Association of hidradenitis suppurativa disease severity with increased risk for systemic comorbidities

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Tattoos and coincidental skin conditions: the example of lymphomatoid papulosis

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Dear Editor, I read with interest the recent report by Haus et al.1 about a patient who developed two lesions of lymphomatoid papulosis (LyP) on the red parts of a tattoo. However, their report deserves a few comments. Many reported pseudolymphomas on tattoos involve T cells or both T and B cells, and are not attributed ‘mainly’ to B cells, as described in the manuscript.2,3 To date, Sangueza et al.4 in 1992 have published the only well-documented report of the malignant transformation of a T-cell pseudolymphoma into a monoclonal B-cell lymphoma related to a chronic tattoo reaction.

It is widely accepted that mercury has disappeared from red ink manufacturing.5 Despite withdrawal of mercury, red tattoo reactions, including pseudolymphoma, still occur, raising the question of the culprit component or by-product leading to such reactions. Beyond the nosological issues that the authors try to discuss (LyP or pseudolymphoma), the present case illustrates an increasingly frequent situation due to the popularity of tattoos, namely the occurrence of coincidental dermatological conditions in tattooed individuals. Indeed, in the vast majority of cases of both pseudolymphoma and other ‘allergic’ reactions, tattoos display either a complete infiltration of the whole culprit colour or an infiltration made by more or less distinct papules or nodules restricted to one colour.2,3 A tattoo ‘allergy’ does not present as one, two or three single lesions on a very little part of the culprit colour. It is hard to conceive that a chronic stimulation of a clonal subset of lymphocytes against a specific component of the colour would be responsible for only an extremely limited reaction on two distant parts of such a wildly coloured area as reported by Haus et al. Besides, despite being rare, localized LyP happens more often among the young.6

It seems rather likely that this patient developed a localized LyP on a fortuitous tattooed area. One could argue the possible presence of specific impurities located specifically on both areas that could have selected a monoclonal population, but it is pushing the speculation rather far, especially as the reaction spontaneously resolved after 2 months and the patient has now been disease free for the past 1.5 years. Pseudolymphomas on tattoos may indeed regress spontaneously,2 but they usually follow a protracted course in the absence of any treatment. The number of anecdotal reactions on tattoos7 will keep on increasing with the popularity of tattoos and the ageing of the tattooed population, due to a fortuitous coexistence of a skin condition and the tattoo. LyP on a tattoo seems to be one of them.

References

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Association of hidradenitis suppurativa disease severity with increased risk for systemic comorbidities

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Dear Editor, Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic, inflammatory skin disease affecting terminal hair follicles in apocrine-gland-bearing skin.1

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### Table 1 Baseline status of enrolled patients with hidradenitis suppurativa (HS)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients, n = 154</th>
<th>High disease burden, n = 60</th>
<th>Medium disease burden, n = 94</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years), mean ± SD</td>
<td>36.3 ± 11.76</td>
<td>37.2 ± 12.90</td>
<td>35.8 ± 11.00</td>
</tr>
<tr>
<td>Age &lt; 40 years, n (%)</td>
<td>98 (63.6)</td>
<td>37 (62)</td>
<td>61 (65)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>110 (71.4)</td>
<td>35 (58)</td>
<td>75 (80)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>110 (71.4)</td>
<td>42 (70)</td>
<td>68 (72)</td>
</tr>
<tr>
<td>Black</td>
<td>29 (18.8)</td>
<td>12 (20)</td>
<td>17 (18)</td>
</tr>
<tr>
<td>Other</td>
<td>15 (9.7)</td>
<td>6 (10)</td>
<td>9 (10)</td>
</tr>
<tr>
<td><strong>Modifiable cardiovascular risk factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>History of diabetes mellitus, n (%)</strong></td>
<td>10 (6.5)</td>
<td></td>
<td></td>
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<tr>
<td>Current tobacco use, n (%)</td>
<td>85 (55.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI ≥ 30 and/or obesity, n (%)</td>
<td>103 (66.9)</td>
<td></td>
<td></td>
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<tr>
<td>TC ≥ 240 mg dL⁻¹ or medical</td>
<td>18 (11.7)</td>
<td></td>
<td></td>
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<tr>
<td>history of hyperlipidaemia, n (%)</td>
<td>39.6 (61.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of risk factors, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>55 (35.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>28 (18.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>7 (4.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2 (1.3)</td>
<td></td>
<td></td>
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</tbody>
</table>

Percentages are based on patients with nonmissing values. BMI, body mass index; DBP, diastolic blood pressure; hsCRP, high-sensitivity C-reactive protein; HS-PGA, Physician's Global Assessment; PHQ, Patient Health Questionnaire; SBP, systolic blood pressure; TC, total cholesterol; VAS, visual analogue scale. *Normal range < 3–1 mg L⁻¹. †VAS ranging from 0 (no pain) to 100 (worst pain). ‡PHQ-9 scores for depression severity: 0–4 none, 5–9 mild, 10–14 moderate, 15–19 moderately severe, 20–27 severe.
Associated comorbidities include depression, obesity and metabolic syndrome. The objective of the current analysis of patients with moderate-to-severe HS was to identify the most common comorbidities, their prevalence according to the level of HS disease burden (high vs. medium) and any association between baseline characteristics and the risk for the comorbidity. These patients, representing one of the largest HS groups to be evaluated to date, were adults from a 52-week, phase 2, randomised, double-blind, placebo-controlled trial of adalimumab treatment, who had at least moderate disease [HS Physician’s Global Assessment (HS-PGA) grade ≥ 3; 0–5 scale]. Additional inclusion/exclusion criteria were published previously.

Baseline comorbidities were identified with patient reports and medical histories. The following conditions were defined: hypertension, use of antihypertensive medication and/or self-reported history; uncontrolled hypertension, systolic/diastolic blood pressure (SBP/DBP) ≥ 140/≥ 90 mmHg; depression, Patient Health Questionnaire 9 (PHQ-9) score ≥ 10; morbid obesity, body mass index (BMI) ≥ 40 kg m–2; hyperlipidaemia, total cholesterol ≥ 240 mg dL–1; high HS disease burden, HS-PGA > 3 and/or Hurley stage III; and medium HS disease burden, HS-PGA ≤ 3 and Hurley stage II.

All patients with available baseline values were included in this analysis. All statistical tests were two-sided and significant at 0.05. Associations between the most common comorbidities and baseline characteristics were evaluated by logistic regression. The odds ratio (OR) with 95% Wald confidence interval (CI) was provided. Final models were chosen by stepwise selection with a P-value of 0.15 for both entry and stay. Model selection was conducted per Akaike information criteria and Bayesian information criteria, which confirmed the final models selected by the stepwise selection method.

Of the 154 patients in this analysis, 60 (39.0%) had high HS disease burden and 94 (61.0%) had medium burden. Mean high-sensitivity C-reactive protein (CRP) was almost four times higher in the high vs. medium disease burden groups (32.7 mg L–1 vs. 8.7 mg L–1). Combining self-report and medical examination results, 39.6% of patients had...
hypertension, 38.3% were morbidly obese and 48.1% had depression. The incidence of modifiable cardiovascular risk factors (Table 1) revealed that >50% of patients were smokers, overweight or had hypertension. Other cardiovascular risk factors included hyperlipidaemia (11.7%) and diabetes mellitus (6.5%). Over one-third of patients (35.7%) had two cardiovascular risk factors (Table 1).

Of the 40.3% of patients who had and/or were diagnosed with hypertension, or were receiving antihypertensive medication (Fig. 1a), 53% had been diagnosed with hypertension, and 31% had been both diagnosed and treated. Of the latter, 53% had reached the treatment goal (SBP/DBP <140/<90 mmHg). Similarly, a minority with hyperlipidaemia were both diagnosed and receiving medication (Fig. 1a).

The percentage of patients with morbid obesity or depression was 14% and 17% higher, respectively, in patients with high vs. medium disease burden (Fig. 1b). The percentage of patients with hypertension was 6% lower in patients with high vs. medium disease burden (Fig. 1b).

Multiple logistic regression identified the most influential factors for morbid obesity and depression. An association with increased odds of morbid obesity was seen for high HS disease burden (OR 2.13, 95% CI 1.00–4.53), and a trend towards association was seen for depression (OR 1.74, 95% CI 0.82–3.68). Smoking was associated with reduced odds of morbid obesity (OR 0.47, 95% CI 0.22–0.99). High HS disease burden (OR 2.12, 95% CI 1.04–4.31), female sex (OR 2.57, 95% CI 1.13–5.85) and smoking (OR 2.35, 95% CI 1.15–4.81) were associated with increased odds of depression.

High HS disease burden was significantly associated with increased prevalence of morbid obesity and depression, but not hypertension, partially contradicting a previous report that also demonstrated the high prevalence of obesity and depression in patients with HS, but not significant association between disease severity and BMI or depression.

Our findings are novel because we demonstrate that the magnitude of HS disease burden appears to be correlated with the risk of depression and morbid obesity, even after controlling for possible confounding variables.

Based on these findings, instructive parallels and differences can be drawn between HS and psoriasis. Positive correlations between psoriasis disease severity and obesity and between psoriasis disease severity and CRP elevation have been demonstrated. However, patients with psoriasis have lower CRP levels, and psoriasis disease severity correlates with hypertension prevalence. More than just skin diseases, both HS and psoriasis are systemic diseases associated with high systemic inflammation and numerous comorbidities.

This analysis had several limitations. A cross-sectional study cannot assess causality. This population may not reflect the entire spectrum of patients with HS because it was limited to clinical trial participants, for whom previous treatment with tumour necrosis factor-α inhibitors, cardiac insufficiency (New York Heart Association class III or greater), active skin diseases and tumours were exclusion criteria. Meaningful correlations were difficult to establish due to the limited population size. Finally, patient-reported prevalence of comorbidities is subject to recall bias.

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References


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of the manuscript, and decision to submit the manuscript for publication.

Conflicts of interest: J.J.C. has received honoraria and grants from AbbVie and Amgen for participation on ad boards and as a speaker and investigator, and grants from Astra-Zeneca, Celgene, Janssen, Lilly, Pfizer, Merck and Regeneron for participation as an investigator. J.R.M. declares no conflicts of interest; his department was reimbursed by AbbVie for his participation as an investigator in this clinical trial. C.C.Z. has received honoraria from AbbVie and Stiefel/GlaxoSmithKline for participation on advisory boards, and as an investigator and speaker, from Galderma for participation on advisory boards; from LEO Pharma for participation as a consultant; and from Bayer Health Care, Bioderma, Biogen-Idec, General Topics and Glenmark for his participation as a speaker; his department received grants from AbbVie, Biogen-Idec, BMS, Immundiagnostik AG, LVMH, Merz, Pierre Fabre and UCB for his participation as an investigator, and from Intendis for his participation on an advisory board. N.S. has received payments from AbbVie and Celgene for participation as an investigator; honoraria from Medicis, Merz, Stiefel and Valeant for participation on advisory boards; and receives a salary as an employee of Optigenex, Inc. A.K. is a consultant and investigator for Janssen, AbbVie and Amgen, and has received fellowship funding from Janssen. F.K. has received honoraria from AbbVie, Amgen, Astellas, Galderma, Janssen and Medicis for participation as a speaker; and has received grants from AbbVie for participation as an investigator. M.S., Y.G. and M.M.O. receive a salary as AbbVie employees, and may also receive AbbVie stock, stock options and/or stock grants.

Some data from this manuscript were presented at the 71st Annual Meeting of the American Academy of Dermatology (AAD) at Miami Beach, FL, U.S.A., 1–5 March 2013.

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**Familial pachyonychia congenita with steatocystoma multiplex and multiple abscesses of the scalp due to the p.As92Ser mutation in keratin 17**

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**Dear Editor,** Pachyonychia congenita (PC) is a rare genodermatosi...