ULTRASONOGRAPHY IN A SENEGALESE COMMUNITY RECENTLY EXPOSED TO SCHISTOSOMA MANSONI INFECTION

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Abstract. Inhabitants of Ndombo (n = 614), a village in an area recently infected with Schistosoma mansoni in Northern Senegal, were examined clinically, parasitologically, and ultrasonographically to investigate the presence and degree of S. mansoni-related hepatosplenic morbidity after a few years of exposure to schistosomal infection of regional canals. Despite previous praziquantel treatment of 56% of the inhabitants prior to our investigation, the prevalence of S. mansoni infection in 1993 was 90%, and 42% of the villagers excreted more than 1,000 eggs per gram of stool. Previously untreated individuals were found to have significantly higher egg counts than treated ones. Despite the high intensities of infection, ultrasonographically detected severe periportal thickening of the liver was infrequent. Grading according to body length-dependent normal values of cross-section diameter of peripheral portal vein branches of a European control group correlated with intensities of infection. Of the total group of patients, 30% (n = 182) had more severe thickening of portal vein branch diameters above the 97th percentile and 70% of these had a splenomegaly. The highest egg counts and the most frequent development of periportal thickening were found in 11–20 year-olds individuals. Praziquantel thickening was less frequent in praziquantel-treated adolescents than in untreated ones. This suggests that early antischistosomal medication may be useful to limit schistosomiasis-induced hepatic morbidity especially in children, even though reinfection seems inevitable.

Ultrasonography is generally accepted as a valuable method for the study of hepatosplenic involvement in schistosomiasis and for monitoring the reversibility of Schistosoma mansoni–related morbidity after treatment with praziquantel. Classically, features of hepatosplenic schistosomiasis arise from periportal thickening of the liver, visualized as echogenic portal vein wall thickening on scanning. Although periportal fibrosis is known to be a chronic complication, the time-lapse for its evolution remains unclear.

The first case of S. mansoni infection in the area of Richard-Toll in northern Senegal was reported in 1988. Transmission was established and the infection spread rapidly as a consequence of ecologic changes after the construction of a dam on the Senegal river.

The rural Ndombo community is currently being investigated for the study of the immunoeopidemiology in early stages of endemicity and also constitutes a unique opportunity to monitor the onset and early development of S. mansoni-related hepatosplenic morbidity in an untreated population. Since parts of the community had received praziquantel prior to our study, the influence of early antischistosomal treatment on the early development of hepatosplenic morbidity could also be studied.

PATIENTS AND METHODS

The present study took place in Ndombo, a rural village of approximately 4,000 inhabitants located 4 km from Richard-Toll along a canal that connects the Senegal River with the nearby Lac de Guers in September–October 1993 at the end of the hot and rainy season. It was part of an epidemiologic study designed by Gryseels and others in which four randomly selected population samples of approximately 400 villagers each were examined at eight-month intervals. Each cohort was a representative selection of the total village population in respects to age, sex, and occupation. We investigated the fourth cohort before treatment, and part of the first cohort, which had been treated twice before within two years. Details of epidemiologic and parasitologic methods are described elsewhere.

From each participant, two stool samples were collected between August and October 1993 and examined by a modified Kato-Katz method using two 25-mg slides per stool sample. The individual egg counts were calculated as the sum of the four Kato slides multiplied by 10 to give eggs per gram (epg) of stools. The clinical examination consisted of a standardized interview in the local language, a physical investigation according to Stelma and others, and a thick blood film to detect malaria infection.

Ultrasonography was performed according to international protocols by experienced observers, using two portable machines (SSD-500; Hellige-Aloka, Freiburg, Germany, with a 3.5-MHz convex transducer, and SDR 1550 XP; Phillips, Eindhoven, The Netherlands, with a 3.0-MHz sector transducer). The ultrasonographic investigation included measurements of liver and spleen, possible signs of portal hypertension, and grading of periportal thickening. The normal range of organ dimensions in growing individuals is closely related to age and body length; thus, to be able to compare organ sizes throughout all age groups, measurements were analyzed using body length–related normal values, and organomegaly was defined as organ size greater than two standard deviations in the respective body length class of a large reference population. The abdomen was carefully examined to rule out congestive changes and liver disorders unrelated to S. mansoni infection. All examinations...
TABLE 1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No.</th>
<th>Group previously untrt.</th>
<th>Group previously treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10</td>
<td>238 (39%)</td>
<td>128 (48%)</td>
<td>103 (31%)</td>
</tr>
<tr>
<td>11–20</td>
<td>149 (24%)</td>
<td>57 (21%)</td>
<td>91 (27%)</td>
</tr>
<tr>
<td>21–40</td>
<td>133 (22%)</td>
<td>47 (18%)</td>
<td>82 (25%)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>94 (15%)</td>
<td>34 (13%)</td>
<td>58 (17%)</td>
</tr>
<tr>
<td>Total</td>
<td>614*</td>
<td>266</td>
<td>334</td>
</tr>
</tbody>
</table>

*No data on previous treatment available in 14/614.

TABLE 2

<table>
<thead>
<tr>
<th>Periportal thickening</th>
<th>Egg excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal, &lt; +2 SDS</td>
<td>0 epg</td>
</tr>
<tr>
<td>+2 to +3 SDS</td>
<td>11%</td>
</tr>
<tr>
<td>&gt; +3 SDS</td>
<td>12%</td>
</tr>
<tr>
<td>Total n (n = 613)</td>
<td>5%</td>
</tr>
</tbody>
</table>

*SDS = standard deviation score; epg = eggs per gram of feces.

were done without the observers being aware of individual parasitologic and clinical findings, or prior ultrasonography results.

For ultrasonographic grading of the echodense zones around the portal tree, the Cairo classification measures cross-section diameters of peripheral portal vein branches at three different locations. Jenkins and Hatz suggested that measurements should be made "after the bifurcation, between the first and the third branching-points" (outer-to-outer measurements). We measured all cross-section diameters after the second intrahepatic branching point. To establish normal values of peripheral portal vein branches, a European control group of 160 healthy people was examined sonographically by one of the observers. Body length dependent normal values were defined and the Senegalese findings were evaluated on the basis of these data. Minor pathology was interpreted as two standard deviations above the mean body length-dependent normal value, more severe lesions as measurements above three standard deviations. To detect interobserver variations for the method, 190 villagers were re-examined by two independent sonographers (RK and YY). After the examination, all S. mansoni-infected participants, except pregnant women, were treated with a single dose of praziquantel (Biltricide; Bayer, Leverkusen, Germany), 40 mg/kg of body weight. If other diseases were detected, the patients were treated according to local standards and referred to the local health service. The studies were approved by the Ministry of Health in Dakar, Senegal, the local health authorities, and the ethical committees of the Universities of Bonn and Hannover.

RESULTS

A total of 614 Senegalese villagers (336 females and 278 males) were enrolled into the study. Their ages ranged from four months to 80 years (Table 1). Although cohort 4 had not yet been examined or treated in the framework of ongoing epidemiologic studies, many individuals of this group reported having received treatment in health centers. Therefore, we regrouped the study population accordingly. Of 600 individuals, 334 (56%) reported a history of previous praziquantel treatment, while 266 subjects (44%) stated not to have been treated before.

In the total study population, the prevalence of S. mansoni infection was 90%. Of those patients not treated before, 45% excreted more than 1,000 epg, compared with 33% in the previously treated group.

On ultrasound scanning, not a single case of severe hepatosplenic pathology was detected. Only mild and moderate periportal thickening was seen. The measurements of normal periportal vein branches in 160 Europeans showed a correlation with body height. The Cairo Score adjusted to these normal values of body length–dependent portal vein branch diameters revealed that 30% (n = 182) of the Senegalese population had cross-section diameters above two standard deviation scores of healthy Europeans. We found values above three standard deviations in 10% (n = 61). As demonstrated in Table 2, the degree of periportal thickening with this classification showed significant differences (P = 0.0018, by chi-square test) according to intensity of S. mansoni infection.

All untreated villagers without S. mansoni infection (n = 34) had normal findings. Previously treated people showed slightly less abnormal branch diameters than untreated villagers (19% and 25%, respectively), even in those with infections more than 1,000 epg (11% and 13%, respectively).

The interobserver variation results of measurements of periportal thickening are summarized in Table 3. The two observers produced identical results in 106 (56%) of the cases. In 74% of the cases, the deviation between the two observers was 1 mm or less, while it was more than 3 mm in 3%.

While sonographically detected splenomegaly occurred in 33% (n = 203) of the total group, 43% of the villagers with enlarged portal vein branches between two and three standard deviations had a splenomegaly, compared with 70% of those above three standard deviations (P < 0.001, by chi-square test). The proportion of height-related spleen enlargement correlated significantly (P < 0.001, by chi-square test) with S. mansoni egg counts (Figure 1). Mainly children four months to ten years of age were affected, with a splenomegaly rate of 54%. Of 350 malaria smears, 16 (5%) were positive for Plasmodium falciparum with 1–5% parasitemia. These cases were evenly distributed among S. mansoni egg count groups.

TABLE 3

| Interobserver variance in measurements according to the Cairo classification |
|--------------------------|--------------------------|
| Periportal thickening    | Grade 0 |
| Observer A              | B Grade 0 |
|                         | ≤2 mm | 3–5 mm | 5.1–7 mm | >7 mm | Total |
| Grade 0                 | 0     | 0      | 0        | 0     | 0     |
| Grade 1                 | 8     | 89     | 16       | 0     | 113   |
| Grade 2                 | 0     | 59     | 17       | 0     | 76    |
| Grade 3                 | 0     | 0      | 1        | 0     | 1     |
| Total                   | 8     | 148    | 34       | 0     | 190   |
No ascites or other signs of congestion were found in any
of the individuals. Hepatomegaly occurred mainly in chil-
dren. Enlargement of the left lobe was detected in 38 indi-
viduals (6%), 34 of whom being S. mansoni-positive. The
right liver lobe was enlarged in 76 cases (12%), 69 of them
being infected.

Enlargement of the gallbladder wall of more than 6 mm
was found in six patients, all of them being infected with 1–
1,000 epg. No hepatic alterations were found in two of them,
whereas three had moderate periporal thickening. The sixth
individual, a young woman, was the only patient with more
severe S. mansoni-related morbidity, portal vein branch di-
ameters above three standard deviation values, splenomeg-
aly, gallbladder wall thickening, and portofugal collaterals.

**DISCUSSION**

The outbreak of S. mansoni infection in the study area,
leading to a 90% infection prevalence within a few years,6-7
presents a unique opportunity to study onset and develop-
ment of S. mansoni-related morbidity in a presumably non-
immune community. The parasitologic results confirm that
the Ndombo population ranks among the most heavily in-
fected in the world.13 Nevertheless, our ultrasound results
demonstrated very little severe hepatosplenic pathology, as
suggested by a previous clinical study9 and an earlier prelimi-
nary ultrasound investigation.16

Ultrasonographic grading of S. mansoni-induced peripor-
tal thickening of the liver is based upon the diameters of
peripheral portal vein branches.11 Our investigation of pe-
ripheral portal vein branch diameters in healthy Europeans
showed that values are age- and body height-dependent. In
the Senegalese population examined, a positive correlation
was found between branch enlargement and egg output. Fur-
thermore, there was a close correlation between branch en-
largement and prevalence of splenomegaly. Thus, using the
Cairo classification modified for a pediatric population, we
detected a mild prevalence of early S. mansoni-related he-
patosplenic alterations. However, the value of our body
length–dependent normal diameters is limited because nor-
mograms of African populations may show a different range.

The lack of ultrasonographically detectable severe hepa-
tosplenic morbidity in this focus mirrors the findings of our
group in endemic regions in Mali.17 For yet unknown rea-
sons, severe morbidity as seen in Sudan, Egypt, Zimbabwe,
and east African foci15,18-20 seems to be rare in western Af-
rica. Possible explanations for these geographic variations
may include immunogenetic factors, parasite strain differ-
ences,21,22 concomitant infections, or toxins. However, in the
Senegalese focus, the recent exposure to S. mansoni would
be an obvious alternative explanation.

While hepatomegaly occurred only in a small number of
children, splenomegaly was present in one-third of the indi-
viduals. The prevalence of splenomegaly correlated with
egg counts. Malaria was infrequent and evenly distributed
among the egg count groups. Thus, schistosomiasis appears
to be the main cause of splenomegaly in this focus. In view
of the minor hepatic alterations, it seems as if splenomegaly
was not caused by portal hypertension, but probably directly
by egg-induced reactions.4

Although many individuals had received praziquantel
treatment prior to the study, a large proportion of these were
heavily infected. However, treated patients had a slightly
lower prevalence of periporal thickening than persons with-
out prior treatment. This may be due to reversibility of pre-
existing lesions after treatment, as demonstrated earlier in
Sudanese children,2 or to a protective effect of early treat-
ment against the early development of lesions, possibly by
shortening the duration of infection.

Untreated adolescents were the most heavily infected and
presented with the highest percentage of periporal thickens-
ing. These findings are in accordance with previous studies
in Sudan2,23 and show the need to focus further treatment
efforts on this age group because even in this recently in-
fected, presumed nonimmune community, children and ad-
ol­eants seem to be at the highest risk for intense infection and
periportal thickening of the liver.
Comparing different ultrasound methods for grading of periportal thickening in schistosomiasis11,12 resulted in
problems exceeding those reported previously by Jenkins and
Hatz.13 It is mainly the distinction between normal and mild
abnormal findings that remain a point of discussion. The
Cairo classification, recently established to minimize inter-
observer variation, is based upon single millimeter differ-
ences of portal vein branches.11 In our study, examinations
by two independent observers gave the same grading in only
56% of the cases, 74% of results differed only up to 1 mm, and
3% deviated more than 3 mm. Thus, even after estab-
lishing of the body length-modified Cairo classification, these
data show that ultrasonicographic quantification of early and
mild S. mansoni morbidity still remains difficult, irre-
respectively of the method used. In conclusion, a second con-
sensus conference seems to be necessary to establish a grad-
ing system of S. mansoni-related morbidity.
In summary, the assumed five-year exposure of the Se-
ne­gal­ese community to S. mansoni resulted in high intensi-
ties of infection. However, this was not paralleled by severe
hepato­splenic morbidity detectable by ultrasound. For detec-
tion of mild periportal thickening, the newly established
body length–dependent modified Cairo classification showed
the best correlation with the number of excruted eggs. Un-
treated adolescents had the highest intensities of infection
and consequently a slightly higher percentage of periportal
thickening. Previously treated individuals had lower morbidi-
ty despite being heavily reinfected. Thus, early anthro-
somatous treatment appears to reduce early and mild hepatic
morbidity although it does not prevent reinfection. The pop-
ulation in our study area as well as those in other new endo-
demic areas have to be closely monitored, since severe peri-
portal thickening may develop as a result of more chronic
infections over the following years.

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