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 acrotrichial, 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>HS severity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
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<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>78 (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>Modifiable cardiovascular risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of diabetes mellitus, n (%)</td>
<td>10 (6.5)</td>
<td></td>
<td></td>
</tr>
<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>
</tr>
<tr>
<td>TC ≥ 240 mg dL⁻¹ or medical history of hyperlipidaemia, n (%)</td>
<td>18 (11.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP ≥ 140 and/or DBP ≥ 90 mmHg or history of hypertension, n (%)</td>
<td>39 (61.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of risk factors, n (%)</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>
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<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>
</tr>
</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, HS 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

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**Fig 1. Comorbidities in patients with hidradenitis suppurativa: study population.**

(a) Number and percentage of patients with hypertension or hyperlipidaemia at baseline (BL). (b) Prevalence of main comorbidities in patients with high disease burden (HDB) vs. medium disease burden (MDB). Hypertension was identified by treatment with antihypertensive medication and/or self-reported history at BL. BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; OR, odds ratio; PHQ, Patient Health Questionnaire; SBP, systolic blood pressure.
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.7 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 obesity8 and between psoriasis disease severity and CRP elevation9 have been demonstrated. However, patients with psoriasis have lower CRP levels,9 and psoriasis disease severity correlates with hypertension prevalence.8 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.9 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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Familial pachyonychia congenita with steatocystoma multiplex and multiple abscesses of the scalp due to the p.Asn92Ser mutation in keratin 17

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Dear Editor, Pachyonychia congenita (PC) is a rare genodermatosis transmitted as an autosomal dominant trait that is caused by mutations in the differentiation-specific keratin genes KRT6a (52%), KRT6b (3%), KRT16 (28%) or KRT17 (17%), which are expressed in the nails, skin, oral mucosa, larynx, hair and teeth.1 Approximately 1000 patients with PC have been identified, of whom 400 have been confirmed genetically to have it. Two subtypes have been classically described: PC-1 (Jadassohn–Lewandowsky type, OMIM#167200), caused by mutations in KRT6a or KRT16, with predominant oral leucokeratosis and palmoplantar keratoderma; and PC-2 (Jackson–Lawler type, OMIM#167210) resulting from mutations in KRT6b or KRT17, with neonatal teeth, pili torti and multiple cysts.2,3 The presence of multiple sebaceous cysts [steatocystoma multiplex (SM)] at puberty has been proposed to differentiate PC-2 from PC-1,2,3 but it is now recognized that there is a considerable overlap between the two classical subtypes of PC, and a new classification based on the mutated keratin gene has now been proposed (PC-6a, PC-6b, PC-16 and PC-17).4,5

A 12-year-old girl presented with a painful inflammatory plaque on her scalp, which had appeared recently without any fever. She had a previous history of microcysts on her face and multiple unsuccessful treatments for suspected fungal infection of fingernails and toenails. She had neonatal teeth. Her mother had multiple steatocystomas on her face and trunk (Fig. 1a), focal plantar keratoderma (Fig. 1b), normal nails and a history of neonatal teeth. She had no history of abscesses. Clinical examination of the scalp of the proband showed multiple suppurative, well-circumscribed, alopecic and cicatricial plaques on her vertex (Fig. 2a) and rough hair. She had multiple microcysts on her face, predominantly on her forehead (Fig. 2b); sebaceous cysts in the armpits; ophryogenes-type keratosis pilaris of the eyebrows; pachyonychia of all finger and toenails (Fig. 2c); and keratosis pilaris on both thighs. The patient had no palmoplantar keratoderma. Histology of the scalp revealed a cystic formation with no content, lined with a thin eosinophilic epithelial lining, highly suggestive of a sebaceous cyst (Fig. 2d). A non-perifollicular polymorphic inflammatory granuloma, rich in neutrophils, lymphocytes and plasmocytes, was seen in the deep dermis. Fungal examination was negative, and bacteriological cultures yielded occasional colonies of Staphylococcus aureus. Microscopical examination of the hair shaft showed normal thickness and a longitudinal fissure giving a flat appearance (in places triangu-