Annular Lichenoid Dermatitis (of Youth) Immunohistochemical and Serological Evidence for Another Clinical Presentation of Borrelia Infection in Patients of Western Austria

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Abstract: Annular lichenoid dermatitis of youth (ALDY) is a more recently described inflammatory disease of the skin of unknown etiology with clinical similarities to morphea. The authors clinically, histopathologically, and immunohistochemically investigated 14 biopsies from 12 patients in western Austria with this disease. There were 6 female and 6 male patients with solitary (n = 7) and multiple lesions (n = 5) affecting the trunk (n = 11), upper arm (n = 2), thigh (n = 1), and calf (n = 1). Clinically, early lesions were erythematous in nature leading to central paleness, scaling, wrinkling, dermal atrophy, slight pigment atrophy, telangiectasia later on. Histopathologically, all specimens showed the typical features of ALDY with a superficial lichenoid process with sprinkling of lymphocytes along the basal cell layer and within the epidermis accompanied by mild fibrosis. Pigment incontinence, superficial fibrosis, and dilatation of superficial capillary vessels are prominent features in more advanced stages of disease. Immunohistochemically, using a polyclonal antibody against Borrelia, 11/14 specimens revealed spirochetes, either vital (n = 4) or degenerated (n = 7), in close proximity to collagen bundles. Thirteen of 14 specimens in addition showed focal (n = 4) or clustered (n = 9) positivity for CD20 in the papillary dermis. Nine of 12 sera tested for Borrelia using a linked immunosorbent assay were positive. Lichen sclerosus et atrophicus, and even necrobiosis xanthogranuloma have been reported to be possibly in part caused by Borrelia. In this regard, the immunohistological investigation of tissue of morphea and lichen sclerosus using focus floating microscopy (FFM) has been found to be more sensitive than the use of polymerase chain reaction. Positive results with FFM were especially observed in inflammatory disease of the skin of unknown etiology with clinical similarities to morphea and early lichen sclerosus et atrophicus.

Key Words: annular lichenoid dermatitis, ALDY, morphea, lichen sclerosus et atrophicus, dermatopathology

INTRODUCTION

Annular lichenoid dermatitis of youth (ALDY) belongs to the more recently described inflammatory dermatoses of the skin only published in 2003 by Annessi et al1 in a series of 23 patients. Since then, also older patients have been reported to suffer from this disease.2,3 Both sexes are equally affected. Clinically, patients present with round to oval, often annular patches with a characteristic erythematous border, and a hypopigmented center mainly involving the groin and trunk. The patches may be solitary or multiple, gradually enlarge in a centrifugal growth pattern, and typically are persistent. The etiology of the disease is still obscure.

In recent years, the spectrum of clinical manifestations of Borrelia infection has expanded considerably. With the advent of immunohistochemistry and molecular genetic methods, diseases such as granuloma annulare, necrobiosis lipoidica, morphea, lichen sclerosus et atrophicus, and even necrobiosis xanthogranuloma have been reported to be possibly in part caused by Borrelia. In this regard, the immunohistological investigation of tissue of morphea and lichen sclerosus using focus floating microscopy (FFM) has been found to be more sensitive than the use of polymerase chain reaction. Positive results with FFM were especially observed in inflammatory disease of the skin of unknown etiology with clinical similarities to morphea and early lichen sclerosus et atrophicus.

To investigate the nature of ALDY, biopsies from patients with this disease have been investigated histopathologically and immunohistochemically for Borrelia using FFM supplemented by blood investigation for Borrelia antibodies.

MATERIALS AND METHODS

A total of 14 biopsies from 12 patients of western Austria with the typical clinical presentation of ALDY have been investigated histologically and immunohistochemically. Four μm thick sections were cut and stained with hematoxylin and eosin, periodic acid-Schiff (PAS), elastic stain, as well as immunohistochemically with a Ventana autostainer (Tucson, AZ) and a polyclonal antibody against Borrelia using focus floating microscopy (FFM) like organisms (Quartett immunodiagnostics, Berlin, Germany) as described previously.7 In addition, sections were investigated for CD20-positive lymphocytes (L26, Dako, Glostrup, Denmark). Two specimens (case no. 2 and 8) were seen in consultation (see acknowledgment). In addition, blood samples were investigated for antibodies against Borrelia using an enzyme-linked immunosorbent assay.

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RESULTS

There were 6 female and 6 male patients with a mean age of 48 years (range 18–78). Lesions were solitary (n = 7) or multiple (n = 5) affecting the trunk (n = 11), upper arm (n = 2), thigh (n = 1), or calf (n = 1) and presented as round to oval annular lesions. Early lesions were erythematous in nature, in time with central paleness similar to erythema chronicum migrans. Later on, the lesions acquired a scale and brownish hue after pigment incontinence, wrinkling, and dermal atrophy. Telangiectasia and fibrosis may become very prominent imitating chronic irradiation dermatitis (Figs. 1A–H). One patient simultaneously had a perianal lesion typical for lichen sclerosus et atrophicus (case no. 4), another subsequently developed morphea (case no. 5). Clinical details including the results of serological testing for Borrelia and FFM are given in Table 1. Nine of 12 sera tested for Borrelia were positive. Other routine investigations including blood count and clinical chemistry were within normal limits. Clinically, patients 1, 2, 3, and 9 reportedly showed improvement with local steroids, case no. 4 with penicillin, whereas no improvement was seen in case no. 5 after treatment with this antibiotic. Patients 1 and 9 showed recurrence after discontinuation of local steroids. In all other cases, there is no clinical follow-up available.

Histologically, 14 specimens from 12 patients were investigated. All of them were rather similar and showed the features of a lichenoid tissue reaction with sprinkling of monomorphous small lymphocytes along the basal layer and within the epidermis accompanied by a superficial, mostly perivascular infiltrate of lymphocytes and macrophages, as well as in more early instances moderate fibrosis and a decrease of superficial elastic tissue. There is focal slight orthohyperkeratosis but no spongiosis (Figs. 2A, B). Older lesions essentially showed the same inflammatory pattern of a lichenoid tissue reaction accompanied by cytoid bodies and more prominent fibrosis with partially wiry bundles of collagen, mild pigment incontinence, and even telangiectasia. The PAS stain in all specimens did not reveal fungi. Immunohistologically, FFM showed 11/14 biopsies to be positive either in the form of vital forms (case no. 1, 3, 6, 11) or degenerated fragments of spirochetes (case no. 2, 4, 6, 7, 8, 9, 12) closely located to collagen bundles, occasionally grouped in clusters (Fig. 2 C). In 13/14 specimens, focal (n = 4) or clustered (n = 9) CD20-positive B lymphocytes in the papillary dermis were present as well.

DISCUSSION

ALDY only described in 2003 is a disease of unknown etiology. In a recent review, similarities to morphea and especially mycosis fungoides have been discussed. With around 50 reported cases to date, the disease is rare but probably underreported because around 20% of all patients described so far are documented in the present observation. The latter frequency might be due to the rising awareness of the disease in a universal and dermatohistopathological referral center. A possible link of the disease to Borrelia infection as discussed herein may be an additional reason due to the high rate of infection with Borrelia burgdorferi in western Austria where our patients came from. Seroprevalence of borreliosis reaches 30% in healthy adult blood donors in highly endemic areas of Austria. In addition, every tenth tick bite in endemic areas causes Borrelia infection. In this respect, 11/14 specimens of our series either showed vital forms or fragments of spirochetes with FFM, 9/12 patients in addition were positive for Borrelia with blood investigation. Serological investigation for Borrelia must always be correlated with the clinicopathological findings because negative results do not exclude previous infection and positive

FIGURE 1. A–H, Early erythematous lesion on the left lower abdomen close to pubic area, later on enlarged and multifocal with a pale center resembling erythema migrans. Left laterally, there is a small scar after biopsy (A, B; case no. 2). More advanced lesions may additionally reveal slight scaling, wrinkling, and brownish pigmentation (C; case no. 3). Multifocal erythematous lesions in this case present with central paleness, atrophy, and wrinkling. There is a small scar after biopsy at the upper part of the back (D, E; case no. 11). Erythema and wrinkling are present on this patient’s left armpit leading to atrophy, prominent wrinkling, and telangiectasia later on. The biopsy site is marked in black (F, G; case no. 1). Telangiectasia, atrophy, and fibrosis resembling chronic irradiation dermatitis may be the predominant clinical feature in very old lesions (H; case no. 5).
Annular Lichenoid Dermatitis (of Youth)

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex/Age</th>
<th>Clinical Diagnosis</th>
<th>Location</th>
<th>FFM</th>
<th>Borrelia/Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/28</td>
<td>Eczema, morphea</td>
<td>Left armpit, 3 mo later Lower abdomen and left flank</td>
<td>+ vital</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>M/31</td>
<td>Morphea, pseudolymphomatous prurigo</td>
<td>Left abdomen 5 mo later right abdomen 6 mo later dorsal hip</td>
<td>+ degenerated</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>F/18</td>
<td>Morphea</td>
<td>Left abdomen</td>
<td>+ vital</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>F/46</td>
<td>Morphea, lichen sclerosus</td>
<td>Left breast</td>
<td>+ degenerated</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>F/71</td>
<td>Morphea, erythema migrans</td>
<td>Left lower abdomen Right upper arm, left breast</td>
<td>- +</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F/28</td>
<td>Morphea, lichen sclerosus</td>
<td>Breast Back</td>
<td>+ degenerated + vital</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M/61</td>
<td>Morphea</td>
<td>Abdomen</td>
<td>+ degenerated</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>F/43</td>
<td>Erythema migrans</td>
<td>Left breast</td>
<td>+ degenerated</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>M/54</td>
<td>Morphea</td>
<td>Right hip</td>
<td>+ degenerated</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>F/66</td>
<td>Morphea</td>
<td>Thigh</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>M/78</td>
<td>Granuloma annulare, tinea</td>
<td>Multiple lesions back</td>
<td>+ vital</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>M/50</td>
<td>Follicular mucinosis</td>
<td>Left calf</td>
<td>+ degenerated</td>
<td>+</td>
</tr>
</tbody>
</table>

results may represent endemic background. In addition, the immunohistological presence of *Borrelia* may be very sparse and false negative in the tissue planes examined. This possibly explains the divergent results of FFM and serological investigation in patients 4, 5 and 8 of our series.

This possible link to *Borrelia* infection has not been substantiated previously but is intriguing because of clinical similarities with early morphea and histopathologically early lichen sclerosus et atrophicus. Interestingly, one of our patients initially presented with ALDY and later on developed typical morphea. Similarly, another patient concomitantly showed the clinical picture of perianal lichen sclerosus et atrophicus. An interesting finding in our patients briefly addressed also in the original series is that ALDY clinically may exhibit time dependant changes—initially erythema resembling erythema chronicum migrans, later morphea, leading to scaling, brownish pigmentation, atrophy, and sometimes prominent telangiectasia. The latter features may even simulate chronic irradiation dermatitis and have not been described before (Fig. 1G and especially Fig. 1H). These time-dependent changes may be attributable to an infectious agent in this disease.

The spectrum of dermatoses in which *Borrelia* may play a role has expanded in recent years. *Borrelia* have been detected not only in cases of morphea but also lichen sclerosus et atrophicus by FFM immunohistochemistry. Both conditions may show overlap not only with respect to their clinical presentation but also to their histopathology, as also suggested by Ackerman. The presence of *Borrelia* in ALDY as reported herein may further expand the clinical manifestation of *Borrelia* infection implying that ALDY may be a very early, comparatively superficial stage of morphea or lichen sclerosus et atrophicus. A possible bacterial etiology of morphea and ALDY is further substantiated because some cases of morphea and lichen sclerosus et atrophicus are known to respond to antibiotic therapy. Ineffective antibiotic treatment, as also demonstrated in one patient of our series of ALDY, may be due to the intracellular presence of bacteria in endothelium, fibroblasts, synovial, and neuronal cells. An inefficient clearance by phagocytic cells and the possible ability of *Borrelia* to form protective biofilm structures may be further explanations for ineffective antibiotic treatment of the disease.

Histopathologically, classic morphea and lichen sclerosus et atrophicus are readily diagnosed because of their distinctive appearance. In morphea, the disease generally affects the reticular dermis (and subcutis) with thickening of collagen bundles, sclerosis, fat atrophy, and loss of appendage structures. Lichen sclerosus et atrophicus in early stages presents as a lichenoid inflammatory process affecting the papillary dermis leading to prominent edema and sclerosis later on. Notably, especially the guttate variant of morphea may show papillary edema as well. The histopathology of ALDY may be very similar to early lichen sclerosus et atrophicus showing a lichenoid inflammatory process with sprinkling of lymphocytes along the basement membrane and within the epidermis accompanied by fibrosis of the papillary dermis. Orthohyperkeratosis, pigment incontinence, more prominent fibrosis with partially wiry bundles of collagen and telangiectasia are signs of older lesions. In all stages a lichenoid tissue reaction is present and seems to be the major histopathological criterium. Thus, there is considerable histopathological overlap in these three conditions.

Comparable to our series of morphea, we found a high prevalence of CD20-positive B lymphocytes in the lichenoid infiltrate in most of our ALDY cases predominantly grouped in clusters, which may be an indicator for an immune response against bacterial infection—a phenomenon which we have previously observed in all forms of “classical” borreliosis and has been shown to be of predictive value for the presence of *Borrelia* also in cases of morphea. We have therefore incorporated the investigation for CD20 in the present series of ALDY. Notably, the clustered presence of CD20-positive lymphocytes
is not an expected finding in mycosis fungoides known as a T-cell–mediated lymphoproliferative disorder. Clinicopathological similarities to ALDY may be challenging, however, and therefore especially CD20-negative cases of ALDY as also described in the literature should be carefully scrutinized for underlying mycosis fungoides.

In conclusion, apart from clinical and histopathological similarities, the presence of Borrelia or Borrelia-like microorganisms in ALDY in patients of western Austria indicate that this disease may represent another form of a superficial stage of morphea besides lichen sclerosus et atrophicus.

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