Annular Lichenoid Dermatitis of Youth: Report of Six New Cases with Review of the Literature

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Introduction

Annular lichenoid dermatitis of youth (ALDY) was firstly described in 2003 in young Mediterranean individuals presenting with sharply demarcated annular erythematous macules and patches with central hypopigmentation [1]. The lesions typically occur on the groin, flanks and sometimes the axillae. The clinical features may suggest inflammatory morphea, mycosis fungoides, vitiligo or annular erythema, whereas histologically the main differential diagnosis includes other lichenoid dermatoses and mycosis fungoides. The histological hallmark of ALDY is an interface dermatitis affecting specifically the tips of the rete ridges, with massive apoptosis of keratinocytes limited to this area and thus configuring a squared base. Since the initial description, other cases have been reported. In this study we describe the clinical and histological features of six patients with ALDY and review all cases published after the initial description [2–11].

Patients

The characteristics of the six patients diagnosed at our institution from 2010 to 2014 are reported in table 1. They were all males, age ranging from 7 to 79 years. Lesions consisted of asymptomatic round-ed, oval or annular red-brown macules or patches, developed from initial erythematous macules with peripheral spreading. Most lesions showed the characteristic annular or archway shape, with a raised erythematous border and a hypopigmented center. Two patients had five (case 1) and four lesions (case 2), respectively, the oldest patient (case 3) had three lesions, whereas three patients had only one lesion (cases 4, 5 and 6). The lesions were located on the side of the trunk, the groin and/or the axillary regions (fig. 1). The duration of the lesions ranged between 2 and 48 months. The main differential diagnosis included eczema, erythema annulare centrifugum, morphea and mycosis fungoides. The patients were otherwise healthy.

Methods

In all six cases, 5-mm punch biopsies were taken from the periphery of the lesions and routinely processed and stained with hematoxylin and eosin; periodic acid-Schiff staining was also performed. Immunohistochemical staining was performed with the Leica Microsystems Bond-Max poly HRP Autostainer System. The primary antibodies used were: CD1a (Dako 010

Key Words
Annular lichenoid dermatitis of youth - Interface dermatitis - Lichenoid dermatitis - Mycosis fungoides

Abstract

Background: Annular lichenoid dermatitis of youth (ALDY) is an uncommon disease clinically reminiscent of morphea, annular erythema or mycosis fungoides. Objective: To describe the histological and clinical features of a small series of patients with ALDY and to review the literature. Patients: We describe the clinical and histological features of six patients (age range 7–79 years) with asymptomatic erythematous macules and patches with a red-brownish border and central hypopigmentation, mostly distributed on the groin and flanks. Histologically, all cases showed lichenoid dermatitis limited to the tips of rete ridges, with many intraepidermal CD8+ and some CD4+ T cells. T cell receptor rearrangement was absent in all cases. A total of 44 patients with a consistent clinical and histological picture have been described. The disease is sensitive to topical and/or systemic corticosteroids. Conclusions: ALDY is a unique lichenoid dermatitis for whose diagnosis a clinical-pathological correlation is essential. The disease typically affects young patients, more rarely adults and elderly.
Table 1. Clinical features of all cases of ALDY reported after the initial description [1]

<table>
<thead>
<tr>
<th>Reference (first author)</th>
<th>Sex</th>
<th>Age, years</th>
<th>Type and number of lesions (in parentheses)</th>
<th>Site</th>
<th>Duration, months</th>
<th>Therapy</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Durdu, 2007 [3]</td>
<td>M</td>
<td>7</td>
<td>asymptomatic annular patches (6)</td>
<td>right flank, left groin</td>
<td>12</td>
<td>TCS</td>
<td>chronic, recurrence of lesions after stopping therapy</td>
</tr>
<tr>
<td>Kleikamp, 2008 [5]</td>
<td>F</td>
<td>12</td>
<td>red-brown macules with lichenoid papules along the margins (&gt;1)</td>
<td>bilateral inframammary</td>
<td>24</td>
<td></td>
<td>chronic, recurrence of lesions after stopping therapy</td>
</tr>
<tr>
<td>Sans, 2008 [6]</td>
<td>M</td>
<td>3</td>
<td>red-violaceous macules (6), annular patches with a red-brownish border and a central area of hypopigmentation</td>
<td>loins, abdomen, upper and lower limbs</td>
<td>12</td>
<td>TCS</td>
<td>chronic, recurrence of lesions after stopping therapy</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>34</td>
<td>erythematous annular patches (multiple symmetric)</td>
<td>abdomen, thorax</td>
<td></td>
<td>TCS</td>
<td>NED after 46 m</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>33</td>
<td>oval brownish patch (1) with erythematous border</td>
<td>right flank abdomen flanks</td>
<td></td>
<td>TCS</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>39</td>
<td>oval desquamative pigmented plaques (multiple)</td>
<td>abdomen, flanks, groin, neck, axillary region</td>
<td></td>
<td></td>
<td>topical tacrolimus</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>45</td>
<td>rounded erythematous plaques (3)</td>
<td></td>
<td></td>
<td></td>
<td>none</td>
</tr>
<tr>
<td>Tsoitis, 2009 [8]</td>
<td>M</td>
<td>3.5</td>
<td>round-oval annular plaques with a brownish border (2)</td>
<td>right thigh, left buttock</td>
<td>12</td>
<td>none</td>
<td>spontaneous regression</td>
</tr>
<tr>
<td>Huh, 2010 [10]</td>
<td>F</td>
<td>2</td>
<td>erythematous annular macules and patches (5)</td>
<td>anterior chest, abdomen, back, waist, inner arm</td>
<td>11</td>
<td>TCS</td>
<td>chronic</td>
</tr>
<tr>
<td>Our case 1</td>
<td>M</td>
<td>45</td>
<td>oval red-brown macules (5)</td>
<td>flanks, left axilla, abdomen axillae and flanks</td>
<td>48</td>
<td>phototherapy and TCS</td>
<td>recurrence of lesions after 25 m</td>
</tr>
<tr>
<td>Our case 2</td>
<td>M</td>
<td>17</td>
<td>annular plaques with central hypopigmentation and erythematous borders (4)</td>
<td>right flank, left groin, abdomen</td>
<td>6</td>
<td>TCS and tacrolimus 0.1%</td>
<td>NED after 2 m</td>
</tr>
<tr>
<td>Our case 3</td>
<td>M</td>
<td>79</td>
<td>annular plaques with central hypopigmentation and erythematous borders (3)</td>
<td>right flank, left groin, abdomen</td>
<td>6</td>
<td>TCS</td>
<td>lost to FU</td>
</tr>
<tr>
<td>Our case 4</td>
<td>M</td>
<td>9</td>
<td>rounded erythematous plaque with central hypopigmentation (1)</td>
<td></td>
<td></td>
<td>TCS and tacrolimus 0.1%</td>
<td>lost to FU</td>
</tr>
<tr>
<td>Our case 5</td>
<td>M</td>
<td>7</td>
<td>red-brown archway macule (1)</td>
<td>left flank</td>
<td>7</td>
<td>TCS</td>
<td>NED after 18 m</td>
</tr>
<tr>
<td>Our case 6</td>
<td>M</td>
<td>8</td>
<td>incomplete rounded erythematous plaque with central hypopigmentation (1)</td>
<td>right flank</td>
<td>2</td>
<td>TCS</td>
<td>in FU</td>
</tr>
</tbody>
</table>

F = Female; M = male; m = months; NED = no evidence of disease; TCS = topical corticosteroid.

Antigen retrieval was performed by incubating slides with the Bond Epitope Retrieval Solution 2 for 15 min at 95°C at pH 6 (CD1a, CD34, CD68) and at pH 9 (CD2, CD3, CD4, CD5, CD7, CD8, CD20, CD30, CD138). In all cases, the following antibodies were used at a dilution of 1:100, CD2 (Novocastra AB75 at a dilution of 1:50), CD3 (Thermo SP7 at a dilution of 1:150), CD4 (Novocastra 4B12 at a dilution of 1:150), CD5 (Novocastra 4C7 at a dilution of 1:200), CD7 (Novocastra CD7-272 at a dilution of 1:50), CD8 (Dako C8/144B at a dilution of 1:200), CD20 (Novocastra L26 at a dilution of 1:100), CD30 (Dako BerH2 at a dilution of 1:30), CD34 (Novocastra QBEND/10 at a dilution of 1:200), CD68 (Dako PG-M1 at a dilution of 1:50), and CD138 (Dako MI15 at a dilution of 1:100).
our cases, molecular analysis of T cell receptor (TCR) gene rearrangement was made using microcapillary electrophoresis, as previously described [12, 13].

Results

At the epidermal level all cases showed mild basket-woven hyperkeratosis, normal granular layer and elongation of rete ridges with a characteristic squared shape at the base of the dermal-epidermal junction; focal to massive basal keratinocyte apoptosis was observed, mostly at the tip of rete ridges (fig. 2). A moderate to marked inflammatory infiltrate in a typical lichenoid pattern of distribution was present in the superficial dermis. The infiltrate was made of small lymphocytes, few histiocytes and scattered melanophages, particularly concentrated at the tip of the rete ridges (fig. 2). Epidermotropism, as either single atypical lymphocytes or lining up of atypical lymphocytes along the basal layer, or Pautrier microabscesses were always absent. Periodic acid-Schiff staining for fungi was negative. Immunohistochemical analysis showed a mixed-cell T cell infiltrate consisting of CD4+ T cells in the dermis, whereas many of intraepidermal T cells were CD8+, particularly those presenting areas of apoptotic keratinocytes (fig. 3). Dermal and intraepidermal T cells were uniformly CD2+, CD5+ and CD7+. No or very few CD20+ or CD30+ cells were observed, whereas scanty CD34+, CD68+ or CD138+ cells were detected. CD1a staining revealed an increased number of suprabasal Langerhans cells within the epidermis. No TCR gene rearrangement was detected. Molecular testing for *Borrelia burgdorferi* and parvovirus B19 was also negative. There was no history of tick bites and the patients were otherwise healthy. Testing for autoimmunity, infections, allergy and family history disclosed no relevant or putative etiologic factors. No seasonal clustering of the cutaneous eruption was reported. All six patients received topical mid-potency corticosteroid twice daily for a period ranging from 3 to 6 weeks. Patients 2 and 4 also received 0.1% tacrolimus ointment once daily and patient 1 was treated with phototherapy for 3 months twice weekly. Complete clearance of skin lesions was observed after 2–48 months of follow-up in 5 out 6 patients. Patient 1 had recurrence of lesions after 25 months.

Discussion

ALDY was originally described in 23 young individuals [1]. An additional 15 patients have been described since [2–11]. Table 1 summarizes all cases reported in the literature after the initial description. Most patients were from the Mediterranean area or had travelled in that region, suggesting an environmental agent as the
causative or triggering factor [11]. However, cases from Central Europe [5] and the Far East (Japan and Korea) [4, 9] have also been reported. The patients’ age ranged from 2 to 79 years, but the mean age was 9–10 years. The disease was more common in males, with a male:female ratio of 1.6:1.

ALDY consistently manifests with solitary or multiple annular patches or plaques located predominantly on the flanks and groin that may extend to the abdomen and more rarely on the axillary region or the neck. Lesions may or may not be distributed in a bilateral and symmetrical fashion [1–11].

Differential diagnosis included primarily morphea [14] and mycosis fungoides, mostly the hypopigmented variant [1–11, 15–21], as well as the recently described variant named hypopigmented interface T cell dyscrasia [22]. Interestingly, hypopigmented mycosis fungoides has been reported in pediatric and young patients, especially in females with darker skin types [15–21]. Hypopigmented mycosis fungoides represents the major clinical as well as histological differential diagnosis. Clues that may be helpful in differentiating ALDY from patch/plaque mycosis fungoides are especially the infiltration of lymphocytes mostly limited to the tips of rete ridges and the massive apoptosis of keratinocytes limited to the rete ridges conferring a square shaped appearance [1, 5, 7]. Frequently the immunophenotype of the epidermal infiltrate in hypopigmented mycosis fungoides is CD8+ and TCR rearrangement is not detected [15–18]. All these considerations may suggest that some cases of hypopigmented mycosis fungoides were indeed ALDY. Molecular analysis of ALDY showed a polyclonal T cell population, in contrast with patch/plaque lesions of mycosis fungoides, where T cell clonality can be detected in 52–75% of cases [1, 5, 15–21, 23, 24]. These data indicate that, in doubtful cases, analysis of the rearrangements of TCR genes represents an adjunctive tool helpful in differentiating ALDY from patch/plaque-stage mycosis fungoides. Hypopigmented interface T cell dyscrasia should also be considered in the differential diagnosis of ALDY. It affects adults and shows cell-poor interface dermatitis featuring lymphocytes with low-grade cerebriform atypia and in 50% of the cases with a predominant CD8+ immunophenotype, but clonality was not identified [22]. Further, ALDY must clinically be distinguished from annular erythema, such as annular erythema of infancy and erythema annulare centrifugum, which, however, do not show histopathological lichenoid pattern.

ALDY may share the same putative pathogenetic mechanism as other lichenoid dermatoses, including lichen planus, graft versus host disease and lichenoid drug eruption. Indeed, ALDY may result from T cell-mediated cytotoxic reaction against rete ridges keratinocytes. The peculiarity of ALDY is that the reaction is restricted to the rete ridges of the keratinocytes [25]. No drug, infection exposure or contact with supposed chemicals has been documented in ALDY cases, with the exception of one case which developed after hepatitis B immunization [6]. All described patients were healthy and without a relevant medical history, with the exception of one patient who had allergic rhinitis and asthma [1]. Moreover, none of the patients had an overt infectious disease in the 2 months before onset of the skin lesions. Routine laboratory parameters including hematology and clinical chemistry, anti-streptolysin titer, rheumatoid factor, antinuclear antibody, C-reactive protein and eosinophilic cationic protein were negative or within normal limits in all patients [1, 3, 7]. Stool examination for ova and parasites, Epstein-Barr virus, Coxsackie/Echo, parvovirus B19, respiratory syncy-

Fig. 2. Band-like infiltrate of small lymphocytes located in the papillary dermis and the lower epidermal layers (a, ×100), with vacuolar alteration and massive necrosis/apoptosis of keratinocytes restricted to the tips of squared rete ridges (b, ×200).
Fig. 3. Immunohistochemical analysis showed a subepidermal mixed-cell CD3+ T cell infiltrate (a) consisting of CD4+ T cells (b) and CD8+ T cells that were mainly intraepidermal (c).

Disclosure Statement

The authors have no conflict of interest to declare.
References


