Prevalence of Cutaneous Disorders in a Population of HIV-Infected Patients

Southwestern France, 1996

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Objectives: To estimate the current extent of cutaneous disorders in a large population of ambulatory and hospitalized human immunodeficiency virus (HIV)–infected patients and to describe characteristics associated with the presence of current skin manifestations.

Design: Cross-sectional survey.

Setting: Hospital units participating in the hospital-based information system of the Groupe d’Épidémiologie Clinique du SIDA en Aquitaine, southwestern France.

Patients: All the patients seen by physicians between November 18 and December 20, 1996, in the participating units (hospital ward, outpatient clinic, or day hospital).

Main Outcome Measures: Prevalence and cumulative incidence of cutaneous disorders.

Results: Four hundred fifty patients at all stages of HIV disease were enrolled; 65.3% had at least 1 skin manifestation during the course of HIV infection. A history of skin disorder was reported for 269 patients (59.8%), and 199 patients (44.2%) had clinical dermatologic manifestations at the time of the study. The most frequent causes of cutaneous disorders were infections (fungal, viral, and bacterial), neoplasia, and miscellaneous disorders. Skin diseases were more likely to be reported in homosexual and bisexual men and in patients with clinically and biologically advanced HIV infection.

Conclusions: Cutaneous disorders occur more frequently as HIV infection advances and immune function deteriorates; however, they are common and of various types throughout the course of HIV disease. Taking cutaneous disorders into consideration for case management is essential to improve quality of life for HIV-infected patients.

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Skin disorders are common manifestations of human immunodeficiency virus (HIV) disease: they affect between 80% and 95% of HIV-infected patients according to the literature,1-5 occurring at anytime in the course of infection. Skin is often the first and only organ affected during most of the course of HIV disease.1,6-7

SAMPLE CHARACTERISTICS

For editorial comment see page 1290

Cutaneous disorders during HIV infection are numerous.3-9 Some have drawn attention because their onset defines some of the Centers for Disease Control and Prevention (CDC) acquired immunodeficiency syndrome (AIDS) clinical categories, eg, oral candidiasis, zoster, herpes simplex, oral hairy leukoplakia, and Kaposi sarcoma,6,9 but most have been documented solely in case reports. In the context of HIV infection, cutaneous disorders can present with particular clinical manifestations: unusual anatomical sites, increased severity, treatment failure, and unusual clinical appearance.11 Moreover, it is argued that some cutaneous disorders reflect the progression of HIV disease,4,6,10 but this relation is still controversial.11

This survey estimated the prevalence of cutaneous disorders in a large population of HIV-infected patients seen in public hospitals in the Aquitaine region, southwestern France, and we studied the link of these skin manifestations with the progression of HIV disease.

RESULTS

Four hundred eighty-eight patients were seen in the participating hospital units during the study, among whom 38 were excluded from the analysis because of a lack
PATIENTS, MATERIALS, AND METHODS

The Groupe d’Épidémiologie Clinique du SIDA en Aquitaine (GECSA) is a coordinated group of clinicians, biologists, and epidemiologists who, since 1987, have developed a hospital-based information system on HIV infection including most of the hospitals of the Aquitaine region. It is an open system in which all patients with HIV infection seen in participating hospital units are enrolled, if they wish to do so, and then are followed up prospectively. At each hospital visit, epidemiological, clinical, biologic, and therapeutic data are collected on a standardized questionnaire. Entry criteria for the GECSA system are HIV-1 infection confirmed by a Western blot test, age older than 13 years, and informed consent; all types of HIV transmission categories and the 2 sexes are included.

All patients seen in hospital units (hospital ward, day hospital, or outpatient clinic) participating in the GECSA system, mainly infectious diseases and internal medicine departments, between November 18 and December 20, 1996, were eligible for this cross-sectional study. During the study, participating physicians (17 specialists in dermatology, internal medicine, infectious diseases, and general practice) were asked to perform a systematic, complete cutaneous examination of all HIV-infected patients in addition to the current clinical examination. Moreover, they were asked to search for a previous history of cutaneous disorders in patients’ medical records. A specific questionnaire about previous and current cutaneous disorders was filled in by physicians as they were examining the patients, as was the standardized GECSA questionnaire providing information about patients’ baseline characteristics (age, sex, and HIV transmission group), HIV disease progression (clinical CDC category and CD4 cell count at the time of the study), and CDC-classifying cutaneous disorders. Patients for whom no CD4 cell count was available in the database during the month preceding the hospital visit were excluded. For patients who were seen more than once during the study, only the first visit was taken into account.

Information on history of CDC-classifying cutaneous disorders was available in the 2 sources of information (survey questionnaire and GECSA database). To take into account both sources and to avoid double counting, the cumulative incidence of these clinical manifestations was estimated by the capture-recapture method. Determinants of skin diseases prevalent at the time of the study were studied by univariate analysis using χ² and Fisher exact tests when appropriate.

of a CD4 cell count. The 450 enrolled patients were predominantly males (71.1%), and their mean age was 38.9 years. Main transmission groups were represented by homosexual and bisexual men (35.3%), intravenous drug users (27.8%), and heterosexuals (24.4%). Clinical and biologic characteristics of patients and their antiretroviral drug treatments at the time of the study are shown in Table 1. According to the CDC 1993 clinical classification, 145 patients (32.2%) were asymptomatic (category A), 182 patients (40.4%) had non–AIDS-defining symptoms (category B), and 123 patients (27.3%) had full-blown AIDS (category C). Median CD4 cell count in the month preceding the study was 0.273 × 10⁹/L (273/µm³) (range, 0.002-1.103 × 10⁹/L); 35.6% of patients had a CD4 cell count below 0.200 × 10⁹/L. More than 80% of patients were prescribed either bitherapy with 2 nucleoside analogs or tritherapy with 1 protease inhibitor and 2 nucleoside analogs at the time of the survey. Among the 183 patients undergoing triple combination therapy, 29 (16%) were prescribed a protease inhibitor for the first time at the time of the study; for the others, the median time of treatment with a protease inhibitor was 4 months (range, 0.5-9.0 months). Of these 183 patients receiving a protease inhibitor, 43.7% had full-blown AIDS and 61.2% had a CD4 cell count below 0.200 × 10⁹/L vs 16.8% and 19.1%, respectively, among those receiving monotherapy or bitherapy. Among the 450 patients in the sample, 271 (60.2%) were seen in a day hospital, 165 (36.7%) were seen in an outpatient clinic, and 14 (3.1%) were seen in a hospital ward.

CUMULATIVE INCIDENCE AND PREVALENCE OF CUTANEOUS DISORDERS

The existence of at least 1 cutaneous disorder during the course of HIV infection was reported for 294 patients (65.3%).

Two hundred sixty-nine patients (59.8%) had a history of at least 1 cutaneous disorder. These 29 previous cutaneous disorders are described in Table 2. The most frequent were caused by fungal infections (oral candidiasis, which had occurred in almost half of the patients), viral infections (zoster, herpes simplex, and oral

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Patients, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC clinical category</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>145 (32.2)</td>
</tr>
<tr>
<td>B</td>
<td>182 (40.4)</td>
</tr>
<tr>
<td>C</td>
<td>123 (27.3)</td>
</tr>
<tr>
<td>CD4 cell count, ×10⁹/L</td>
<td></td>
</tr>
<tr>
<td>0-0.049</td>
<td>35 (7.8)</td>
</tr>
<tr>
<td>0.050-0.199</td>
<td>125 (27.8)</td>
</tr>
<tr>
<td>0.200-0.349</td>
<td>131 (29.1)</td>
</tr>
<tr>
<td>≥0.350</td>
<td>159 (35.3)</td>
</tr>
<tr>
<td>Antiretroviral drug therapy</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>53 (11.8)</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>18 (4.0)</td>
</tr>
<tr>
<td>Bitherapy†</td>
<td>189 (42.0)</td>
</tr>
<tr>
<td>Tritherapy‡</td>
<td>183 (40.7)</td>
</tr>
<tr>
<td>Others</td>
<td>7 (1.5)</td>
</tr>
</tbody>
</table>

*CDC indicates Centers for Disease Control and Prevention. †Bitherapy includes 2 nucleoside analogs. ‡Tritherapy includes 1 protease inhibitor and 2 nucleoside analogs.
of the 10 more frequent cutaneous disorders was associated with the progression of HIV disease (Tables 2 and 3). The most frequent cutaneous disorders were caused by herpes simplex (13%), Kaposi sarcoma (13%), seborrheic dermatitis (13%), and pruritus (11%). The other skin diseases were observed in less than 10% of patients of this subgroup.

### **CLINICAL AND BIOLOGIC DETERMINANTS OF CUTANEOUS DISORDERS (KAPOSI SARCOMA EXCLUDED)**

Altogether, prevalence and cumulative incidence of cutaneous disorders were higher in homosexual and bisexual patients than in the other transmission groups: 78.5% of homosexual and bisexual patients reported at least 1 cutaneous disorder during the evolution of HIV infection vs 64.0% of intravenous drug users and 54.6% of heterosexuals (P<.001). Moreover, the prevalence of skin diseases was associated with the progression of HIV disease regardless of CD4 cell count: overall, 31.0% of patients in CDC category A had cutaneous symptoms at the time of the study vs 41.2% in category B and 62.2% in category C (P<.001), and this association remained significant after adjustment for CD4 level. Biologically, 81.8% of patients with a CD4 cell count below 0.050 × 10⁹/L had a skin disorder vs 51.7% of patients with a count of 0.050 × 10⁹/L.
Our prevalence estimate of skin disorders, 65.3%, is much lower than that in previous reports: Pitche et al reported a prevalence of 82.5% in HIV-infected patients hospitalized in Togo, West Africa; Coldiron and Bergstresser observed a prevalence of 92.0% among 100 serial outpatients in Texas; and Goodman et al reported higher prevalence figures of all skin diseases among 117 HIV-infected outpatients and inpatients. However, in these 3 studies, patients were much more advanced in HIV disease than in our sample: most patients had full-blown AIDS or had at least non–AIDS-defining symptoms. Similarly, the prevalences of cutaneous disorders reported by Uthayakumar et al and Goldstein et al were higher than those in our study; however, in the former the study population included almost exclusively homosexual and bisexual men, and in the latter, the study setting was a department of dermatology, with an obvious referral bias.

The GECSA hospital-based information system deals with at least 80% of the HIV-infected patients known in the Aquitaine region. Thus, our results provide an estimation of the frequency of skin disorders among a sample that is representative of the current population of HIV-infected patients followed up by the hospital wards in Aquitaine, the third region in France for AIDS reporting.

Using data from a specific questionnaire filled in by participating physicians in addition to results of the regular medical examination may still have led to an underestimate of the frequency of cutaneous disorders: skin diseases present at the time of the study but for which diagnosis requires a careful examination, eg, dermatophyte infections, may have been missed by a nonspecialist. Moreover, history of minor cutaneous disorders may have been underestimated in relation to a recall bias, and previous cutaneous disorders whose occurrence defined a CDC clinical category were more likely to be well remembered by physicians. In addition, our estimation of prevalence of previous skin disorders used 2 sources of information for the classifying conditions but only 1 source for the others because they were not reported in the GECSA standardized questionnaire: the capture-recapture method used when information was provided by the 2 sources took into account the cases notified by each of the 2 sources but corrected the possible overlap.

The overall predominance of skin disorders in homosexual and bisexual men compared with the other HIV transmission groups, even after exclusion of Kaposi sarcoma, may be explained by the fact that these patients usually report more easily their discomfort than the others. Moreover, some skin disorders, such as condyloma or molluscum contagiosum, are known to be caused by sexually transmitted agents.

Our results show that cutaneous disorders are more and more frequent as HIV infection clinically advances and immune function deteriorates, ie, in patients with full-blown AIDS, with a low CD4 cell count, and whose status justifies the prescription of a tritherapy of antiretroviral drugs.

### Table 4. Prevalence of the 6 Most Frequent Cutaneous Disorders According to Clinical Stage of HIV Infection and CD4 Cell Count, Groupe d’Épidémiologie Clinique du SIDA en Aquitaine, November to December 1996 (N = 450)*

<table>
<thead>
<tr>
<th>Cutaneous Disorder</th>
<th>CDC Category</th>
<th>CD4 Cell Count, $10^9$/L</th>
<th>$&lt;0.200$ (n = 290)</th>
<th>$&lt;0.200$ (n = 160)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerosis</td>
<td>A (n = 145)</td>
<td>B (n = 182)</td>
<td>C (n = 123)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 (5.5)</td>
<td>21 (11.5)</td>
<td>15 (12.2)</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
<td>10 (6.9)</td>
<td>17 (8.3)</td>
<td>14 (11.4)</td>
<td>0.44</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>9 (6.2)</td>
<td>12 (6.6)</td>
<td>11 (8.9)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>0</td>
<td>0</td>
<td>32 (26.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>0</td>
<td>8 (4.4)</td>
<td>11 (8.9)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Molluscum contagiosum</td>
<td>1 (0.7)</td>
<td>6 (3.3)</td>
<td>10 (8.1)</td>
<td>0.006</td>
<td></td>
</tr>
</tbody>
</table>

* Patients may have more than 1 diagnosis. Values are given as numbers (percentages). HIV indicates human immunodeficiency virus; CDC, Centers for Disease Control and Prevention.
† Value has not been computed.
rovirral drugs. However, the median CD4 cell count of patients who have skin disorders in our study is high, close to 0.200 × 10^9/L, suggesting that most of these cutaneous manifestations can occur even early in the course of HIV disease. The analysis restricted to the subgroup of patients who had begun a threerapy of antiretroviral drugs with a protease inhibitor before the study did not reveal any particular pattern of skin diseases among these patients compared with the others.

In conclusion, our report underlines the extent of the cutaneous disorders throughout the course of HIV infection. This implies that the occurrence of these skin disorders in patients not known to be HIV infected must lead to HIV testing. Moreover, looking systematically for these troubles in known HIV-infected patients seems essential: their occurrence may reflect a deterioration of the immune system, and prescription of specific symptomatric treatments should be considered because the length of life of HIV-infected patients is increasing and because their quality of life is emerging as an important aspect to take into account in case management. Finally, it will be interesting to study the future impact of the recent introduction of new antiretroviral drug therapies on the incidence and prevalence of these skin disorders at each stage of HIV disease.

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