ONCHODERMAL SKIN DISEASE IN A HYPERENDEMIC ONCHOCERCIASIS FOCUS IN WESTERN UGANDA

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Abstract. To assess the degree of skin disease in Simulium neavei s.s.-transmitted onchocerciasis, 72 patients infected with Onchocerca volvulus in the Kabarole district of Uganda were studied. They were clinically and parasitologically evaluated. Onchocercal skin lesions were determined using a modified Murdoch skin assessment, and skin scores were calculated. The chronic skin score (4.0) was associated with age, and the acute skin score (8.5) was significantly higher in males. The burden of onchocercal skin lesions was found to be high in most patients. The number of nodules (median number 1.9) and the microfilarial load (geometric mean of microfilaria 11.5) were not determinants for the burden of onchocercal skin disease in infected individuals. The study concludes that onchodermatitis is a serious medical condition in Kigoyera Parish and needs to be considered in all efforts to control onchocerciasis

INTRODUCTION

In spite of the concentrated efforts to control and eliminate onchocerciasis in sub-Saharan Africa by programs such as the Onchocerciasis Control Program (OCP) in West Africa, the disease still causes a high burden of morbidity and disability in many African countries. The public health importance of onchocerciasis is derived from its devastating effect on human vision. The World Health Organization (WHO) estimated 17.7 million total onchocerciasis cases worldwide in 1995, of which 270,000 victims were blind and 500,000 were severely visually impaired.1 The WHO Expert Committee on Onchocerciasis Control considers these data to be underestimated. While implementation of a multilateral-funded OCP dramatically reduced cases in West Africa, the number of cases in Uganda, Tanzania, Zaire, Equatorial Guinea, and other countries has reportedly increased.1

Onchocerciasis transmitted by Simulium damnosum s.l. has been studied extensively in the OCP areas of West Africa where blindness presents a major public health problem. However, less information is available from areas where blindness is not a major feature of onchocerciasis and where skin disease is more severe. The public health importance of skin lesions, including acute and chronic papular dermatitis, subcutaneous nodules, hanging groins, depigmentation, and lichenification (leopard skin), has not been evaluated systematically. Most efforts to control blindness have been made through the OCP and non-governmental organizations by use of mass ivermectin treatment in areas where blindness is common. Some 8.6 million people infected with onchocerciasis live in areas where blindness is rare but severe skin disease is believed to be common. In many of these areas, no systematic control efforts are in place because of the low priority given to skin disease by health professionals and government agencies.

In 1993, WHO and the World Bank initiated a multicenter study on the importance of onchocercal skin disease in Tanzania, Ghana, Nigeria, Cameroon, and Uganda. Reports from the Nebbi district in Uganda show that onchocercal skin disease was highly prevalent in infected persons (48%) and that the most important association with skin disease was troublesome itching. Forty percent of Onchocerca volvulus-infected persons reported severe itching.2 Since onchocercal skin disease was perceived by local people as a consequence of poor personal hygiene, it created a stigma with negative social and psychological effects for those suffering from it. Furthermore, onchocercal skin lesions were often mistaken for those of leprosy, which carries a high burden of social discrimination.3 Brieger et al. report from Nigeria that in communities situated in endemic onchocerciasis areas, onchocerciasis patients considered themselves stigmatized because of their disfiguring onchocercal skin lesions. Healthy community members rated the importance of onchocercal skin disease between that of leprosy and fungal infection of the skin.4

In 1996, the African Program for Onchocerciasis Control (APOC) was initiated with major support from the World Bank. It aims to control onchocerciasis in areas outside the OCP. Many countries participating in APOC are in central and eastern Africa. The program has continually emphasized the importance of onchocercal skin disease, but to the best of our knowledge, no attempts have been made to measure the intensity and scope of onchocercal skin infection in onchocerciasis patients who are living in areas where the vector is Simulium neavei s.l. We used a modified Murdoch skin assessment to describe in detail the observed skin lesions in onchocerciasis patients in Kigoyera Parish, Kabarole district, western Uganda.5 This pilot study was part of a larger ongoing study in the Kabarole district from 1991–1994.

METHODOLOGY

Kigoyera Parish is 40 miles northeast of Fort Portal, the district capital. Details of the study design and other results are published elsewhere.5,7 According to 1991 census data, Kabarole district had a population of 749,000 and Kigoyera Parish had a population of 6,973. Kigoyera Parish lies within the onchocerciasis belt stretching north to south along the Ruwenzori Mountains where S. neavei s.s. is the main transmitting vector. In Kigoyera Parish, overall prevalence of infection with O. volvulus was 78% in 1991. The prevalence of onchocercal skin disease ranged from 16–45% in the villages. Levels of infections were high with microfilaria (mf) loads of up to 1,000 mf per skin snip. Onchocerciasis was viewed by most people in Kigoyera Parish as an important health problem. Skin disease and itching were seen as especially troublesome by most parishioners infected with O. volvulus.
Study participants, who had confirmed infection with *O. volvulus* and skin disease due to *O. volvulus* infection, were selected at the examination sites, using systematic sampling. On a randomly selected clinic day, every consecutive person attending the clinic who was infected with onchocerciasis and had clinical signs of onchodermatitis was included in the study until the sample size of 72 was achieved. The size was chosen to let us assess characteristics of this population with a prevalence of 10% with 95% confidence intervals of 5–15% (SE = 0.0503). We considered this sufficient precision for our pilot study. We also did a *post hoc* secondary analysis using multivariate regression with the skin score as the dependent variable.

An onchocerciasis-infected person was defined as a person having microfilaria of *O. volvulus* in a skin snip. Each participant was clinically examined with a focus on onchocercal skin involvement. Acute and chronic skin lesions, and their severity and localization, were recorded according to experiences from Murdoch et al. (See also Table 1.) Murdoch et al. have developed a clinical classification and grading system for recording the cutaneous lesions of onchocerciasis, and have proposed that the system be used as a standard method for describing onchocercal skin changes. This would allow clinical information to be communicated among workers in all endemic areas to aid local and comparative research. The system consists of three components: location of skin lesions; clinical classification of the lesions, e.g., acute papular onchodermatitis (APOD), chronic papular onchodermatitis; and grading of severity, e.g., for APOD, 0 = absent, 1 = infected area scattered with small papules, 2 = infected area covered with papules, vesicles, or pustules with diffuse edema. We counted only skin lesions with an extension of more than 20×20 cm and/or more than 20 spots or papules.

This clinical classification and grading system has shown itself to be useful for standardizing the assessments of onchocercal skin changes. The inter-rater agreement for the assessment method was found to be acceptable, with kappa values of 0.7 and greater.\(^5\) We rated the onchocercal skin changes as severe, moderate, or mild, thus using a modified version of the Murdoch classification, e.g., APOD as 1 = infected area scattered with small papules, 2 = infected area covered with papules, vesicles, or pustules with diffuse edema. We counted only skin lesions with an extension of more than 20×20 cm and/or more than 20 spots or papules.

This table of a data collection sheet for the assessment of onchocercal skin disease shows the severity and localization, were recorded according to experiences from Murdoch et al. (See also Table 1.)

<table>
<thead>
<tr>
<th>Acute inflammatory skin score (pruritus, scratch marks, fresh papules, old papules, edema): 28</th>
<th>Chronic degenerative skin score (Hyperkeratosis, hyperpigmentation, depigmentation, atrophy): 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total skin score: 28 + 5 = 32</td>
<td></td>
</tr>
</tbody>
</table>

### Table 1

Example of a data collection sheet for the assessment of onchocercal skin disease

<table>
<thead>
<tr>
<th>Head</th>
<th>Upper torso front</th>
<th>Upper torso back</th>
<th>Arms</th>
<th>Lower torso front</th>
<th>Lower torso back</th>
<th>Legs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Scratch marks</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Fresh papules</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Old papules</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Edema</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hyperkeratosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Depigmentation</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Atrophy</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

All data were entered into an IBM microcomputer with EPI INFO software. Distributions and logic checks of the data were done. After completion of data entry, the data were transferred to Stata version 5.0 for further analysis. After checking and clearing in Stata 5.0, the data were analyzed. Skin scores were not normally distributed. Even after subjecting the scores to log normal transformation, normal distribution was not achieved. Therefore, the data were analyzed using the median. We used the median regression models for multivariate analysis, with the skin scores as the dependent variables. The objective of the median regression is to estimate the median of the dependent variable, conditional on the values of the independent variables. Median regression finds a line that minimizes the sum of the absolute residuals rather than the sum of the squares of the residuals as in ordinary regression.\(^9\)

Throughout the study, all residents of Kigoyera Parish and surrounding parishes were given medical care for the most common diseases. This included people who were not participating in the study, especially children and the elderly. The study was explained to everyone in the Rutooro language. The informed consent information was read in the local language, and those who participated in the study signed the consent form. Parents signed on behalf of subjects younger than 18. Participants who could not sign for themselves were assisted by a witness, who verified the subjects’ agreement and noted it in writing on the consent form. In addition to the individual consents, the chiefs of the 13 villages in Kigoyera Parish consented on behalf of their communities. All procedures met the requirements of the Ugandan Ministry of Health. The study protocol was submitted to the Ethical Review Board and the Ministry of Health, and formal approval was given by the permanent secretary of the Ministry of Health.

All patients infected with *O. volvulus* were treated with ivermectin tablets according to the protocol of the Mectizan Expert Committee (single dose of 150 µg/kg body weight, excluding children younger than 5, pregnant women, women...
in the first week of breast feeding, and persons with severe illnesses). To assess the drug's side-effects, all onchocerciasis patients treated with ivermectin were visited at home after 48 hours, and were treated if they had side-effects. Late side-effects of ivermectin treatment were reported to the survey team by village leaders. Patients who had been reported to have late side-effects were then visited, examined, and treated.

RESULTS

The mean age of participants was 29.5 (SD 14.6, years, range 8–69 years). Thirty-eight (52.8%) were female and 34 (47.2%) were male. All adult participants were engaged in subsistence farming. Thirty-nine (54.2%) were of the major ethnic group, while 33 (45.8%) were of other ethnic origin. Fourteen participants (19.4%) had received formal schooling, while the remaining 58 (80.6%) never attended school. The participants’ average duration of residence in Kigoyera Parish was 14.9 years, with a range of 1–35 years. The geometric mean of the mf load was 11.5 (SD 5.4). The mf load per mg skin was higher for men (geometric mean 17.8, SD 6.0) compared with women (geometric mean 7.8, SD 4.3). Thirty-four of the patients (47.2%) had nodules, with an average of 1.9 nodules for each person and a range of 1–18 nodules. Fourteen patients (19.4%) showed swollen lymph nodes, mostly in the femoral region. Only one person had hanging groins.

Ten onchocerciasis patients (13.9%) had acute signs of onchodermatitis, while 13 (18.1%) showed mainly a chronic stage of dermatitis due to *O. volvulus* infection. Most patients (68%) had a mixed form of onchodermatitis with acute and chronic symptoms. The medians of the skin scores were as follows: total skin score 13.5 (range 9.0–18.6), acute skin score 8.5 (range 4.0–14.0), and chronic skin score 4.0 (range 3.0–6.0). Twenty participants (27.8%) reported having pruritus. Pruritus was reported with similar frequency in males and females. Of the 20 patients reported to have pruritus, five said it was severe, eight said it was moderate, and seven said it was mild. Scratch marks were observed in 18 patients; they were moderate in 10, mild in six, and severe in two. Seven patients who reported pruritus did not show any scratch marks. The frequency and severity of skin changes were rated as follows: Thirty-one participants (43.1%) had severe skin disease, 31 (43.1%) had moderate skin disease, and 10 (13.8%) had mild skin disease.

Table 2 shows the localization of onchocercal skin lesions.

Acute skin lesions seemed to be more evenly distributed over the body than the chronic lesions, which were more prevalent on the lower body and legs.

Table 3 shows the extent of skin lesions.

Acute and chronic skin lesions extended to major parts of the body in many patients. Localized dermatitis was seen less frequently. Localized hyper-reactive onchodermatitis (“Sowda”) was not observed. Pruritus was reported as general by most participants, and as being restricted to part of the body by only a few.

Table 4 shows the results for the skin scores of acute and chronic onchodermatitis.

Skin scores were also tested in multivariate models with the dependent variables being acute skin score, chronic skin score, and total skin score. Covariates tested in the model were age, sex, educational level, ethnic group, duration of residence, and mf load. Age, duration of residence, and mf load were entered as continuous variables. Stepwise forward regression was applied. The results of the multiple regression and the final models with the significant covariates are shown below:

- **Acute skin score** = no association with the covariates.
- **Chronic skin score** = 6.97 + 0.104 age.
- **Total skin score** = no association with the covariates.

Intensity of infection (mf load per mg skin) was not associated with onchocercal skin scores. Gender was not a significant covariate for the acute skin score.

DISCUSSION

We present detailed clinical data on onchocercal skin disease from 72 onchocerciasis patients in the Kabarole district of western Uganda, where *S. neavei* s.s. is the main transmitting vector. To the best of our knowledge, this is the first detailed description of skin disease from an *S. neavei* s.s.-transmitted onchocerciasis focus. Our study is in line with efforts of the World Bank and WHO to assess the impact of onchocercal skin disease. The socioeconomic impact of onchocercal skin disease has only recently been recognized as a serious manifestation of infection with *O. volvulus*. The World Bank’s multicenter studies in West and East Africa to assess the importance of onchocercal skin disease indicate severe social implications for people suffering from it, and are just one example of these current efforts.

We found the clinical classification and grading system of cutaneous symptoms in onchocerciasis patients used by Murdoch (which we slightly modified) to be a useful research instrument to assess skin changes in onchocerciasis patients. It lets researchers better standardize the assessment of onchocercal skin lesions, thus making the results more comparable. We also see the value of this grading system in the potential to assess the relationship of skin scores (as a continuous variable) with other covariates and to establish a causal framework for the etiology of onchocercal skin disease in this focus. It also allows differentiation between the acute and

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**Table 2**

<table>
<thead>
<tr>
<th>Skin change</th>
<th>Upper torso front</th>
<th>Upper torso back</th>
<th>Arms</th>
<th>Lower torso front</th>
<th>Lower torso back</th>
<th>Legs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>17 (24%)</td>
<td>18 (25%)</td>
<td>18 (25%)</td>
<td>18 (25%)</td>
<td>19 (26%)</td>
<td>17 (924%)</td>
</tr>
<tr>
<td>Acute</td>
<td>28 (39%)</td>
<td>29 (40%)</td>
<td>39 (54%)</td>
<td>30 (42%)</td>
<td>36 (50%)</td>
<td>34 (47%)</td>
</tr>
<tr>
<td>Chronic</td>
<td>12 (17%)</td>
<td>18 (25%)</td>
<td>36 (50%)</td>
<td>17 (24%)</td>
<td>43 (60%)</td>
<td>46 (64%)</td>
</tr>
</tbody>
</table>
chronic skin manifestations and the calculation of both these proportions of the total burden of skin disease.

Since we examined only onchocerciasis patients with skin involvement, we could not determine the prevalence of onchocercal skin disease. Data from earlier studies indicate that the prevalence of dermatitis varied from 19–45% in the 13 villages of Kigoyera Parish. This is lower than the prevalence of 48% Okello in the Nebbi district in the West Nile region of Uganda. Ovuga described a severe negative social impact on people with onchocercal skin disease.3

In Kigoyera Parish, 86% of onchocerciasis patients with skin involvement showed severe or moderate skin disease, and 49% of those had generalized skin symptoms on the arms, legs, and torso. This high percentage of persons with significant skin changes due to onchocerciasis may indicate that some 1,800 residents of the parish, with a total population of 6,973, may suffer from severe skin disease. These patients may experience social deprivation and be less able to interact socially with other family and community members, and less able to live a satisfactory life. However, troublesome pruritus was lower in this sample compared with the findings from the Nebbi district (28% versus 40%).

Onchodermatitis in Kigoyera Parish presents mainly as a generalized form for both the acute and chronic manifestations. The chronic onchodermatitis is more often located on the lower parts of the body while the acute form is more evenly spread over the entire body. This is most likely caused by the biting habits of S. neavei s.s., which tend to prefer biting on the lower trunk and legs. Lymphadenopathy, leoparding, and hanging groins are not important manifestations of onchocercal skin disease in this focus. Skin atrophy is the major feature of chronic onchocercal skin disease. Acute forms of skin disease contribute more to the overall skin morbidity than chronic skin manifestations caused by O. volvulus infection (72% versus 28%).

We also examined the relationship between skin scores (measuring the severity of onchocercal skin disease) and other variables such as age, sex, educational level, duration of residence, ethnic group, number of nodules per person, and mf load as part of our secondary data analysis. Skin scores were independent of the microfilarial load and the mean number of nodules per patient in the multivariate analysis. This confirms findings from other studies which did not find an association between intensity of infection with O. volvulus and skin involvement.1,10,11 Males had higher skin scores than females. This contrasts with findings from Nigeria where females suffered more often and more severely than males from onchocercal skin disease.5 Gender-related differences in skin involvement could not be explained by any other demographic variable.

A limitation of our pilot study is that the small sample size made it impossible to draw definite conclusions from our multivariate model. In addition, we cannot exclude the possibility that we occasionally diagnosed onchocercal skin disease incorrectly, leading us to overestimate its burden in this focus. However, other causes for dermatitis such as scabies, eczema, senile atrophy, etc. were excluded. Our rationale is that all our patients had microfilaria of O. volvulus in the skin snip, and other tropical parasitologic infections (e.g., other microfilarial diseases than O. volvulus) were rare or absent in the focus under investigation. In addition, our comparisons of the photographs we took of our patients’ skin lesions with photos of patients with proven onchocercal skin disease validated our skin classification process. Based on this process of classifying onchocercal skin disease, we conclude that a very high proportion of our patients indeed had dermatitis due to onchocerciasis rather than other agents.

### CONCLUSIONS

In spite of these limitations, we believe that onchocercal skin disease is a severe health problem in Kigoyera Parish, Uganda, where S. neavei s.s. is transmitting O. volvulus. Our finding that onchodermatitis presents as severe skin disease emphasizes further the need to control S. neavei s.l.-transmitted onchocerciasis in the APOC area of central and eastern Africa. As this was a pilot study, our findings have to be confirmed by another study with an adequate sample size and the inclusion of a control group for more valid comparisons and conclusive results.

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