Incidence of Cancer Among Patients With Hidradenitis Suppurativa

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Background: On the basis of some case reports, a relationship has been suggested between hidradenitis suppurativa (HS) and the development of nonmelanoma skin cancer.

Objectives: To confirm this relationship and to explore the risk of other cancers among patients with HS.

Patients: Patients with a discharge diagnosis of HS were obtained from the computerized database of hospital discharge diagnoses from January 1, 1965, through December 31, 1997. A total of 2119 patients with HS were identified.

Setting: All hospitals in Sweden.

Design: With record linkage to the Swedish National Cancer Registry, standardized incidence ratios (SIR [the ratio of the observed to expected incidence]) were calculated to estimate relative risk.

Results: The risk of developing any cancer in the cohort with HS increased 50% (95% confidence interval of SIR, 1.1-1.8, based on 73 observed cases). Statistically significant risk elevations were observed for nonmelanoma skin cancer (5 cases; SIR, 4.6; 95% confidence interval, 1.5-10.7), buccal cancer (5 cases; SIR, 5.5; 95% confidence interval, 1.8-12.9), and primary liver cancer (3 cases; SIR, 10.0; 95% confidence interval, 2.1-29.2).

Conclusions: This study confirms an increased risk of nonmelanoma skin cancer among patients with HS. The risk for buccal cancer and primary liver cancer was also elevated among this cohort, but these associations should be interpreted cautiously because the combination of multiple significance testing and the few observed cases may have generated chance findings.

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Hidradenitis suppurativa (HS) is a chronic, suppurative, and cicatricial inflammatory disease, mainly affecting apocrine gland–bearing areas of the skin. Several case reports of co-occurrence of HS and nonmelanoma skin cancer have implied a causal relationship, but firm epidemiological data are lacking. In an attempt to confirm this association and to look for other cancer associations as well, we performed a retrospective cohort study of patients hospitalized for HS in Sweden. The patients were followed up for up to 32 years to examine the subsequent risks of cancer.

On average, the patients with HS were followed up for 9.8 years, yielding 20801 accumulated patient-years at risk. During the observation period, we ascertained a total of 81 cases of cancer (52 among women, 29 among men). The average age at diagnosis of cancer was 51.2 years for women and 55.0 years for men (Table 1). Among all 2119 patients, 134 (6%) had a diagnosis of alcoholism and 152 (7%) had a diagnosis of diabetes mellitus. About one third (652) of the patients had ever undergone surgical excision of the affected skin areas.

After excluding 8 cancer cases accumulated during the first year of follow-up (SIR, 1.9; 95% CI, 0.8-3.8), including 1 case of squamous cell carcinoma of the skin, the risk for any cancer (all sites) was increased by 50% among patients hospitalized for HS, compared with the age and sex-matched general Swedish population during the time of the study (Table 2). The estimated relative risks for cancers of different sites with at least 2 observed cases are also listed in Table 2. There was a significantly increased relative risk for nonmelanoma skin cancer (5 cases; SIR, 4.6; 95% CI, 1.5-10.7), but no excess risk was observed for melanoma skin cancer.
PATIENTS AND METHODS

STUDY COHORT

In 1964-1965, the National Board of Health and Welfare started collecting data on individual hospital discharges in the Inpatient Register. In addition to the national registration number (unique personal identifiers assigned to all Swedish residents), each record—corresponding to one in-hospital episode—contains administrative and medical data such as hospital department and discharge diagnoses. The diagnoses are coded according to the International Classification of Diseases, 7th Revision (ICD-7) through 1968, the eighth revision until 1987 (ICD-8), the ninth revision (ICD-9) until 1996, and the 10th revision (ICD-10) thereafter. The number of hospitals providing data to the register has increased steadily: the register covered 60% of the Swedish population in 1969, 75% in 1978, and 85% by the end of 1983. From 1987, the register attained complete nationwide coverage.

All patients recorded in the Inpatient Register with a discharge diagnosis of HS (ICD-7 = 714.07, ICD-8 = 705.91, ICD-9 = 705.W, and ICD-10 = L732) were initially selected for inclusion in the study. A total of 2259 unique national registration numbers were registered at least once with this diagnosis between January 1, 1965, and December 31, 1997. During the period 1987 through 1996, the ICD-9 code, 705.W, contains also other diseases, namely, pompholyx, bromhidrosis, and chromhidrosis. However, the incidence of these 3 diagnoses in Swedish inpatients is very low.

FOLLOW-UP DATA

Record linkage of the study cohort to the nationwide Register of Causes of Death, using the national registration numbers as identifiers, provided information on dates and causes of death among those deceased through 1997. Corresponding linkage to the emigration register identified dates of emigration. The National Swedish Cancer Register, founded in 1958 and close to 98% complete,17 was used to ascertain for inclusion in the study. A total of 2259 unique national registration numbers were registered at least once with this diagnosis between January 1, 1965, and December 31, 1997. During the period 1987 through 1996, the ICD-9 code, 705.W, contains also other diseases, namely, pompholyx, bromhidrosis, and chromhidrosis. However, the incidence of these 3 diagnoses in Swedish inpatients is very low.

Follow-up time (person-years) was calculated from the date of enrollment in the cohort (date of the first discharge from the hospital having a diagnosis of HS) until the occurrence of a first cancer diagnosis, emigration, death, or the end of the study (December 31, 1997). To avoid possible ascertainment bias associated with differential autopsy rates between the cohort members and the general population, we did not count cancers found incidentally at autopsy. Relative risk was estimated as the standardized incidence ratio (SIR), defined as the ratio of the observed number of cancers to that expected. The expected number of cancers was calculated by multiplying the number of observed person-years, divided into age- (in 5-year groups), sex-, and calendar year–specific strata, by the corresponding cancer incidence rates. These incidence rates, derived from the relevant strata in the entire Swedish population and aggregated by 5 calendar years to avoid instability in rates of rare cancers, were calculated by dividing number of the first primary cancers excluding those discovered incidentally at autopsy by person-years at risk (number of midyear population without reported cancer). The 95% confidence interval (CI) of the SIR was calculated on the assumption that the observed number follows a Poisson distribution.18 For selected cancer sites, stratified analyses were also performed to detect any difference of risk pattern across sex, duration of follow-up, period at discharge, status of comorbidities, and whether patients had ever undergone surgical excision of the affected skin areas. An approximate χ² test was used to test the difference between 2 SIRs.19 We also calculated standardized mortality ratios for selected causes of death. Patients with prevalent cancers (ie, those who had a previously registered diagnosis of cancer) were included in the mortality analyses. In the main analyses, we excluded cancers and person-years accumulated during the first year of follow-up to minimize the possible influence of selection bias. Such bias occurs if patients with HS and a subclinical cancer are more likely to be hospitalized than those without a subclinical cancer. If this is the case, these cancers are most likely to be diagnosed within the first year of follow-up.

STATISTICAL ANALYSIS

No obviously increased risk was observed for colon, rectum, breast, female genital system, and brain cancers in our cohort (Table 2). Nine cancers are not accounted for in Table 2 and they occurred in the following sites: stomach (1 patient), ampulla of Vater (1 patient), pancreas (1 patient), prostate (1 patient), testis (1 patient), thyroid (1 patient), and unspecified (3 patients).

Stratified analyses for selected cancer types among patients hospitalized for HS from January 1, 1965, through December 31, 1997, in Sweden by sex, follow-up dura-
tion, and calendar period of hospitalization are given in Table 3. Small numbers of observed and expected cancers hampered interpretation of these data. Men seemed to have a higher relative risk for all-site cancer, but a lower relative risk for nonmelanoma skin cancer and buccal cancer than women, although these differences were not statistically significant. The observed excess risk for primary liver cancer was seemingly confined to men, with a borderline significant difference between sex (P = .07). Except for buccal cancer, where the excess became more obvious after more than 10 years of observation (P = .05), there was no clear tendency of increasing or decreasing relative risks with time. Nor did the relative risks vary materially with calendar period of enrollment. The findings remained practically unaltered after removal of patients with a co-diagnosis of alcoholism, and the excesses seemed to be essentially independent of whether a surgical excision of the hidradenitis had been carried out (although only one case of buccal and no cases of primary liver cancers were observed among operated on patients). Cancer cases were clearly overrepresented among patients with a co-diagnosis of diabetes mellitus (P = .01 for all-site cancer and P < .01 for buccal cancer), but the excesses of all-site cancer, nonmelanoma skin cancer, and primary liver cancer remained (the latter nonsignificantly) after removal of the patients with diabetes mellitus.

To our knowledge, no other large-scale follow-up study of patients with HS has been published. The association between HS and the risk of nonmelanoma skin cancer has, however, been suggested in some case reports. The lack of proper denominators in measures of occurrence and of correct unexposed comparison groups make case reports a shaky basis for qualitative or quantitative inferences regarding cause-and-effect relationships. In our cohort of patients with HS, we observed a 4.6-fold increase of non-melanoma skin cancer, but among females than males, leading to a longer duration of the chronic disease in females.

The earliest inflammatory event in HS is a rupture of the follicular epithelium, followed by the spilling of foreign body material such as corneocytes, bacteria, sebum products, and hair into the dermis. The dumping of foreign products initiates an inflammatory response to cause a foreign body granuloma. Epithelial strands form sinuses in this inflammatory tissue. Secondary bacterial colonization in this milieu can intensify the chronic inflammation, a similar picture as seen with intravascular catheters and prosthetic devices, but in HS the process is long standing, and the presence of a foreign body enhances the pathogenetic properties of coagulase-negative staphylococci that are found in a high proportion of hidradenitis lesions. Thus, although it is not fully understood why HS predisposes to skin cancer, the suspicion has centered on the role of chronic irritation and infections that may lead to proliferative epidermal changes, including cancer. The reason for the greater risk among female patients than among male patients, although not clearly ascertained statistically in our data, is unclear. It may be related to hormonal factors or to the fact that HS has an earlier debut among females than males, leading to a longer duration of the chronic disease in females.

In our study, for the first time, it was possible to investigate other cancer risks in a relatively large group of patients with HS over 3 decades. Increases were found for several cancer types, most importantly buccal cancer and primary liver cancer. We have no information of the alcohol-drinking habits of our cohort, and, to our knowledge, no such studies exist, but the increased incidence of primary liver and buccal cancer might be an...
Buccal Cancer
Primary Liver Cancer

Therefore, substantial confounding by smoking habits and HS were found in a recent retrospective study. Similar results regarding smoking habits and HS were found in a matched-pair control group. Similar results regarding smoking habits and HS were found in a matched-pair control group.

We have shown a statistically significant 50% excess of malignant neoplasms among patients with HS. The greatest relative excess among patients with HS was for nonmelanoma skin cancer, buccal cancer, and primary liver cancer, but the confounding by smoking and possibly alcohol abuse might explain some or most of these excess risks. The increased frequency of skin cancers, the site

**Table 3. Standardized Incidence Ratio (SIR) and Its 95% Confidence Interval (CI) for Selected Cancer Types Among Patients Hospitalized for Hidradenitis Suppurativa, 1965-1997, Sweden, Stratified by Various Cofactors**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All-Site Cancer</th>
<th>Nonmelanoma Skin Cancer</th>
<th>Buccal Cancer</th>
<th>Primary Liver Cancer</th>
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<tbody>
<tr>
<td></td>
<td>Obs†</td>
<td>SIR</td>
<td>95% CI</td>
<td>Obs†</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26</td>
<td>1.7</td>
<td>1.2-2.5</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>47</td>
<td>1.4</td>
<td>1.0-1.8</td>
<td>4</td>
</tr>
<tr>
<td>Follow-up duration, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-9</td>
<td>43</td>
<td>1.4</td>
<td>1.0-1.9</td>
<td>2</td>
</tr>
<tr>
<td>10+</td>
<td>30</td>
<td>1.5</td>
<td>1.0-2.2</td>
<td>3</td>
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<tr>
<td>Period of enrollment in the cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1965-1986</td>
<td>55</td>
<td>1.5</td>
<td>1.1-2.0</td>
<td>3</td>
</tr>
<tr>
<td>1987-1997</td>
<td>18</td>
<td>1.3</td>
<td>0.8-2.1</td>
<td>2</td>
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<tr>
<td>Alcohol abuse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>70</td>
<td>1.5</td>
<td>1.2-1.9</td>
<td>5</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>1.0</td>
<td>0.2-2.9</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>61</td>
<td>1.3</td>
<td>1.0-1.7</td>
<td>4</td>
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<tr>
<td>Yes</td>
<td>12</td>
<td>2.8</td>
<td>1.5-5.0‡</td>
<td>1</td>
</tr>
<tr>
<td>Surgical excision</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>40</td>
<td>1.5</td>
<td>1.1-2.1</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>33</td>
<td>1.4</td>
<td>1.0-2.0</td>
<td>4</td>
</tr>
</tbody>
</table>

* Data exclude the first year of follow-up. Ellipses indicates not applicable.
† Observed (Obs) cases of cancer.
‡ Differences of SIRs between 2 strata, P < .05.
§ Differences of SIRs between 2 strata, P < .01.

**CONCLUSIONS**

We have shown a statistically significant 50% excess of malignant neoplasms among patients with HS. The greatest relative excess among patients with HS was for nonmelanoma skin cancer, buccal cancer, and primary liver cancer, but the confounding by smoking and possibly alcohol abuse might explain some or most of these excess risks. The increased frequency of skin cancers, the site
of the chronic inflammation, and bacterial colonization, support a possible etiopathologic link between the disease and neoplasia. Clinicians caring for patients with HS should be aware of their propensity to develop these tumors. Whenever atypical clinical manifestations of HS occur, histopathologic examination of representative skin biopsy specimens are recommended.

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