Diagnostic Standard for Atopic Dermatitis

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Abstract: For a dermatologist, the diagnosis of atopic dermatitis (AD) is relatively easy. In view of the fact that the increase and exacerbation of AD, confusion over its treatment and prevalence of abundant but not necessarily correct information are creating social issues in Japan, diagnosis and treatment of AD based on precise cognition are extremely important. While Hanifin and Rajka's diagnostic standard is known worldwide, a standard that is easily appreciated and handy for use by non-dermatologists is needed as many AD patients are being treated in departments of pediatrics, allergy, etc. In this context, the diagnostic standard established by the Japanese Dermatological Association is quite meaningful. By comparing the standard with other previously published diagnostic standards, this paper discusses in detail the main items of "pruritis", "exanthematous features and their distribution" and "chronically relapsing course", and emphasizes differential and exclusion diagnoses.

Key words: Atopic dermatitis; Diagnostic standard; Pruritis; Differential diagnosis

Introduction

Atopic dermatitis (AD) is diagnosed with relative ease based on its clinical symptoms regardless of sex or age of the patients. But not all the diagnoses are correctly rendered. The concept of AD proposed by Wise *et al.* (Table 1)[1] in 1933 has been accepted worldwide, and AD is now defined as "a disease mainly consisting of eczematous lesions with itch, following the course of exacerbations and remissions, and many of the patients have

Table 1 Concept of AD by Wise and Sulzberger[1]

(1)	Family history of atopic diseases
(2)	Preceded by infantile eczema
(3)	Localization to cubital and popliteal fossae, forehead, anterior thorax and face, particularly eyelids
(4)	Presence of gray to brownish skin
(5)	Absence of clinical and histological vesicles
(6)	Instability or easy irritability of vasomotor nerves
(7)	Patch tests with many irritating contact substances are usually negative
(8)	Instant positive wheal reaction against many scratch or intradermal tests
(9)	Presence of much serum regains

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Table 2 Definition and Diagnostic Criteria for Atopic Dermatitis by The Japanese Dermatological Association

Definition

Atopic dermatitis is a pruritic, eczematous dermatosis, the symptoms of which chronically fluctuate with remissions and relapses. Most individuals with atopic dermatitis have atopic diathesis.

Atopic diathesis: (1) Personal or family history (asthma, allergic rhinitis and/or conjunctivitis, and atopic dermatitis), and/or (2) Predisposition to overproduction of immunoglobulin E (IgE) antibodies.

Diagnostic Criteria for Atopic Dermatitis

1. Pruritus
2. Typical morphology and distribution:
   (1) Eczematous dermatitis
   - Acute lesions: erythema, exudation, papules, vesiculopapules, scales, crusts
   - Chronic lesions: infiltrated erythema, lichenification, prurigo, scales, crusts

   (2) Distribution
   - Symmetrical
     Predilection sites: forehead, periorbital area, perioral area, lips, periauricular area, neck, joint areas of limbs, trunk
   - Age-related characteristics
   * Infantile phase: starts on the scalp and face, often spreads to the trunk and extremities
   * Childhood phase: neck, the flexural surfaces of the arms and legs
   * Adolescent and adult phase: tendency to be severe on the upper half of body (face, neck, anterior chest, and back)
3. Chronic or chronically relapsing course (usually coexistence of old and new lesions):
   * More than 2 months in infancy
   * More than 6 months in childhood, adolescence, and adulthood

Definite diagnosis of atopic dermatitis requires the presence of severity. Other cases should be evaluated on the basis of the clinical course with the tentative diagnosis of acute or chronic, non-specific eczema.

Differential Diagnosis

- Contact dermatitis • Seborrheic dermatitis • Prurigo simplex • Scabies • Miliaria • Ichthyosis
- Xerotic eczema • Hand dermatitis (non-atopic)

Diagnostic Aids

- Family history (bronchial asthma, allergic rhinitis and/or conjunctivitis, atopic dermatitis)
- Complications (bronchial asthma, allergic rhinitis and/or conjunctivitis)
- Follicular papules (goose-skin)
- Elevated serum IgE level

Clinical Types (not applicable to the infantile phase)

- Flexural surface type • Extensor surface type • Dry form in childhood • Head · face · upper neck · upper chest · back type
- Prurigo type • Erythroderma type • Combination of various types are common

Significant Complications

- Ocular complication (cataracts and/or retinal detachment): especially in patients with severe facial lesions
- Kaposi's varicelliform eruption
- Molluscum contagiosum
- Impetigo contagiosa

atopic predisposition."[2] AD is, however, a complex inflammatory disease with Type I and IV allergies combined in a complicated manner, and not all the patients have atopic predispositions. In view of these points, it is necessary to recognize that AD is clearly different from other atopic diseases such as bronchial asthma and allergic rhinitis.

As the increase and exacerbation of AD, confusion over its treatments, and abundance of not necessarily correct information over AD are creating social problems today, the diagnosis and treatment based on precise cognition of AD is extremely important. As many AD

patients are being treated in non-dermatology departments such as pediatrics and allergy, a diagnostic criterion that is easily appreciated and handy for use by non-dermatologists is needed, and the significance of the diagnostic standard prepared by the Japanese Dermatological Association (Table 2)[2] is quite meaningful in this context.

Particular attention should be paid, however, to "diagnoses for exclusion" in the standard. Even after seven years since its publication, we often encounter patients with contact dermatitis caused by external preparations and non-drugs that have been prescribed for treatment purposes, or those whose AD has become exacerbated by non-drugs.[3] A physician unable to diagnose eczema lesions accurately by differentiating them as true AD lesion or complication of contact dermatitis is not qualified to diagnose AD.[4,5]

I would like to discuss the diagnostic standards of AD, its clinical features, and useful items for diagnosis.

Diagnostic Standards[4,5]

Several standards and guidelines for the diagnosis of AD have been published, all of which are substantially the same as the disease concept of AD published by Wise *et al.*[1] (Table 1). Rajika published the diagnostic standard of AD in 1961 for the first time in the world. Although it is somewhat insufficient from the contemporary standpoint, its historical significance is enormous.

In 1977, Hanifin *et al.* cited three essential features of (1) pruritis, (2) typical morphology and distribution of eruptions, and (3) chronic course of dermatitis. They further cited 13 features related to Type I allergy, physiological functions of the skin and complications, divided them roughly into two groups (four and nine), and proposed to diagnose AD when the patient meets two out of the four features of the former group or at least four out of nine of the latter group.

Table 3 Diagnostic Standard of Hanifin & Rajika[6]

1. Must have three or more basic features described below
   (1) Pruritus
   (2) Typical morphology and distribution
   Flexural lichenification in adults
   Facial and extensor eruptions in infants and children
   (3) Chronic or chronically relapsing dermatitis
   (4) Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis)

2. Must have three or more following minor features:
   (1) Xerosis
   (2) Ichthyosis/palmar hyperlinearity, keratosis pilaris
   (3) Immediate (type I) skin test reaction
   (4) Elevated serum IgE
   (5) Early age of onset
   (6) Tendency toward cutaneous infections (especially *staph. aureus* and *herpes simplex*), impaired cell-mediated immunity
   (7) Tendency toward non-specific hand or foot dermatitis
   (8) Nipple eczema
   (9) Cheilitis
   (10) Recurrent conjunctivitis
   (11) Dennie-Morgan infraorbital fold
   (12) Keratoconus
   (13) Anterior subcapsular cataracts
   (14) Orbital darkening
   (15) Facial pallor, facial erythema
   (16) Pityriasis alba
   (17) Anterior neck folds
   (18) Itch when sweating
   (19) Intolereance to wool ad lipid solvents
   (20) Periofollicular accentuation
   (21) Food intolerance
   (22) Course influenced by environmental and emotional factors
   (23) White dermographism, delayed blanch

In 1980, Hanifin and Rajka modified and combined their respective standards and proposed a new diagnostic standard (Table 3).[6] This standard cited the essential three features of Hanifin plus the individual or the family history of atopic disease as an essential feature, and proposed to diagnose AD when the patient meets at least three of these four items and also at least three of 23 minor features. This diagnostic standard is being relied on worldwide today, but many minor features are somewhat tedious. These minor features are being re-

examined currently, and we also reported the significance of infra-auricular fissures (fissures of the ear) in diagnosing AD.[7)]

Subsequently, the American Academy of Dermatology has published the diagnostic standard for AD, which is substantially the same as that of Hanifin & Rajika.[6)] Firm diagnosis of infantile AD is quite difficult and should be studied further. Seymour *et al.* reported a revised version of Hanifin & Rajika's standard[6)] for infants younger than 20 months old. The standard by the Japanese Dermatological Association[2)] notes that chronically relapsing course lasting at least two months as the basis for diagnosing infantile AD.

In Japan, the standards published so far include those of Masuda, of Hongou, of Uehara *et al.*, and more recently "Guideline for diagnosis of atopic dermatitis" of the Japanese Ministry of Health & Welfare (MHW).[4,5)]

The standard of Uehara *et al.* is quite concise as it cites (1) unique clinical picture and (2) chronic course repeating the seasonal cycle of exacerbations and remission, and is easy to understand by dermatologists who have precise cognition of clinical picture of AD. MHW's guidelines were prepared not necessarily for physicians only, have problems in the science of dermatology, and may mislead diagnoses of all eczema lesions in infants as AD.

The diagnostic standard for AD (Table 2) deliberated by the Academic Committee of the Japanese Dermatological Association[2)] cites (1) pruritis, (2) exanthematous features and their distribution, and (3) chronically relapsing course as the three features that should be manifested for diagnosing AD. The standard is concise and focuses on clinical symptoms of eruptions. Eight diseases such as contact dermatitis, seborrheic dermatitis, etc. are mentioned as those to be excluded in the diagnosis. Those physicians without adequate knowledge of diseases to be excluded may not be able to use the standard properly.

Items Important for Diagnosis

1. Pruritis

Pruritis is a symptom commonly seen in many cutaneous diseases, and there exists no AD without pruritis or traces of itch-induced scratching. Itchiness becomes intense toward night and often prevents sleep.

All of the diagnostic standards in which Hanifin and Rajika were involved[4–6)] and that of the Japanese Dermatological Association[2)] cite pruritis as the primary and essential feature. Although various causes are cited for pruritis in AD such as abnormality in cutaneous barrier function, increase in dermal mast cells, and increase of epidermal nerve ends, there remain many unclear points.

2. Features, distribution and course of exanthema

Dermatological symptoms of AD change with advance in age, and patients manifest uniquely different features according to their age. It is therefore essential to give full consideration to the age of the patient in diagnosis.

In infancy, exudative erythema, papules, exfoliative scales, and crusts are observed from the forehead, the cheeks to the front of ears accompanying traces of itch-induced scratching. Similar signs are observed from the forehead toward the parietal region, often accompanying adhesion of yellowish soft crusts. Eruptions are often observed also in the neck, trunk and limbs, but no exudation is observed except in the neck, cubital and popliteal fossae. At this period, differentiation from seborrheic dermatitis always presents a problem and diagnosis should be established after careful observation of the course.

In early childhood, exudative or erosive lesion decreases and xerosis increases. Lichenification appears in the cubital and popliteal fossae, nuchal region, shoulders, and hips, and because of intense itchiness, itch-induced scratch traces and crusts are apparent. Other features characteristic to this period include erythma with

lichenification in the forehead and infra-auricular fissures.[7)]

From pubescence to adulthood, lichenified erythema spreads from the cubital and popliteal fossae and neck to thoracodorsal region, upper limbs, lumbar and femoral regions. Compared to infancy, prurigo-like papules are more notable. As exanthema continues for long, it is often accompanied by complex and mixed phases of secondary thickening, pigmentation, and depigmentation. In adulthood, eruptions often appear at places other than the cubital and popliteal fossae where eruptions usually to appear. Recently, patients with relatively light eruptions in the trunk and limbs manifested severe eruptions in the face, neck, and upper thoracodorsal part.[3)]

While various signs characterize the respective age groups, there exist general and common findings of AD in all the groups that are easily recognized as such by any dermatologist. Eruptions in AD are mainly eczematous lesions, often accompanied by diffuse and symmetrical erythema. Another feature is that such exanthema takes a chronically relapsing course. These features are commonly described in the diagnostic standards for AD of the Japanese Dermatological Association and of Hanifin and Rajka,[2,6)] indicating that remissions by adequate treatment are followed by flare-ups. The important question is how to judge the degree of chronicity in infants and children. At any rate, it should always be remembered that AD subsides with advance in age if given adequate and proper treatment.[8)]

3. Laboratory tests

AD patients often manifest high total serum IgE, are positive against mite-specific IgE antibody, and experience peripheral blood eosinophil increase. It is reported that adult AD patients manifest a high positive ratio against *Pityrosporum*-specific IgE antibody, the incidence of *Staphylococcus aureus* detected from the diseased skin of AD patients is high, and the value of IgE antibody specific to the toxins produced thereby is also high.[9)] These matters related to type I allergy are not necessarily observed in all the AD patients. Although one cannot avoid diagnosing according to the standards focusing on clinical features, one should use these tests results as references only in order to avoid confusion in diagnosis since the disease entity of AD is already established.

The patients with higher than moderate degree of AD often manifest high serum LDH values, but they should be regarded as references to determine the degree of severity rather than for establishing diagnosis. Various intracutaneous tests for such as mites and foods are performed, but one should be aware that the results of food allergen tests do not necessarily correlate to RAST values while those of inhaled allergens do.

4. Differential diagnosis

Differentiating infantile AD and seborrhic dermatitis is quite difficult, and special care is taken in the diagnostic standard of the Japanese Dermatological Association. Although it may be necessary to consider the infancy separately from other periods as in the standards of Seymour *et al.*[4,5)] diagnoses during this period need to be established by careful observation of the course. Those patients who are subsequently diagnosed as AD tend to have lesions spread beyond the face and head from early days.

The standard of the Japanese Dermatological Association[2)] cites eight diseases such as contact dermatitis for differentiation, but others such as hyper IgE syndrome and Wiskott-Aldrich syndrome should also be differentiated. There are quite a few patients who develop contact dermatitis by external preparations prescribed for AD and whose dermatitis is being overlooked.[3)] Special care should be taken in this regard.

Conclusion

Diagnosis of AD should be made by refer-

ring to adequate diagnostic standards as well as by taking detailed history (the age at onset, clinical course, histories of treatment, family, past diseases, and occupations, living environment, life style, etc.). Diagnosing AD may be described as diagnosis by exclusion, and differential diagnosis is, as discussed above, very important. By being aware that factors for exacerbation differ from patient to patient in AD, one should take meticulous care in treating them.

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