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HEPATIC AMEBIASIS: EXPERIENCE IN THE THERAPY OF 56 CASES*

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SUMMARY

The results of therapy in 56 consecutive cases of hepatic amebiasis are reviewed. In retrospect, the results in patients receiving metronidazole alone, dehydroemetine combined with chloroquine, and dehydroemetine combined with chloroquine and metronidazole were compared. No deaths occured.

Our results confirm the great efficacy of metronidazole alone. The response to treatment was similar in patients receiving dehydroemetine combined with chloroquine but the average number of days of hospitalization was greater in these patients.

No advantage was demonstrated for the combination of metronidazole with dehydroemetine and chloroquine. In retrospect these patients proved to have a more severe and protracted course with more frequent surgical complications and a greater need for closed aspiration of the abscess.

Closed aspiration, not used routinely, has not reduced the number of days of hospitalization. Significant side effects were not observed.

Amebicidal drug therapy has dramatically changed the prognosis of hepatic amebiasis, nowadays a readily curable disease (Powell, 1971).

Enduring landmarks in the development of drug therapy were the introduction of emetine hydrochloride (Rodgers, 1912), followed by chloroquine (Conan, 1948) and later by metronidazole (Powell et al, 1966). The efficacy of these drugs, in single or combined drug regimens has been well proved (Powell, 1971; Adams and MacLeod, 1977).

The purpose of the present study is to review in retrospect our experience with three drug regimens in 56 consecutive cases of hepatic amebiasis.

MATERIAL AND METHODS

Case records of 56 patients admitted to the Luanda University Hospital, Department of Medicine I, from January 1970 to June 1974, were reviewed. Clinical, laboratory and chest-X-ray findings in these cases were previously reported (Carneiro Chaves et al, 1977 a, 1977 b). Every patient satisfied at least three of five diagnostic criteria for hepatic amebiasis proposed by Lamont and Pooler (1958).

In retrospect the patients were divided in three groups according to therapy. Group 1 received oral metronidazole 750 mg thrice daily for ten days. In one patient the drug was administered in two courses for a total of seventeen days. In group 2 intramuscular dehydroemetine 1 mg per kg. daily for ten days was combined with chloroquine diphosphate 250 mg twice or thrice daily for four to ten weeks. In group 3 intramuscular dehydroemetine 1 mg per kg daily for ten days was combined with oral metronidazole 750 mg thrice daily for ten days and oral choroquine diphosphate 250 mg twice or thrice

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daily for four to ten weeks. A dose of dehydroemetine above 60 mg daily was never prescribed.

In those patients in whom subclinical amoebic colitis or *E. histolytica* cysts were demonstrated, tetracycline 1 to 2 g daily for one to two weeks, concomitantly with the other drugs, followed by oral diiodohydroxiquinoline 650 mg thrice daily for three weeks, were prescribed.

Needle aspiration was not performed routinely but only when a point of maximal tenderness persisted after at least five days of therapy.

Results of treatment were evaluated by: 1 — The number of days to become afebrile; 2 — The number of days taken to achieve absence of liver tenderness; 3 — A significant reduction of hepatomegaly; 4 — The need of needle aspiration or surgical treatment for complications; 5 — The number of days of hospitalization.

Liver function tests, hematological studies and chest X-ray were performed weekly. Only after an increase in hemoglobin, a decrease of erythrocyte sedimentation rate, normalization of leucocyte counts, hepatic function tests and chest X-ray, was discharge permitted.

In all patients receiving dehydroemetine, E.C.G. was made on admission and ten to fourteen days after the beginning of treatment.

For statistical studies the χ^2 test, with Yates correction, for comparison of symptoms and signs and abnormal fluoroscopic and chest X-ray findings, and the Student's t test for all other results, were used. Differences were considered significant for $P<0.05$.

RESULTS

Total number of patients, sex, race and age in years (Table 1), the number of patients with symptoms and signs (Table 2), the length of symptoms in days at the time of admission (Table 3), the values of hemoglobin, leucocyte counts, ESR, serum albumin, bilirubin, SGOT and SGPT, alkaline phosphatase, prothrombin time (Table 4) and the number of patients with abnormal fluoroscopic and chest X-ray findings (Table 5), in the three groups are represented in Tables 1 to 5.

Table 1

Total number of patients, sex, race and age

	Groups		
	1	2	3
Number of patients	14	30	12
Males	13	26	11
Females	1	4	1
Whites	3	6	2
Blacks	10	22	10
Mulattos	1	2	—
Age	31.9[a]±10.9[b]	35.4±9.2	32.2±6.2

(a) Average in years (b) Standard deviation

Table 2

Number of patients with symptoms and signs

	Groups		
	1	2	3
Feverishness	11	24	9
Abdominal pain	13	29	11
Diarrhea	9	15	4
Fever	11	25	7
Painful percussion	10	27	9
Painful hepatomegaly			
<5cm	3	6	2
5-10cm	8	19	5
>10cm	—	2	4
Abnormal pulmonary auscultation	7	16	12

Statistically significant differences were observed only for the greater number of patients with abnormal pulmonary auscultation in group 1, when compared with group 3, and for serum albumin, which was lower in group 3 than in the other two groups. For all other results, differences are not statistically significant.

The results of treatment in the three groups are summarized in Table 6. There is no statistical difference between the three groups for the number of days taken to become afebrile . Pain persisted for a significantly greater number of days in group 3 than in groups 1 or 2. The number of days of hospitalization was significantly greater in group 3 than in groups 1 and 2.

The number of patients in whom closed aspiration was performed is significantly greater in group 3 when compared with group 2, but the difference between group 1 and group 2 is not statistically significant (Table 7). The average number of days of hospitalization in the patients submitted to closed aspiration and those in whom it was not done, in the three groups, (Table 8) was compared and no statistical difference was detected.

The number of patients submitted to surgery is significantly greater in group 3 than in groups 1 and 2 (Table 7). In a patient in group 1 and another in group 3 surgical drainage of the pleura for intrapleural rupture was performed. Another patient in group 3 was submitted to surgical peritoneal drainage for intraperitoneal rupture. The third patient in group 3 was operated on by open drainage of multiple hepatic abscesses for suspected pyogenic transformation. In all patients submitted to surgery an uneventful recovery was observed.

In another patient in group 3 *E. histolytica* was found in pus aspirated after a complete course of the three drugs. However, after closed aspiration and a new course of therapy, resolution was observed.

No deaths ocurred in these patients.

Significant side effects leading to interruption of drug therapy was never observed.

Table 3

Length of symptoms in days at the time of admission

	Groups		
	1	2	3
Feverishness	20.66[a]±23.00[b] (3-75)[c]	37.68±46.74 (2-180)	51.80 ± 41.51 (10-120)
Abdominal pain	21.08 ±23.18 (3-75)	45.55 ±58.23 (2-180)	95.38±194.58 (7-730)

(a) Average in days (b) Standard deviation (c) Range

Table 4

Results of laboratory tests

	Groups		
	1	2	3
Hemoglobin (g/dl)	11.8[a]±2.4[b] (14)[c]	11.2±2.0 (30)	10.6±2.0 (12)
Leucocytes (n.º/l)	(10.23±5.04)×10^9 (14)	(8.82±3.62)×10^9 (30)	(8.60±5.09)×10^9 (12)
E.S.R. (mm)	75±36 (14)	91±33 (30)	100±40 (12)
Albumin (g/dl)	2.33±0.68 (8)	2.54±0.65 (22)	1.86±0.29 (9)
Bilirubin (mg/dl)	0.73±0.38 (14)	2.27±6.19 (29)[d]	1.01±0.65 (12)
SGOT (Karmen U./dl)	47.07±24.65 (14)	55.43±37.56 (30)	171.08 ±419.39 (12)[e]
SGTP (Karmen U./dl)	35.71±24.52 (14)	35.23±33.53 (30)	40.41±5.96 (12)
Alkaline phosphatase (Bessey-Lowry U.)	2.87±1.30 (9)	4.37±2.72 (29)	5.09±3.61 (12)
Prothrombin time (% of normal)	74.64±20.72 (11)	77.65±22.30 (23)	64.30±17.21 (10)

(a) mean values (b) standard deviation (c) number of cases collected, in brakets (d) in one case the value of 34 mg/dl was obtained (e) in one case where typical anchovy «pus» was aspirated the value of 1500 U./dl was obtained.

Table 5

Fluoroscopic and chest x-ray findings

	Groups		
	1	2	3
Reduced motility of right hemidiaphragm	4	14	6
Right hemidiaphragm elevation	6	22	12
Right pleural effusion	3	15	8
Right base parenchymatous condensation	3	3	2

Table 6

Number of days of therapy when patients became afebrile and without pain and number of days of hospitalization

	Groups		
	1	2	3
Afebrile	7[a]± 4[b]	5± 3	4± 3
Without pain	11 ± 4	12± 5	25±17
Days of hospitalization	27 ±18	41±25	71±45

(a) Average (b) Standard deviation

Table 7

Number of patients in whom closed aspiration of pus or surgical drainage for complications was performed

	Groups		
	1	2	3
Closed aspiration	1(7.1%)	6(20.0%)	9(75.0%)
Surgical complications	1(7.1%)	0(0.0%)	3(25.0%)

Table 8

Average number of days of hospitalization

	Groups		
	1	2	3
Closed aspiration	80	37	86
No closed aspiration	21	41	26

DISCUSSION

Our results confirm the efficacy of drug therapy in hepatic amebiasis. In 56 consecutive cases no deaths were observed. Even in the presence of such severe complications as intraperitoneal or intrapleural rupture, amebicidal therapy has been effective when associated with pleural or peritoneal drainage.

Open drainage of amebic liver abscess is an operation with a high mortality rate (Ochsner and DeBakey, 1943; DeBakey and Ochsner, 1951) and it must be performed only for suspected pyogenic transformation (Turril and Burnhan, 1966) as in one of our patients.

The value of closed aspiration is debatable. Investigators in South Africa (Adams and MacLeod, 1977b) still propose closed aspiration as a routine procedure in all cases in which a point of maximal tenderness is elicited by palpation. However, in our experience, even when this sign is present a prompt and complete therapeutic response to amebicidal drug therapy may be observed.

Closed aspiration seems not to influence the evolution of amebic liver abscess. The time of resolution is not hastened (Sheehy et al, 1968) and in our experience, the average number of days of hospitalization is not statistically different in those patients submitted to closed aspiration compared with those in whom it was not done. In the group taking metronidazole alone, closed aspiration was performed in only one patient and the average length of hospitalization was 27 days, while in another report (Ruas and Ramalho Correia, 1970) where closed aspiration was associated routinely with metronidazole, it was 26 days.

In our opinion closed aspiration must not be used as a routine procedure. It is indicated only for patients in whom a prompt response to drug therapy is not observed.

Since the original report of Powell et al (1966) many accounts have been published confirming the efficacy of metronidazole in hepatic amebiasis. (Powell et al, 1967; Chhetri et al, 1968; Rao et al, 1968; Chhetri et al, 1969; Antani and Srinvas 1970; O'Holohan and Hugoe-Mathews, 1970: Vig et al, 1971; Rao et al, 1971; Powell and Elsdon-Dew, 1971; Monges et al, 1973; Everett, 1974; Cohen and Reynolds, 1975; Shabot and Patterson, 1978).

Although high dose regimens are usually prescribed for five to ten days, single and low dosage administration has also proved to be effective (Powell, et al, 1969).

Even in the relatively large doses used in treating amebiasis the drug is well tolerated and side effects are minimal (Adams and MacLeod, 1977 a). In our patients side effects leading to reduction in dosage or interruption of the drug were not observed. The possible carcinogenic and mutagenic effects of the drug observed in experimental studies have not been confirmed in man (Beard et al, 1979).

Despite the high efficacy of metronidazole, a few reports of treatment failures with the drug have appeared (Henn and Collin, 1973; Wilde, 1973; Griffin, 1973; Stillman et al, 1974; Gregory, 1976) and alternative regimens with other drugs may be necessary.

The efficacy of chloroquine alone has been demonstrated (Conan, 1948; Sodeman et al, 1951; Cohen and Reynolds, 1975). A ten week course of the drug may have the same efficacy as metronidazole (Cohen and Reynolds, 1975). However in short courses of 28 days it is less effective than emetine and dehydroemetine (Powell et al, 1965). A comparable efficacy to metronidazole has been reported for the combination of a four week course of chloroquine with dehydroemetine, (Wilmot et al, 1964).

Our results confirm that the combination of chloroquine for four to ten weeks and dehydroemetine are similar to those for metronidazole alone. Despite the doubts about lesser cardiotoxicity of dehydroemetine relatively to emetine (Powell, 1971) significant electrocardiographic changes were not detected in our cases.

Although Tsai (1973) in a retrospective study observed the lowest mortality using a combination of emetine or dehydroemetine, chloroquine and metronidazole, in our experience the association of the three drugs has not proved useful. In retrospect these patients had a more severe course. They needed a greater number of days of hospitalization and surgical complications and closed aspiration were more frequent. It was also with this drug regimen that treatment failure was demonstrated in one patient in whom *E. histolytica* in aspirated pus obtained after a full course of therapy was observed.

From our study we can confirm that by its high efficacy, low cost, ease of administration, absence of significant side effects and lesser mean length of hospitalization, metronidazole is the first drug of choice. The combination of dehydroemetine and chloroquine is a satisfactory alternative for treatment failures with metronidazole.

Although no deaths occured in these series a low mortality still persists in endemic areas (Tsai 1973; Adams and McLeod 1977 b). Most deaths result from failure or delay in diagnosis particularly in non endemic areas where physicians may not be familiar with the characteristic clinical picture (Wright 1966; Stamm 1975).

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