Biopsy-Proven Amebic Colitis Treated with Metronidazole

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NOTES AND COMMENTS

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Amebiasis was diagnosed in a Vietnam veteran and treated in a conventional manner with diodoquin and tetracycline. Symptoms persisted over the next three and one-half years despite repeated courses of diodoquin. Amebic colitis was confirmed by biopsy through a sigmoidoscope. The patient then received a ten-day course of metronidazole (Flagyl®). Studies are cited proving this single agent is the drug of choice in the oral therapy of all clinical forms of amebiasis.

Amebiasis remains an important consideration for the physician faced with the patient with a diarrheal illness. Recent review articles1,2 have pointed out the importance of this (and other) communicable diseases, especially in those returning from Vietnam.

In the late 1960s numerous authors3-6 reported work on a new therapeutic modality, metronidazole (Flagyl®), in treating amebiasis. Since then, the drug has become FDA-approved for this use but most physicians remain unaware of this since most clinical data was gathered in other countries and from Armed Forces personnel treated in Vietnam. In reviewing our case of amebiasis, we again draw attention to this new, simple, and highly effective form of therapy.

Case Report

This 35-year-old white man was first seen at USAF Hospital, Hahn, Germany, in December 1971, complaining of tiredness, eight watery stools per day, and a 5.45-kg (12-lb) weight loss in 19 days. There was no history of “bloody flux” or fever. While stationed at Nha Trang AFB, Vietnam, in May 1967, he had first experienced a diarrheal illness. Although this had persisted over the next 11 months accompanied by a weight loss of .18 kgs (40 lbs), he had sought little medical attention until April 1968. Sigmoidoscopy at Grissom AFB, Indiana, had revealed multiple ulcerations below 12 cm, barium enema was negative, but stool specimens revealed the cysts of entamoeba histolytica. The patient was treated with tetracycline and diodoquin and was discharged improved.

Although military public health authorities examined the entire family, their baby sitter, close friends, and the water supply of the trailer park in which the patient lived, no other cases or evidence of contamination were found.

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For the next three years he had normal stools when using diodoquin and recurrent diarrhea when the medicine was discontinued. However stool specimens were no longer positive for cysts. In March 1971, when a repeat sigmoidoscopy suggested the possibility of ulcerative colitis, he was hospitalized and a rectal biopsy was performed. This was non-diagnostic and diodoquin therapy was resumed. In October 1971, he was assigned to Germany. By late November, he exhausted his supply of diodoquin. When Lomotil (diphenoxylate hydrochloride) proved unsuccessful in controlling the diarrhea, he reported to the USAH hospital.

There, physical examination revealed no evidence of jaundice, hepatomegaly, or abdominal masses. A number of typical isolated ulcers were found by sigmoidoscopy scattered throughout the upper rectum and lower sigmoid. They varied from 4 to 15 mm in diameter and were round, oval, or buttonhole shaped with a punched-out appearance. Biopsy specimens were taken from two such lesions. (Figures 1 and 2) The mucosa in uninvolved segments appeared normal. A saline preparation of bowel wall scrapings showed mobile trophozoites, a few of which contained ingested RBCs.

On December 17, 1971, the patient began taking metronidazole, 750 mg orally, every eight hours for ten days. His diarrhea quickly abated; he experienced no side effects and has remained symptom-free since then. When he was rehospitalized in April, 1972, repeat warm stage stool examinations were normal. Sigmoidoscopy showed no evidence of the previously observed abnormalities. Barium enema and liver function tests were normal. Stool examinations of the entire family were also negative.

Discussion

Amebiasis is transmitted only by fecal contamination of water, food, or articles of daily living. The cyst is the only infective form. After being ingested, cyst encasement is digested in the small intestine. By the time it reaches the terminal ileum, the quadraruclear metacyclic ameba has been released and then divides into four motile trophozoites. These are the forms responsible for clinically manifested disease. The motile trophozoites continue to pass along with bowel traffic.
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Figure 1B

High-power view of the trophozoite seen in Figure 1A, demonstrating an ingested red cell. (Hematoxylin and eosin; original magnification, X400.)

until they reach favorable conditions for colonization, usually in the area of the Cecum. Trophozoites either re-encyst to be passed in the stool causing no symptoms and continuing the life cycle, or they can invade the bowel wall. Of the colonic lesions, 79% occur in the cecal region and 29% in the rectosigmoid area.8

Usually only the mucosa and muscularis mucosa are invaded forming the typical flask-shaped ulcer.9 However, more rarely, the trophozoites continue their invasion through the bowel wall causing perforation and peritonitis. Other frequently seen complications result from the trophozoites entering the circulation through portal venules causing amebic hepatitis, liver abscess, and more rarely brain or skin abscesses.

Correct diagnosis is best achieved by prompt examination of saline wet mount preparations of freshly passed stool specimens or proctoscopic scrapings.9 Invading trophozoites with ingested red blood cells seen in biopsy specimens are diagnostic, as was shown in our case report. In addition, liver scan and serologic tests are of value in diagnosing extra-intestinal amebic disease.10

In the past, no single drug cured both the intestinal and extra-intestinal forms of the disease. Emetine and chloroquine act primarily on extra-intestinal disease. Arsenicals and halogenated hydroxyquinolines act only on the intestinal phase, as do broad spectrum antibiotics which alter the bowel flora.11 In the United States, diodoquin has been used alone for the therapy of the asymptomatic cyst carrier.12 While the preferred therapy for symptomatic amebic dysentery or amebic colitis has been diodoquin (Vioform) and tetracycline11 or emetine, Carbarsone, and Vioform.13
The most significant recent advance in the treatment of this protozoal infection is the use of metronidazole. As is true for all other amebicides except emetine, the exact mechanism of antiprotozoal activity is unknown. Metronidazole was first introduced into clinical medicine in 1959 by Cosar and Julou and in 1960 by Durel et al. for the successful treatment of trichomonal infections in men and women.

In 1966 Powell and co-workers found encouraging results in the treatment of amebiasis with nidadazole, a compound chemically related to metronidazole, but found the side effects were intolerable at therapeutic dosages. The same year Powell et al. conducted clinical trials with metronidazole in the treatment of intra- and extra-intestinal amebic infections. The results of these first encouraging studies and others indicate that metronidazole is the initial oral drug of choice in the treatment of all forms of amebiasis. Table 1 summarizes the results of the best-known studies.

Establishment of optimal dosage schedules and assurance that such doses would cause no serious side effects have delayed until recently the acceptance of metronidazole as the drug of choice in the treatment of amebiasis in North America. Currently, the pharmaceutical manufacturer recommends for treatment of acute dysentery in adults 750 mgs orally three times daily for five to ten days. This same dosage schedule, which is also recommended for amebic abscess, is about three times that used for trichomonal infections in adults. For children 35 to 50 mgs per kilogram per 24 hours in three divided daily doses is recommended.
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Because it is a nitroimidazole, the drug is contraindicated in patients with a history of blood dyscrasia. No persistent hematologic abnormalities have been observed, but mild reversible neutropenia may be frequently seen. Alcoholic beverages should not be consumed by patients taking metronidazole because a reaction similar to that induced by antabuse may occur. Abnormal cerebellar signs such as ataxia and dizziness are the third and final major side effect. If neurological complications are observed, the drug should be discontinued promptly. Minor gastrointestinal side effects and headaches have been reported.

Summary

Metronidazole has proven to be safe and effective in amebiasis. It is presently the only safe direct-acting amebicide with activity at all required sites. The reported case illustrates the successful outcome of such therapy. Other studies indicate that this single agent is the drug of choice.

Table 1. Summary of Pertinent Studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Daily Dosage</th>
<th>Number Patients</th>
<th>Success</th>
<th>Failure</th>
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<tbody>
<tr>
<td>Powell et al, 1966</td>
<td>800 mg tid x 10 days</td>
<td>25</td>
<td>22</td>
<td>3</td>
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<tr>
<td>Powell et al, 1969</td>
<td>2.4 gm one dose daily x 2</td>
<td>30</td>
<td>26</td>
<td>4</td>
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<tr>
<td>Taylor 1968</td>
<td>500-750 mg tid x 10 days</td>
<td>13</td>
<td>12</td>
<td>1</td>
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<tr>
<td>Minvielle et al, 1969</td>
<td>800 mg tid x 10-20 days</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Scott and Miller 1970</td>
<td>250 mg tid x 10-14 days</td>
<td>5</td>
<td>5</td>
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</tbody>
</table>
of choice in oral therapy of all clinical forms of amebiasis. The treatment is especially convenient when compared to the necessary combinations of other drugs. Significant side effects occur less frequently.

Acknowledgements
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References