The Treatment of Pleuropulmonary Amebiasis with Metronidazole*

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One hundred forty patients with pleuropulmonary amebiasis were classified radiographically in order to rationalize therapy based on the use of metronidazole. Amebic testing with gel diffusion, serial chest x-ray films, and observation of the patient's response to treatment have dominated management of the patients, 135 of whom made a successful recovery. Five patients died. Sixty percent of the surviving patients have been reviewed at a follow-up clinic, and there has been no instance of recurrence of amebiasis.

This review presents the results of treatment with metronidazole in 140 patients, 128 of whom had invasive pleuropulmonary amebiasis and 12 of whom had pleural effusion secondary to amebic abscess of the liver. A course of antibiotic therapy was given, and surgery was undertaken only when specifically indicated. The patients came from the province of Natal, South Africa, where amebiasis is hyperendemic. One hundred nineteen were male patients, and 21 were female patients, with ages ranging from 2 to 75 years. The male-to-female ratio and the age distributions are closely similar to those found by Rodriguez in Venezuela. Apart from conditions attributable to amebiasis (such as anemia), other significant disease was present in 12 of the patients.

It has been customary to classify pleuropulmonary amebiasis in terms of its pathogenesis. Since the present series derives from patients referred to a thoracic surgical unit, there is a preponderance of atypical or complicated lesions, and it has been found more convenient to use a classification based on serial chest x-ray films. From this classification, from amebic testing with gel diffusion, and from observation of the patient's clinical response to treatment with metronidazole, it has been possible to evolve a straightforward approach to the diagnosis and therapy of pleuropulmonary amebiasis.

Radiographic Classification and Clinical Management

Pleural Effusion

Right-sided pleural effusion is the most common intrathoracic sign of amebiasis. With antiamebic treatment, the effusion is usually a benign lesion that resolves spontaneously with healing of the underlying amebic hepatitis or hepatic abscess. The effusion is often associated with elevation of the right hemidiaphragm and plate atelectasis at the pulmonary base.

In this series, 12 patients initially had only an effusion. The number involved underestimates the frequency of the lesion, since an effusion with atypical features was the common reason for referral. Each patient was given a standard course of therapy with metronidazole, augmented by a single aspiration if the effusion was massive and causing dyspnea.

Amebic Empyema

Thirty-five patients initially had a collection of anchovy sauce pus in the right pleural cavity. Clinically, these patients were more severely ill than those with a sympathetic pleural effusion, but radiographically, both groups of patients were alike. Pleural aspiration was diagnostic.

A course of therapy with metronidazole and a single aspiration to dryness was adequate treatment in four patients. Thirty-one patients were managed with therapy with metronidazole and intercostal intubation. Of the 31 patients, two died (one during an epileptic convolution 48 hours after intubation and the other from aspiration of vomit). In our experience with patients with uncomplicated amebic empyema, a constricting cortex does not develop on the visceral pleura; and, therefore, intercostal intubation has been effective in emptying the pleural cavity of amebic pus and in achieving complete pulmonary reexpansion.

Bacterial Thoracic Empyema

Twenty patients initially had a secondarily infected amebic empyema. On the chest x-ray film the

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Empyemas were classic D-shaped posterior opacities contiguous with the diaphragm and were without any features that allowed recognition of their amebic origin.

Bronchographic studies were performed on 14 patients before surgical treatment of their empyema. One patient had an ectatic basal segmental bronchus; the others had normal bronchi, although they were displaced by the pleural lesion. Under cover of therapy with metronidazole, eight patients were managed by decortication and 12 by rib resection and open drainage. Three patients died; one died from intraoperative hemoptysis, one died from bacteremic shock, and the other, who had chronic pyelonephritis, died from renal failure.

**Pulmonary Lesions**

Extension of an amebic hepatic abscess through the diaphragm into neighboring pulmonary tissue occurred in 72 cases. There was one case of hematogenous spread involving the right upper lobe. Pulmonary amebiasis was seen radiographically as either a homogeneous opacity (49 cases) or as a cavitated lesion (24 cases); and the sites involved were the right lower lobe (43 cases), the middle lobe (24 cases), the left lower lobe (three cases), and the left upper lobe and lingula (two cases). The apical segments of the lower lobes were commonly spared. The profile of the diaphragm related to the pulmonary opacity was disfigured by a peaked elevation contiguous with the pulmonary lesion. This abnormality was clearly seen on lateral chest x-ray films. Pleural effusion was visible in 20 cases.

Forty-seven patients with pulmonary lesions were treated with metronidazole alone. Radiographic improvement lagged behind clinical improvement, which occurred within days of the start of treatment; resolution of fever and malaise was the most evident feature. The other patients also had courses of antibiotic therapy, either before admission when a diagnosis of bacterial pulmonary infection had been made or after admission when secondary infection of cavitated pulmonary amebiasis was found. Parenchymal disease was managed by thoracotomy in seven patients; in five of these, secondary infection had caused lobar destruction, and in two patients, lesions thought before surgery to be bronchial carcinoma proved to be amebic.

**Amebic Test with Gel Diffusion**

This test yielded positive results in all but five patients. Although the most sensitive serologic test for amebiasis is by indirect hemagglutination, its accuracy of over 98 percent in extraintestinal invasive amebiasis is the same as that of the test using gel diffusion. Four of the patients with negative results on the test with gel diffusion had convincing evidence of amebic infection on other grounds; three had a hepatic abscess shown on the scintiscan, with anchovy sauce pus recovered on aspiration, and the other patient underwent pulmonary resection, and amebae were demonstrated histologically in the specimen. The fifth patient was a two-year-old girl who was also suffering from kwashiorkor. Anchovy sauce pus was drained from her pleural cavity, and pneumoperitoneum confirmed fusion of the liver to the hemidiaphragm.

<table>
<thead>
<tr>
<th>Type of Amebiasis</th>
<th>No. of Cases</th>
<th>No. with Secondary Infection</th>
<th>Management*</th>
<th>Stay in Hospital</th>
<th>Follow-Up Rate, percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural effusion</td>
<td>12</td>
<td>0</td>
<td>A B C</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A</td>
<td></td>
<td>2</td>
<td>10</td>
<td>None</td>
<td>10</td>
</tr>
<tr>
<td>Amoeba</td>
<td>35</td>
<td>0</td>
<td>26</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Bacterial</td>
<td>20†</td>
<td>45</td>
<td>6</td>
<td>26</td>
<td>7</td>
</tr>
<tr>
<td>Pulmonary lesion</td>
<td>73</td>
<td>31</td>
<td>22</td>
<td>45</td>
<td>6</td>
</tr>
</tbody>
</table>

*Entries are numbers of patients.

Schedule A, 800 mg of metronidazole three times daily for either five or seven days; schedule B, 400 mg of metronidazole three times daily for either ten or 14 days; and schedule C, two courses of therapy with metronidazole, given at intervals.

†Two with E. coli.
RESULTS OF TREATMENT

The results are summarized in Table 1. The regimens of treatment with metronidazole were based on the experience of Powell7 in the management of hepatic amebiasis. The choice of schedule A (800 mg of metronidazole three times daily for five or seven days) or schedule B (400 mg of metronidazole three times daily for ten or 14 days), as described in Table 1, was arbitrary, and no distinction could be made between the results achieved. The dosages were adjusted to children. Six patients were given repeat courses of therapy with metronidazole because there was negligible resolution of the radiographic lesion after the first course of treatment. Four of the six patients had a secondary infection of pulmonary amebiasis, and *Escherichia coli* was isolated from two to them. Since *E coli* and other bacteria may be capable of inactivating metronidazole,8 such secondary infection may provide an explanation for slow resolution and a reason for repetition of a course of therapy with metronidazole. Surgical management, including therapeutic pleural aspiration, was combined with a single course of therapy with metronidazole in 62 patients. In this group, there were five deaths, of which only the patient who died from bacteremic shock could be classified as a failure of treatment. Various courses of therapy with antibiotic drugs were given to 33 patients. Thirty-five percent of the patients with pulmonary amebiasis were treated with antibiotic drugs in response to evidence of secondary infection or because of misdiagnosis. Patients who underwent decortication received routine antibiotic therapy as a cover during the surgical phase.

With the exception of the five patients who died, all were discharged from the hospital clinically well, with serial chest x-ray films showing impressive or complete resolution of the lesions (Fig 1). Abnormalities of the diaphragmatic profile and of the pleura persist indefinitely. Parenchymal opacities, after initial and nearly complete resolution, may then leave residua that clear slowly over the ensuing months. Patients with uncomplicated pulmonary amebiasis were, therefore, frequently discharged from the hospital before radiographic resolution was complete. In Natal, South Africa, attendance at outpatient follow-up clinics is erratic. Eighty-three patients attended out-patient reviews at intervals ranging from three months to two years, and no recurrence of disease was observed.

DISCUSSION

The management of amebiasis has been revolutionized by the introduction of therapy with metronidazole;9 however, the use of this drug in pleuropulmonary amebiasis has not been reported previously. The efficacy of therapy with metronidazole and its safety when used in surgical practice has allowed simplification of the diagnosis of amebiasis, a disease which can be difficult to recognize clinically18 and where morphologic identification of *Entamoeba histolytica* may be problematic.10,11 In this series, when evidence of hepatic amebic abscess has been lacking and when amebae or anchovy sauce pus were not found in the sputum or pleural aspirate, the combination of (1) positive results on the test with gel diffusion, (2) an initial chest x-ray film suggestive of amebiasis, and (3) rapid resolu-

![Figure 1. A (left), Left lower lobar amebiasis on initial chest x-ray film. B (right), Radiographic resolution after 12 days of treatment with metronidazole (schedule B).](image-url)
in response to subphrenic amebiasis will subside on treatment of the hepatic lesion; (2) intercostal intubation and a course of therapy with metronidazole is effective treatment of amebic empyema; (3) in bacterial thoracic empyema, bronchographic studies should be carried out to exclude the presence of bronchial damage, and surgical management by rib resection or decortication is then required with a cover of metronidazole therapy invariably and antibiotic therapy if indicated; and (4) pulmonary lesions without secondary infection resolve with metronidazole alone, and there is no radiographic evidence in this series of postamebic bronchial or parenchymal destruction that requires resection (Fig 2). With secondary infection a true pulmonary abscess develops, which is treated appropriately.

REFERENCES


FIGURE 2. Right lateral bronchogram in patient with middle lobar amebiasis. Right hemidiaphragm is typically deformed.