risk factors
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Online First : October 2020

Abstract

Atopic dermatitis (AD) or atopic eczema is one of the most common forms of pediatric dermatological skin conditions, primarily beginning in childhood with a variable natural course characterized by intense pruritus and eczematous lesions. This condition requires multifactorial interplay and risk factors to explain the pathogenesis. We hereby report a case of a two-month-old male who presented with widespread erythematous lesions, excoriations, and dry skin since one day before admission. The antenatal history showed use of antibiotics during pregnancy, familial history of atopy, and non-exclusive breastfeeding which are all known risk factors. Dermatological examination revealed skin phototype III with diffuse erythematous patches scattered on the face, trunk, upper and lower limbs, and groin followed with excoriations and palmar hyperlinearity. Further laboratory and histopathological examinations were not conducted. The patient was treated with topical corticosteroid and emollients, resulting in a notable improvement without any further flares. A thorough history taking and physical examination must be conducted to establish the diagnosis based on the Hanifin and Rajka criteria and identify risk factors such as genetic factors, impaired skin barrier, and environmental factors and microbial exposure, which may play a protective or harmful role in AD development. Holistic treatments consist of pharmacological and non-pharmacological treatments, with significant emphasis on education to the patient and caregiver(s) to improve quality of life and prevent exacerbations and infectious complications while minimizing potential medication side effect

Introduction

Atopic dermatitis (AD) is a chronic, relapsing-remitting inflammatory skin disease characterized by pruritic eczematous lesions. The pathogenesis of AD is multifactorial consists of immune dysregulation, genetic susceptibility, environmental factors, and impaired barrier function.[1] With an estimated global prevalence of nearly 230 million, AD is considered one of the most common chronic conditions.[2] AD affects 10-20% of children and roughly 60% of cases manifested during the first year of life, posing a significant burden on health-care resources and patients' quality of life.[3] In developing countries, AD prevalence appears to be increasing, likely due to an increase in urbanization, pollution, Western diet consumption, and obesity.[4]

This report describes a case of a two-month-old male with a diagnosis of AD. Owing to the peculiarity and risk factors of the case, it serves as a unique opportunity to present the risk factors interplaying in the pathogenesis leading to the development of the disease.

Case Illustration

A two-month-old male brought to the emergency department presented with generalized erythematous macules, excoriations, and dry skin first appeared one day before admission. The macules started on the patient's cheeks spreading to the trunks, upper and lower limbs, and groin area. The patient cried inconsolably during scratching episodes, particularly during night time. The patient was born full-term at 40 weeks and two days by vaginal delivery with a birth weight of 3000 grams. Pregnancy was complicated due to intrauterine infection necessitating the use of oral antibiotics. Nutritional history revealed non-exclusive breastfeeding with the use of formula milk due to parents' concern of inadequate breast milk. Growth and development and immunization history were unremarkable. He has non-consanguineous Balinese parents and there was a history of similar illness in the family from the mother (atopic dermatitis). The personal hygiene of the baby was maintained with regular twice-daily baths with baby soap.

The physical examination comprising of vital signs and general examination were within normal limit. Nevertheless, dermatological examination showed skin phototype III with diffuse erythematous patches scattered on the face, trunk, upper and lower limbs, and groin followed with excoriations and palmar hyperlinearity (Figure 1). A skin biopsy and laboratory examinations were not performed due to the disapproval of the parents.

Diagnosis of infantile AD was concluded based on the history taking and physical examination following Hanifin and Rajka criteria. The patient was given hydrocortisone 2.5% cream q12hr and emollient of urea 10% q12hr. Appropriate education was discussed with the patient's family. After one week of treatment, the condition has improved and resolved with no further flare noticed.

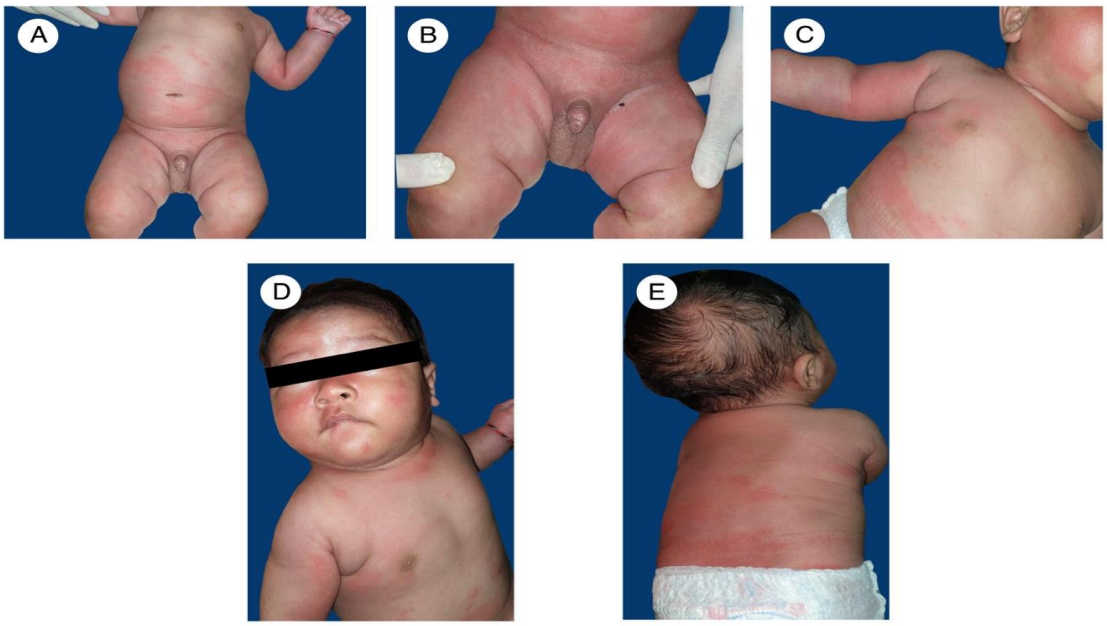

Figure 1. Clinical appearance and dermatologic findings of the patient where diffuse erythematous patches were observed over the face, trunk, upper and lower limbs, and groins area (A-E)

Discussion

In this case, we presented a case of the first flare episode of AD in a previously healthy young baby. The case represented several proposed risk factors of developing atopy, subsequently manifesting as AD. These risk factors are 1) genetic factors, 2) impaired skin barrier function, and 3) environmental factors and microbial exposure (**Figure 2**).[5, 6]

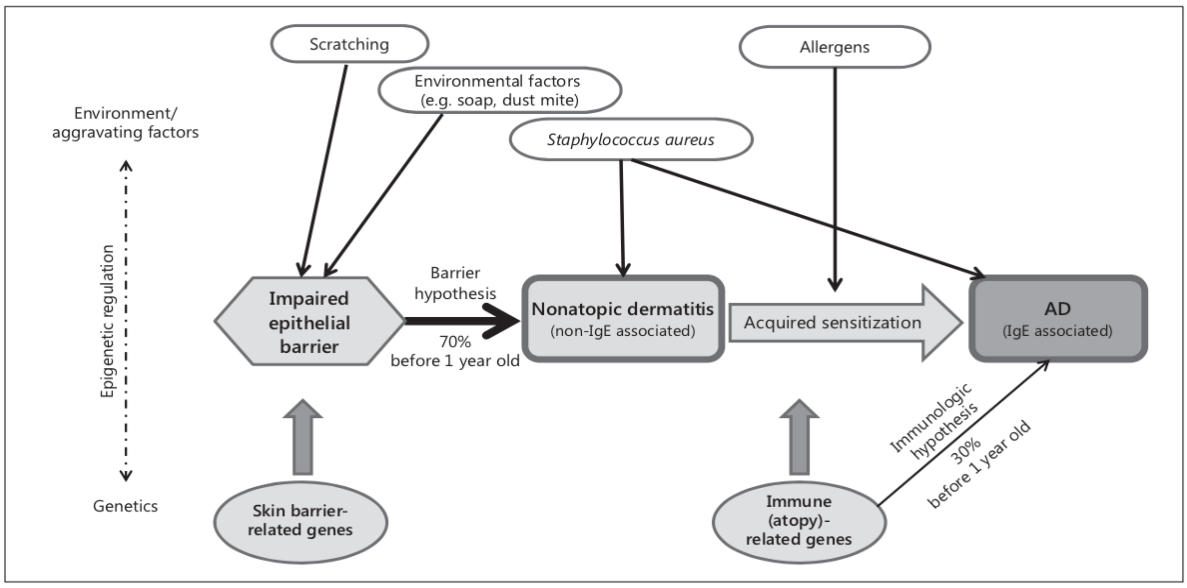

Figure 2. Risk factors contributing to the natural history of AD[5]

Genetic factors serve as an essential risk factor for AD in which positive parental history in AD patients and in twin studies showed a higher concordance rate in monozygotic twins compared to dizygotic twins. Genetics also plays a role in filaggrin (FLG) gene encoding the epidermal barrier protein, filaggrin, in which it is reported that loss-of-function mutations and downregulation of FLG lead to impairment of barrier function.[6, 7]

Essentially, an intact epidermal is needed for the skin to function as a physical and chemical barrier. The genetically altered epidermis or lipid composition prevented the skin barrier function leading to dysfunction and inflammation. Additionally, altered epidermal barrier allows easier and complemented environmental allergen penetration through the skin, facilitating the recognition of the allergens with the local antigen-presenting cells and immune effector cells leading systemic immunoglobulin E sensitization and transition from the non-atopic state to the atopic state of the disease. The defective skin barrier in AD also predisposes to colonization or infection by pathogenic microbes whose exogenous proteases can also further damage the skin barrier[5, 7]

Lastly, environmental factors and microbial exposure shared its role as a risk factor in which it was found that environmental risk factors such as climate, urban versus rural setting, diet, breastfeeding and time of weaning, obesity and physical exercise or tobacco smoke and pollution have been proposed (**Table 1**).[5]

Table 1**.** Environmental risk factors for AD[5]

Factor	**Associated Effect**
Climate	
Low outdoor temperature	Increased risk
UV light exposure	Protective
Urban vs. rural setting	Increased risk
Diet	
Fresh fruits	Protective
Fish (During pregnancy)	Protective
Fast-food	Increased risk
Breastfeeding	Protective
Delayed weaning	Increased risk
Obesity	Increased risk
Pollution/tobacco smoke	Increased risk

Exclusive breastfeeding and avoidance of complementary feeds during the first 3-4 months of life have shown a protective risk against atopic dermatitis during infancy and childhood asthma, but not in later life.[8] Association between atopy and exposure of cigarette smoke during in utero and early childhood is not yet clear, but exposure to parental smoking increase risk of AD and early childhood wheeze.[8-10] Obesity plays a role in the immune system that modulates the severity of the atopic disease. The retrospective case-control pediatric cohort study demonstrated that obesity persisting more than five years and starting early in life (before 5) is associated with increased risk for AD and AD severity.[6]

Studies also suggested that microbial exposure could play its part in the development of AD. Antenatal antibiotics exposure associated with increased risk of AD in a dose-related manner.[10] Postnatal antibiotics exposure in a meta-analysis study estimated increased odds of AD in children. It also plays a role in microbiota changes, knowing that the microbiota takes part in the immune response. In addition, skin microbiota is also found to be involved in the homeostasis of the immune system of skin and may also have an impact on AD.[5] While a study suggests an association between the skin microbiome and AD, it remains unknown whether dysbiosis of the skin directly causes AD or simply reflects the impaired epidermal barrier and immune dysregulation of AD.[10] These risk factors further support the underlying immune mechanisms in AD.

Immunopathogenesis of AD involved alteration of the innate and adaptive immune system. In AD, a decrease in the antimicrobial peptides has been observed and may contribute to the susceptibility towards infections in AD patients. A biphasic inflammation also characterizes immune response in AD, in which a Th2-biased immune response (Interleukin [IL]-4, IL-13, thymic stromal lymphopoietin [TSLP], and eosinophils) is predominant in the initial and acute phase of AD. In contrast, in chronic AD skin lesions, a Th1/Th0 dominance has been described (interferon [IFN]-γ, IL-12, IL-5, and granulocyte-macrophage colony-stimulating factor [GM-CSF]). Additionally, a lesional and healthy skin of AD patients is frequently colonized with *Staphylococcus aureus* which exacerbates or aggravates skin lesions.[5]

Dermatological manifestations of AD are characterized by multiple erythematous papulovesicles with distribution varying following with the patient's age and disease activity. Based on age, AD can be classified into three groups, infancy (0-2 years), older childhood (2 years-puberty), and adulthood. Collectively, with the history taking, dermatological manifestation, age of manifestation, and/or supportive examinations and in unison based on Hanifin and Rajka criteria, AD can be diagnosed.[7]

Management of AD is based on the five pillars of therapy constituting of 1) education and empowerment of patients and caregiver(s), 2) avoidance and modification of environmental trigger factors, 3) rebuilding and maintenance of optimal barrier function, 4) clearance of inflammatory skin disorders and 5) control and elimination of the itch-scratch cycle.[11]

Education plays a vital role in the management of AD in which physicians must emphasize the importance concerning the disease, therapy (why and how to take care of the skin), trigger factor, and prognosis. AD skincare routine involved bathing using lukewarm water, no longer than 10 minutes, using non-soap cleansers (low pH, hypoallergenic, and fragrance-free). Moisturizers should be applied soon after bathing to improve skin hydration as the application of moisturizers showed strong evidence that their use can reduce disease severity and the need for pharmacologic intervention. Type of moisturizers contained humectant(s),

emollient(s), and occlusive(s) or newer generation containing anti-inflammation and anti-pruritus (glycerrhectinic acid, temestein, and vitis vinifera) or containing physiological component (lipid, ceramide, natural moisturizing factor).[11-14]

Avoidance of triggering factors based on history taking (irritant(s), allergen(s), extreme temperature, food, stress), clinical manifestation, and allergic panel test results. Rebuilding and maintenance of optimal barrier function can be achieved through the application of moisturizer after bathing, carried out throughout every phase of the disease.[11, 13]

Clearance of inflammatory skin disorders can be achieved through the application of corticosteroid. Corticosteroids can be prescribed for manifesting AD as reactive therapy (twice-daily application) or for subclinical AD as proactive therapy. As for maintenance therapy, the corticosteroid can be applied to hot spots as weekend therapy (1-2 times per week). Nevertheless, care should be appropriately addressed to the potential side effects for both topical and systemic corticosteroids, including possible hypothalamic-pituitary-adrenal axis suppression, particularly in children with AD in whom corticosteroids are used. Control and elimination of the itch-scratch cycle can be managed through the use of sedative antihistamine for babies and children, or non-sedative antihistamine as adjuvant therapy for life pruritus.[11-13] Nevertheless, the prognosis of AD is unpredictable due to the nature of the disease and the risk factors interplaying in its course.[15, 16]

Conclusion

Atopic dermatitis is a multifactorial, chronic inflammatory and heterogenous dermatological disorder resulting from the interplay between genetic, immune, and environmental factors. Advancement in the understanding between risk factors, pathogenesis, and five pillars of AD therapy expectantly will aid for a better holistic and comprehensive approach among physicians treating AD.

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