The differential diagnosis of atopic dermatitis in childhood

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ABSTRACT: Atopic is the most common of the dermatitides seen in infancy and childhood, but there are numerous other diseases that can mimic the skin findings. These include seborrheic dermatitis, immunodeficiency, and psoriasis in infancy; scabies, tinea corporis infection, perioral, nummular, contact, and molluscum dermatitis in childhood. It is sometimes extremely difficult to differentiate between ichthyosis and AD, and it is also important to differentiate AD from erythrodermic conditions including acrodermatitis enteropathica, biotin deficiency, and Netherton syndrome. A rare condition in children that may mimic AD is mycosis fungoides.

KEYWORDS: atopic dermatitis, immunodeficiency, nutritional diseases

Introduction

Atopic dermatitis (AD) is a pruritic skin disease that typically starts early in life. It is probably inherited, but to date has no cure. The hallmark of the disease is a pruritic dermatitis that localizes in different areas depending on age. In infancy it affects the face and extensors of the lower legs (FIG. 1); in childhood the flexural areas are commonly involved, and the eruption has a more diffuse distribution in adulthood. Other important clues to diagnosis include xerosis of the skin, early age of onset, and a chronic, relapsing course. The incidence and prevalence of AD decreases with increasing age. There are numerous skin conditions that can mimic AD, these include seborrheic dermatitis and psoriasis, immunodeficiency, erythrodermic conditions such as acrodermatitis enteropathica (AE) and Netherton syndrome in infancy; scabies, tinea corporis infection and contact, nummular, perioral, and molluscum dermatitis in childhood. At times it is difficult to tell ichthyosis from AD and they may occur together. Rarely in children, T cell lymphoma (mycosis fungoides) presents with dermatitis, although the condition is usually seen in adults. This article will discuss the diseases that may be mistaken for AD in infancy and childhood, and provide methods of distinguishing among them.

Seborrheic dermatitis and psoriasis

Seborrheic dermatitis (SD) was a common disease seen in infants in the latter part of the 20th century. There is an impression that the severe forms of SD are not seen with the same frequency in North America or the UK as 10 years ago. The reason for this decrease is unknown, but may be related to the etiology of SD, which is possibly caused by an overgrowth of the yeast like organism, Pityrosporum ovale (1). This is a lipophilic organism requiring lipid surroundings in which to grow; nowadays, mothers wash their infant's hair on a daily basis, preventing the accumulation of lipid material. It is unlikely that adult SD has any relationship to the childhood variant.

The eruption primarily involves the scalp, face, and flexures. Both AD and SD usually begin soon after birth in the first 8 weeks of life, and may affect the same areas (2). In both conditions the vertex or frontal area of the scalp is often the first
area to be involved. In SD the lesions are usually an asymptomatic accumulation of greasy scale with an occasional associated erythema (FIG. 2). This is known as cradle cap. Many physicians use the term cradle cap synonymously with SD, but cradle cap may be seen as a frequent isolated sign in normal infants, where it is caused by the retention of keratin. It is also frequently observed in infants with AD, where the scale is dryer, adherent, and often crusted. The scalp lesions in AD are extremely pruritic and scratch marks are often seen. Hair loss is rare in SD but common in AD, probably the result of scratching and rubbing.

The face is commonly affected in both conditions. In SD the lesions are located over the eyebrows and the nasolabial folds. There is asymptomatic accumulation of greasy scale with an occasional associated erythema. In AD the cheeks and chin are characteristically affected and there is dry exudative erythema and scale. The lesions are pruritic in AD and there may be erosions where the baby rubs the chin against a hard surface.

In full-blown SD the flexures may be involved, particularly the retroaural and axillary areas. The lesions are erythematous and surmounted by a greasy yellow scale. In patients with AD the flexures, particularly the antecubital and popliteal fossae, are also affected early in the course of the disease with erythema that is exudative and at times crusted. The diaper area is involved in SD, whereas it is typically spared in AD. Infants with SD may have extensive lesions but are “happy babies”; those with AD are irritable and itchy.

Psoriasis in infants is not infrequent and is often mistaken for AD and SD. It may also present in childhood; one-third of psoriasis cases present before the age of 19. Many cases that were previously diagnosed as SD are now known to have been psoriasis that may recur later in life. Psoriasis often presents in the same areas as SD – in the scalp, folds, and diaper area (FIG. 3); it does not have the thick silvery scale seen in adults, and resolution is often rapid (3). Other areas that are involved include the face and periumbilical areas in children, but lesions may also affect the trunk with well-demarcated erythematous patches and plaques surmounted by a thin white scale. AD is unusual in the diaper area and is always pruritic;
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this is usually not a feature of psoriasis in infants. The diaper lesions of psoriasis are well demarcated, in AD they are poorly demarcated (4). A rare condition of candidiasis with a psoriasiform ID is sometimes encountered. There is severe candidiasis in the diaper area with an explosive psoriasiform eruption elsewhere on the body. It is unknown whether this is a forme fruste of psoriasis and may indicate a Koebner reaction in an infant with a psoriatic diathesis.

Immunodeficiency

Before it was recognized that many immune disorders have associated skin findings suggestive of AD, any dermatitis that occurred in the context of an immune disorder was labeled AD. This diagnosis was made despite the absence of immunoglobulins, particularly IgE. The most common immune disorders with skin signs are Wiscott–Aldrich syndrome, Omenn syndrome, and hyper-IgE syndrome. Severe combined immunodeficiency may also be associated with a macular-papular, erythrodermic, or eczematous eruption reminiscent of AD.

Infants have severe pruritus with a generalized eczematous eruption, but without the localizing features generally seen in AD (FIG. 4). Internal organ involvement with lymphadenopathy and hepatosplenomegaly may be present, as well as recurrent infections and failure to thrive; these are helpful features that allow distinction between AD and immune disorders.

Omenn syndrome is a T cell-deficient state with infiltrates of abnormal histiocytic cells and eosinophilia. Infants usually present in the neonatal period with a generalized, eczematous, papular, and pruritic eruption (FIG. 5a,b). There is usually extensive lymphadenopathy and hepatosplenomegaly (5). AD patients may have a generalized reactive lymphadenopathy, but to a lesser extent than in Omenn syndrome, and hepatosplenomegaly is not seen with AD. In addition, in Omenn syndrome there is alopecia, eosinophilia, recurrent infections, and failure to thrive. Bone marrow transplant is curative.

Wiscott–Aldrich syndrome is an x-linked disease almost always affecting male children. The gene is present on Xp11–13. The cell surface marker CD43 (sialophorin) is absent from most cells. In adults there is an association with nephropathy and lymphoproliferative malignancies. Infants usually present with purpura, ecchymoses, and bloody diarrhea. These signs, signifying low and/or abnormal platelets, usually precede the skin changes that are characterized by a pruritic, generalized dermatitic eruption with hemorrhagic crusts and bloody scratch marks (FIG. 6). The dermatitis is indistinguishable from AD except for the obvious bleeding diathesis and lack of localizing signs. Recurrent skin abscesses with pneumococci, meningococci, and Haemophilus influenza are common, and infections with mollusca contagiosa, verrucae, and herpes simplex also occur. Bone marrow transplant is curative (6, 7).

Hyper-IgE and Job syndrome are both immunodeficiency states with an unknown inheritance pattern, characterized by a chronic dermatitis that presents in babies. In addition, there are skeletal and dental abnormalities, cold abscesses, eosinophilia, and very high levels of IgE; these usually occur after the neonatal period. There are often inflammatory papules on the face mimicking cephalic pustulosis. Coarse facies and cranial synostoses may be seen. Job syndrome is a variant of hyper-IgE syndrome occurring mainly in red-haired and fair-skinned women. Mucocutaneous candidiasis, recurrent pneumonia, and osteomyelitis are also features of the disease (8).

All forms of severe combined immunodeficiency (Di George syndrome, Bruton’s hypogammaglobulinemia, and common variable hypogammaglobulinemia) can have an associated pruritic skin eruption that may be macular papular, eczematous, or erythrodermic. The skin findings usually start in early infancy before other symptoms and signs become evident, AD is often initially considered to be the diagnosis. Associated features that help differentiate these conditions from AD are fever, diarrhea, recurrent infections, and failure to thrive. Di George syndrome affects branchial pouch development and may have features of chronic mucocutaneous candidiasis and hypoparathyroidism (9,10).

FIG. 4. Infant with severe combined immunodeficiency syndrome.
Nummular dermatitis

One of the most common misdiagnoses of AD is nummular dermatitis, so named because the lesions are “coined shaped.” Unlike AD, it is unusual to develop nummular dermatitis in the first few years of life. It commonly starts around 5 years of age and presents with small, pruritic, follicular papules that coalesce into large, exudative, crusted plaques. Lesions occur anywhere on the body although the face is not commonly affected. When the lesions are very inflammatory a secondary ID reaction affects other areas and dermatitic lesions may be seen in the antecubital and popliteal fossae. Although nummular patches may occur in AD, the natural history of these conditions is very different. There is no xerosis of the skin in patients with nummular dermatitis and the disease does not commonly continue beyond puberty in children. The etiology is unknown and management consists of potent topical steroids with systemic antibiotics. Nummular dermatitis in children is different from the dry patches of nummular dermatitis seen in adults.

Zinc and biotin deficiency

Zinc and biotin deficiency can present as an eczematous eruption or an erythroderma, and are often misdiagnosed as AD before other symptoms and signs become evident. The most common cause of zinc deficiency occurs in premature
infants whose mothers continue to breast-feed their infants. At around 3 months the zinc levels in breast milk drop and the zinc requirements of the infant go up. This is when the typical pattern of zinc deficiency is seen in the skin. Other causes of zinc deficiency include the very rare entities of the recessively inherited condition of AE, the occasional mother who has an absence of zinc in her breast milk, and the now redundant condition of parenteral feeding with no zinc added to the alimentation solution (11). AE is caused by an absence of a ligand in cow’s milk (Zip7 protein) that allows zinc to be transported across Paneth cells in the small intestine (12).

The skin eruption consists of dermatitis on the face that has a typical horseshoe appearance on the cheeks and around the chin (FIG. 7). There is often crusting and erosions. Lesions are also common in the perianal area where there is a diffuse dermatitis with a peripheral edge of scale. There are often paronychial lesions around the nails caused by either bacteria or Candida. Children are particularly irritable as in AD, but there is no xerosis of the skin and pruritus is not a feature of zinc deficiency. In older children the lesions are seen on the elbows and knees, whereas in AD the flexures are usually involved.

Other associated features of zinc deficiency include alopecia, diarrhea, recurrent skin infections, and irritability. In the relative zinc deficiency infants, treatment with zinc sulfate improves the symptoms and signs until solid food is introduced when it is unnecessary to continue the zinc supplement. Patients with AE need to be on zinc supplements for life.

Biotin deficiency (multiple carboxylase deficiency) is a rare autosomal recessive disorder seen both in the neonatal period as a holocarboxylase deficiency, or in late infancy where there is an absence of biotinidase (13). The etiology is attributed to a decreased activity in any or all three carboxylases; these are all biotin-dependent enzymes in which biotin acts as a cofactor. The absence of carboxyl enzymes leads to an accumulation of carboxyls in the urine, resulting in lactic acidosis and ketosis. Biotin deficiency is also seen in patients who require parenteral feeding in which no biotin has been added. The latter is no longer seen. Lastly it is associated with patients who have diets of raw eggs.

The skin lesions are similar to those seen in zinc deficiency with lesions around the eyes, periorificial area, hands, feet, and perianal area. Lesions are eczematous, psoriasiform or in the neonatal form, erythroderma may occur (14). Chronic candidiasis may supervene and this is unresponsive to treatment until the biotin deficiency has been corrected. Other symptoms and signs include vomiting, seizures, developmental delay, hypotonia, and eventually ataxia. Treatment with biotin leads to rapid improvement.

**Scabies**

Scabies can be seen in both infants and young children and is commonly mistaken for AD. Although the epidemic that was prevalent about 7 years ago is not seen with the same frequency, there are still many sporadic cases and it is important to consider the diagnosis in anybody with a pruritic dermatitis. The lesions are an allergic reaction to the Sarcoptes scabiei mite. The face is usually spared, unlike in AD where it is frequently involved. Lesions are polymorphic (FIG. 8a); there are dermatitic lesions; nodules that are seen mainly in the flexural areas of the axillae and inquinal areas (FIG. 8b), and on the penis; small vesicles and pustules on the feet and hands in infants are
typical of scabies (FIG. 8c); urticaria; and the diagnostic feature of scabies the burrow where the organisms are found. The latter is a small linear scale that is seen in intertriginous areas such as the webs of the fingers and toes in children and on the palms and soles in infants. Xerosis is not seen as opposed to AD where it is a major sign of the disease. It is very helpful to get a family history of other members who are itchy, and the demonstration of the eight-legged mite at the end of the burrow is diagnostic. Scabies that is treated with the chronic use of steroids may eventuate into Norwegian scabies where there are thousands of mites (FIG. 8d). Normally an individual’s mite count does not exceed 6–10 organisms. Treating the whole family is mandatory and 5% permethrin is safe and effective when used overnight on two occasions 1 week apart (15).

Contact dermatitis

Irritant contact dermatitis may occur in infants and children but it is unusual. The most common
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is lip licking that often affects children in the winter months. It is localized to the area around the mouth and should not be confused with AD, although this is seen with some frequency in patients with AD, who often have an associated nasal congestion and breathe through their mouth. The saliva and air cause a dryness that may become inflamed.

Despite the ability to mount a normal immunological response, allergic contact dermatitis is not seen in infants with any frequency, possibly through lack of exposure. Nickel is the most common allergic reaction in infants. It produces a dermatitis that is difficult to differentiate from AD. Both contact dermatitis and AD are extremely pruritic. In contact dermatitis, a dermatitic pattern is seen at the site of exposure and this is most helpful in differentiating the eruption from AD. The midline of the chest where the infant has exposure to nickel snaps in undershirts is the most frequent area of involvement (FIG. 9a). There is no xerosis of the skin as seen in AD. Contact dermatitis may produce an ID reaction that affects areas far from the site of exposure, particularly in the antecubital fossae where AD is also seen. In older children the nickel snap on the waistline of jeans causes a typical eczematous or lichenoid eruption just below the umbilicus that is classic for allergic nickel dermatitis (FIG. 9b). It has been argued that this may be a sign of AD, but in the authors’ opinion it is typical of nickel dermatitis. Another cause of an allergic contact that may mimic AD is the usually unilateral eruption around the eye resulting from an allergy to nail varnish. The only cure for a contact dermatitis is removal of the offending substance. It may take months for the eruption to completely disappear, even with the use of topical steroids (16).

Perioral dermatitis

Perioral dermatitis is quite common in childhood. It presents as an eruption around the mouth that spares the vermillion border (FIG. 10). It can also affect the eyes both unilaterally and bilaterally and there are occasional reports of extra-facial involvement including the vulva. It is unusual in infancy and is not particularly pruritic. Although the eruption is mainly dermatitic, a granulomatous pattern may also be seen. The etiology is unknown but the eruption is worsened by the use of fluorinated topical steroids. Initially there is a response to topical corticosteroid treatment only to recur when the medication is stopped. Treatment with either oral or topical antibiotics for some weeks causes a resolution of the eruption (17). The disease starts later than AD and is usually confined to the face.

Ichthyosis

Ichthyosis is usually seen early in life. It is an accumulation of keratin either from excess skin turnover or from reduced desquamation. Although the end result is keratin build-up, ichthyosis is a group of diseases with a different inheritance pattern and presentation. Xerosis of the skin in AD is
at times difficult to differentiate from ichthyosis and at times they may be seen together. Most of the patients with ichthyosis do not complain of itch and do not have the typical pattern seen in AD. The lesions of AD are inflamed, which is unusual in ichthyosis, except in Netherton syndrome.

**Netherton syndrome**

This rare recessively inherited condition caused by a defect in the spink-5 gene presents soon after birth (18). This gene encodes LEKTI (a serine protease inhibitor) that regulates barrier function and immunity (19). Initially the infant has an erythroderma with scaling, that over 1–2 years eventuates into an ichthyosis with a typical pattern of a double-edged scale known as ichthyosis linearis circumflexa. Other characteristic features of the disease are specific hair abnormalities – trichorrhexis invaginata (although trichexis nodosa is also seen) and an atopic diathesis mostly manifest as a high-IgE and acute allergic reactions to food, particularly peanuts (20). Because the differential diagnosis of an erythroderma always includes AD, it is important to look for the bamboo hairs of trichorrhexis invaginata that are so typical of Netherton syndrome. There may be a big problem with feeding in the first year of life and there have been a number of reports of hypernatremia in infancy (20), but the disease becomes less erythematous with time. Repeated infection is not uncommon and at these times the eruption may revert to the erythrodermic state.

**Molluscum dermatitis**

Mollusca contagiosa is a common viral condition on the skin, caused by in infection with a poxvirus. Children between the ages of 3–9 years present with a few scattered flesh-colored papules usually localized to one area. After a few months the eruption may spread and many more lesions appear. These last for a variable period of 1 to 2 years and then spontaneously disappear with an inflammatory response. An interesting phenomenon in some patients is the appearance of a circular pruritic dermatitis surrounding some of the mollusca (FIG. 11). The child scratches the lesions and may scratch off the mollusca. It is easy to miss the small papules in the dermatitis and because of the itch, these patients are diagnosed with AD. It is not known whether the dermatitis associated with the mollusca occurs primarily in patients with AD. Treatment of the mollusca varies, but in
small children it is too traumatic to use liquid nitrogen effectively. Canthrene can be applied by the physician with the wooden end of a Q tip. This causes blistering and crusting of the lesions with subsequent disappearance. The dermatitis responds well to a mild or mid-strength topical steroid.

**Tinea corporis**

Tinea corporis was less prevalent for some years, but many forms of fungal infection have reappeared including a resurgence of tinea corporis. This is an acquired disease that is seen infrequently in infants in the diaper area; it is much more commonly in children. The offending organism is mainly *Microsporum canis* or *Trichophyton mentagrophytes*. Lesions are well-demarcated patches or plaques in a circular pattern with an active peripheral border. This is commonly treated as eczema with topical steroids, resulting in the patches spreading peripherally and resembling AD (21). A high index of suspicion is warranted, and potassium hydroxide and culture will confirm the diagnosis. Treatment with a topical antifungal is curative in a few weeks.

**Mycosis fungoides**

Mycosis fungoides (MF) is a chronic T cell lymphoma that is being recognized much more frequently in children. It is not known whether this is because of the increased knowledge of its existence in this population, or whether there is a real increase in the number of cases. MF presents with varied patterns in the skin; the most recognized is with hypopigmented patches (FIG. 12) (more easily recognized in black skin) but a chronic dermatitis is also seen that may be extremely itchy and easily confused with AD. In the later stages of the disease plaques and tumors supervene, but this is much more likely in adults than in children. Treatment is difficult; the most commonly used is narrowband ultraviolet B or psoralen plus ultraviolet A (22). It is unknown what the ultimate prognosis is in children with MF (23).

**Conclusion**

AD is a very frequently encountered disease in children and a wide variety of scaly, inflammatory, infectious, and even lymphomatous conditions are easily and often ascribed to this common skin disease.

**References**

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