Lichen Aureus

Clinicopathologic Features, Natural History, and Relationship to Mycosis Fungoides

Regina Fink-Puches, MD; Peter Wolf, MD; Helmut Kerl, MD; Lorenzo Cerroni, MD

Background: A possible association between lichen aureus (LA) and mycosis fungoides (MF) has been suggested in the past. We evaluated the clinicopathologic features of LA and its relationship to MF. Data from 23 patients with a clinicopathologic diagnosis of LA were reviewed.

Observations: Lesions were asymmetrically localized on 1 area of the body (mostly 1 extremity) and were characterized histologically by dense, bandlike lymphocytic infiltrates. A monoclonal T-cell population was detected in half of the cases. After a mean follow-up of 102.1 months, 14 patients had no sign of skin disease, 7 patients had unmodified skin lesions, and 2 other patients with unmodified skin lesions had died of unrelated conditions. Treatment modalities did not affect the outcome. There was no relationship between the presence or absence of monoclonality and patient status at follow-up assessments.

Conclusion: Patients with classic lesions of LA do not show progression to MF.

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METHODS

PATIENTS

Data from 23 patients from the files of the Department of Dermatology, Medical University of Graz, were included in this study. In each case, the original histopathologic sections were reviewed by one of us (L.C.). Lichen aureus was diagnosed according to clinicopathologic correlation by reviewing clinical photographs when available or by reviewing medical records. Clinical data analyzed included age, sex, date of first diagnosis, duration of follow-up, and status of disease at the last follow-up assessment.

HISTOLOGIC, IMMUNOHISTOLOGIC, AND MOLECULAR BIOLOGIC EVALUATION

Sections with a maximum thickness of 4 µm and stained with hematoxylin-eosin, Giemsa, and periodic acid–Schiff were available for standard histologic evaluation. In all cases in which a paraffin block could be retrieved, analysis of the T-cell receptor was performed using polymerase chain reaction (PCR) techniques and primers as published previously with minor modifications. Details about PCR procedures have been published previously.

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RESULTS

Twenty-three patients (11 male and 12 female) were included in the study. Age at diagnosis ranged from 1 to 77 years (mean age, 43.2 years; median age, 47 years). Clinical data are given in the Table.

In 18 patients, the lesions were asymmetrically distributed at a single body site on the lower (n=15) or upper (n=3) extremities (Figure 1). Five patients had solitary lesions located on the buttocks, back, shoulder, trunk, or breast.

All cases histopathologically revealed variably dense, bandlike lymphoid infiltrates with slight fibrosis of the papillary dermis and the presence of hemorrhage and siderophages (Figure 2). Lymphocytes were the predominant cells in all cases. True epidermotropism of atypical lymphocytes was not observed, but most cases showed variable exocytosis of lymphocytes. A clear-cut grenz zone of uninvolved papillary dermis was not observed. In 1 case, 2 biopsy specimens from a persistent, unchanged skin lesion obtained 17 years apart revealed identical histopathologic pictures (Figure 3).

Analysis of the T-cell receptor-γ gene rearrangement performed in 16 cases revealed a monoclonal band in 8 cases and a smear in the other 8 cases. There was no relationship between the presence or absence of monoclonality and the presence or absence of skin disease at follow-up assessments. In 1 patient, a monoclonal population of T lymphocytes was demonstrated in 2 biopsy specimens obtained 17 years apart. Although the lengths of the PCR products were similar, we could not sequence the products to check whether the same T-cell clone was persistent for such a long period.

Follow-up data were available for all 23 patients (mean follow-up period, 102.1 months; median, 76 months; range, 11-382 months). No patient developed skin lesions of MF. Fourteen patients were alive without any sign of skin disease. Five of them had received local corticosteroid treatment, 5 had undergone surgical excision, and 1 had received light therapy (UV-B at 311 nm). Seven patients were alive with skin disease. In all of these patients, skin lesions had remained largely unchanged during the follow-up period. Four of them had received local corticosteroid treatment, 2 had obtained no therapy, and 1 had received psoralen–UV-A therapy. Two patients had died of unrelated conditions after follow-up periods of 30 and 25 months. In both of these, skin lesions were unchanged at the time of death according to information given by relatives.

COMMENT

To our knowledge, this is the largest follow-up study on LA and its relationship to MF. Our data show that 9 patients (39%) had persistent skin disease after a mean follow-up of 102.1 months. However, there were no substantial changes in the clinical picture, and classic MF developed in none of these patients. In the literature, an association between PPPD (including LA, Shamberg disease, and other variants difficult to classify) and MF, as well as progression of PPPD to MF, is reported. In this context, it is notable that the first patient with LA described in the American literature subsequently died of MF. In the study by Toro and coworkers, histopathologic examination and analysis of the T-cell receptor gene rearrangement in 56 patients with PPPD raised

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y</th>
<th>Site</th>
<th>T-Cell Rearrangement</th>
<th>Follow-up, mo</th>
<th>Status</th>
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<tr>
<td>1/M/37</td>
<td>Heel</td>
<td>Polyclonal</td>
<td>11</td>
<td>A−</td>
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<td>204</td>
<td>A+</td>
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<td>Buttocks</td>
<td>Monoclonal</td>
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<td>A−</td>
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<td>Monoclonal</td>
<td>51</td>
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<td>37</td>
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<tr>
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<td>64</td>
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<td>41</td>
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<td>Right trunk</td>
<td>ND</td>
<td>382</td>
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Abbreviations: A−, alive without skin disease; A+, alive with skin disease; D+, dead of unrelated conditions with persistent skin disease; ND, not done.
the suspicion that this condition is biologically related to MF. Barnhill and Braverman described 3 patients with PPPD evolving to MF during follow-up periods averaging 8.4 years. Lipsker et al evaluated 17 patients who were diagnosed clinically and histologically as having chronic pigmented purpura. Two of these patients developed cutaneous T-cell lymphoma within a few years. However, our results indicate that conventional cases of LA have an excellent prognosis and do not eventuate into MF. Viseux et al describe a patient with PPPD who developed MF after 24 years, but lesions in our patients were stable or regressed spontaneously, a finding that would be unusual for classic MF. In fact, 5 patients had skin lesions that resolved without any treatment and did not recur during the follow-up period (range, 37-168 months), indicating possible spontaneous resolution of the dis-

Figure 1. A-G. Different clinical presentations of patients with lichen aureus.
ease. Although lesions of MF can regress spontaneously as well, recurrences are the rule. However, the median follow-up period (76 months) among our patients may be too short to completely rule out the possibility of evolution to MF.

It is intriguing that histopathologic features of LA are sometimes indistinguishable from those of MF. In this context, in half of our cases a monoclonal population of T lymphocytes was observed, confirming previous observations by Toro and coworkers\textsuperscript{11} and by Crowson and coworkers.\textsuperscript{23} A similar finding was recently published by Magro and coworkers.\textsuperscript{24} However, their inclusion criteria differed, and approximately 40% of patients with PPPD having monoclonal populations of T lymphocytes were reported to have clinicopathologic features consistent with MF. A similar rate of clonal cases (about 50%) is found in follicular mucinosis–alopecia mucinosa, a disease that is linked to MF.\textsuperscript{25} The interpretation of rearrangement studies in these cases is controversial. Detection of a clonal T-cell receptor rearrangement has been observed in certain inflammatory benign skin disorders such as pityriasis lichenoides\textsuperscript{26,27} or lichen planus\textsuperscript{28} and is obviously not synonymous with malignant neoplasms. On the other hand, 1 of our patients had a monoclonal T-cell infiltrate in a lesion that had persisted unchanged and revealed identical histopathologic features in biopsy specimens obtained 17 years apart. It may be that LA is a clonal dermatosis in which the clone is kept under control by immune surveillance but in a few patients may escape immune surveillance and become a dominant clone. In this context, LA treatment should continue until complete resolution, or patients should be kept under regular follow-up observation. Recently, LA has been included in a group of “cutaneous T-cell lymphoid dyscrasias” with potential for progression to cutaneous T-cell lymphoma.\textsuperscript{29}

The cause of PPPD and LA remains unknown. Familial cases\textsuperscript{30} and associations with hematologic diseases, hepatic diseases,\textsuperscript{31} and diabetes mellitus\textsuperscript{32} have been reported. In some cases, LA has been related to allergic contact allergens such as paraphenylenediamine, cobalt, benzoyl peroxide, balsam of Peru, and glass wool.\textsuperscript{21} Treatment in our patients varied, including local corticosteroid use, surgical excision, light therapy, and no treatment, but persistence or resolution of skin lesions was unrelated to the type of therapy. Given the reported possible association with MF,\textsuperscript{7-11} patients with PPPD or LA should be treated according to schemes efficacious for both diseases.

In conclusion, we showed that no progression to MF was observed in our group of patients with conventional LA. However, LA belongs to the expanding spectrum of so-called clonal dermatoses, and a possible evolution to MF cannot be ruled out. Therefore, close patient follow-up observation is recommended.

\textbf{Figure 2.} Patient 14 in the Table. Dense bandlike infiltrate of lymphocytes with hemorrhage (hematoxylin-eosin, original magnification ×10).

\textbf{Figure 3.} Patient 3 in the Table. A, Appearance of skin lesion in 1990. B, A biopsy specimen obtained in 1990 showed a bandlike infiltrate. C, Note sparse hemorrhage and coarse bundles of collagen in the papillary dermis. D, Appearance of the lesion in 2007. E, A biopsy specimen obtained in 2007 revealed persistence of the lymphocytic infiltrate. F, Note features similar to those of the biopsy specimen obtained in 1990. Hematoxylin-eosin, original magnification ×10 (B), ×20 (C and F), and ×4 (E).
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Author Contributions: Drs Fink-Puches, Wolf, Kerl, and Cerroni had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Cerroni.

Acquisition of data: Fink-Puches and Cerroni.

Analysis and interpretation of data: Fink-Puches, Wolf, Kerl, and Cerroni.

Drafting of the manuscript: Fink-Puches.

Critical revision of the manuscript for important intellectual content: Wolf, Kerl, and Cerroni.

Study supervision: Cerroni.

Financial Disclosure: None reported.

References


Correction

Notice of inadvertent duplicate publication. The article “Skin surface electron microscopy in Pityrosporum Folliculitis: The role of follicular occlusion in disease and the response to oral Ketoconazole” by Hill et al was inadvertently published twice in the Archives of Dermatology in 1990, once in February (1990;126[2]:181-184) and again in August (1990;126[8]:1073-1074). This was through no fault of the authors; rather, it appears to have been the result of a database error in the publisher's office, with the article not appearing to have been published and, consequently, being published again.