

DIAGNOSIS OF AMOEBIC INFECTION OF THE LIVER: REPORT OF 36 CASES

by

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Summary — The classical clinical picture of amoebic infection of the liver consists of fever, right upper quadrant pain and hepatomegaly. In recent years, the widespread availability of ultrasound and serology made an early diagnosis possible, which could result in less prominent clinical pictures.

Thirty six cases of liver amoebiasis diagnosed in Antwerp between 1985 and 1992, were reviewed. Three patients acquired their infection in Belgium. For the other patients, the average delay between arrival in Belgium and the first symptoms was 5.64 months. The classical triad of clinical signs (fever, right upper quadrant pain and hepatomegaly), was observed in only 13.9% of the patients, whereas it was much more frequent in earlier studies (68-75%). The right lobe was the most frequently affected (94%). The colour of the liquid, obtained by puncture, was brown in 61% of patients in whom it was reported. Amoebic cysts were found in the stools of only one patient. Amoebic serology was initially negative in only one patient, but became positive on second testing. Chest X-rays were abnormal in 34% of the patients.

All patients who develop unexplained fever during the year after a stay in tropical countries should undergo an abdominal ultrasound examination and serological testing for *Entamoeba histolytica*.

KEYWORDS: Amoebiasis; Liver abscess; Case reports.

Introduction

Liver amoebiasis is one of several clinical manifestations of *Entamoeba histolytica* infection. After oral ingestion of cysts, trophozoites of an invasive strain infect the colon. Through the portal veins they colonise the hepatic parenchyma, where they cause a localised cytolysis mimicking macroscopically an abscess. The term "liver amoebiasis" is preferred since there is no real abscess, defined as an accumulation of polymorfonuclear white blood cells contained within a capsule (Manson-Bahr).

The classical clinical picture of liver amoebiasis includes fever, right upper quadrant pain and hepatomegaly, and often a history of dysentery. In recent years, the widespread availability of ultrasound and serology allows an early diagnosis, which could result in less prominent clinical pictures. Thirty six cases of liver amoebiasis, diagnosed in the Institute of Tropical Medicine Antwerp or in other hospitals of the Antwerp region between 1985 and 1992, are described. The results are compared with results of similar studies of invasive amoebiasis in Western countries.

Patients and methods

Patients were considered to have liver amoebiasis in the presence of a suggestive ultrasound examination and a positive indirect immunofluorescence test (IFAT) for *Entamoeba histolytica* (dilution 1/100 or more) (1). The medical records of 36 cases of liver amoebiasis diagnosed in the Institute of Tropical Medicine Antwerp or in other hospitals of the Antwerp region between 1985 and 1992 were reviewed for a history of foreign travel or stay, the time between arrival in Belgium and the appearance of the first symptoms, the presence of fever ($>38^{\circ}\text{C}$, measured axillary), fatigue, weight loss, diarrhoea or dysentery during and after travel or stay, pain in the right upper quadrant, in the right shoulder or in the right scapular region, jaundice, hepatomegaly, painful palpation or percussion of the liver.

The following laboratory tests were reviewed: the erythrocyte sedimentation rate, the leukocyte count, the percentage of segmented granulocytes, the liver enzymes and the indirect immunofluorescence test for *E. histolytica*. Stool samples were examined for cysts or vegetative forms of *E. histolytica* by the SAEX concentration technique (13).

The chest X-rays and the ultrasound reports were reviewed for localisation, number, size and kind of the lesions.

The different therapeutical approaches and the final outcome were not the objective of the study.

Results

The ratio male/female was 26/3 of the 29 files in which the sex was noted. Of 27 patients the age was known. We obtained a mean age of 39.7 years.

Sixteen cases acquired their *E. histolytica* infection in Africa, 12 in Asia, 1 in Latin America, 1 in Poland and 3 in Belgium. In 3 sailors it was impossible to determine where they acquired their infection. The delay between arrival in Belgium and the appearance of symptoms varied between 1 and 60 months with an average of 5.64 months.

The five clinical symptoms or signs with the highest sensitivity for liver amoebiasis were: fever (83%), pain in the right upper quadrant (53%), history of dysentery (47%), liver tenderness on palpation (44%), and hepatomegaly (44%) (table 1). The classical triad of fever, painful right upper quadrant and hepatomegaly was present in only 5 patients (13.9%).

TABLE 1
Signs and symptoms

Signs or symptoms	Frequency (n = 36)	Percentage
Fever	30	83%
Right upper quadrant pain	19	53%
Pain in the right shoulder	6	17%
History of dysentery	17	47%
History of watery stools	14	39%
Diarrhoea on admission	9	25%
Hepatomegaly	16	44%
Painful palpation	16	44%
Painful percussion	15	42%
Jaundice	1	3%

A parasitological stool examination was performed in 30 cases: amoebic cysts were observed only once (3.3%). Laboratory tests that were nearly always abnormal were a sedimentation rate of >20 mm/h (94.4%), leucocytosis of >10.10⁹/l (88.5%) and alkaline phosphatase of >170 U/l (93.3%) (table 2).

TABLE 2
Haematological and biochemical values

Parameter	Number and frequency of patients with abnormal results		Mean value (SD)	Normal value
Sedimentation rate	34/36	94.4%	66.2 (31.7)	<20 mm/h
Haemoglobin	32/35	91.4%	12.6 (1.9)	≥ 11 g/dl
Leukocytes	31/35	88.5%	15.1 (12.7)	< 10 × 10 ⁹ /l
Non-segmented neutrophils	18/35	51.1%	9.3 (11.3)	<3%
Segmented neutrophils	31/35	88.5%	67.9 (9.5)	<56%
ALAT	28/32	87.5%	31.6 (22.4)	<23 IU/l
Alkaline phosphatase	31/33	93.3%	255.6 (124.1)	<170 IU/l
Gamma GT	30/34	88.2%	80 (71.8)	<28 IU/l

SD: standard deviation; ALAT: alanine aminotransferase; gamma GT: gamma glutamyltranspeptidase.

Thirty-one patients had an indirect immunofluorescence test result for *E. histolytica* of 1/100 or more on presentation. Four patients were not tested initially: they had a positive test later in the course of their disease. In one patient the test was initially negative, but became positive after repeated testing. The geometric mean antibody titer was 1/317 on presentation, and 1/515 maximally.

Fifteen patients underwent a diagnostic or evacuating puncture, and five patients underwent a percutaneous continuous drainage. The colour of the liquid (reported in 18 cases) was chocolate or brown in 11 cases, yellow or green in 5, and mixed with blood in 2 cases. A chest X-ray was available in 35 patients (table 3). It was normal in 23 cases (65%). An elevated right diaphragm was observed in 10/35 (28%) patients, a pleural effusion in 5/35 (14%), and pulmonary infiltrates in 6/35 (17%). A combination of all three findings was found in 3/35 (17%).

TABLE 3
Chest X-ray findings

Normal findings	Pleural effusion only	Elevated right diaphragm only	Elevated right diaphragm with pulmonary infiltrate without pleural effusion	Elevated right diaphragm, pulmonary infiltrate and pleural effusion
23/35 65%	2/35 5.7%	4/35 11.4%	3/35 8.6%	3/35 8.6%

The ultrasound of the liver identified the process predominantly as an abscess (27/36, 75%); the current localisation was in the right lobe (28/36, 77%) (table 4). The mean diameter was 7.1 cm, the largest diameter 13 cm. A detailed description of the ultrasound findings has been published elsewhere (21).

TABLE 4
Ultrasound examination of the liver; localisation and appearance of lesions

Right lobe	Left lobe	Right and left lobe	Lobe not specified	Ill-defined infiltration	Infiltration resembling metastasis	Well circumscribed fluid collection	Presentation not specified
28/36 77.7%	2/36 5.7%	5/36 13.8%	1/36 2.7%	5/36 13.8%	3/36 8.3%	27/36 77.0%	1/36 2.7%

Discussion

Four cases acquired their infection in Western Europe. One of them was a girl who reported coprophagy with an Asian friend. This suggests that the amoebiasis was in fact imported. Endemic cases are described in many series of invasive amoebiasis in Western countries (4).

In the imported cases the mean time between arrival in Belgium and the appearance of symptoms was 5.64 months. In 2 studies in France, this interval was 2.8 months and 2 months (4, 12).

In this study the most frequent symptom or sign was fever (83%). Pehrson and Lapierre also mention fever as the key clinical sign (11, 19) (table 5). In other series pain or hepatomegaly were the most prevalent clinical signs (16, 17).

TABLE 5
Comparison of symptoms and signs in different series

	Number of patients	Key sign	Only fever	History of dysentery	Jaundice
Our series 1994	36	fever 83%	14.7%	54%	3%
Laverdant (1986)	171	pain 92%	1.9%	NM	7.9%
Peters (1979)	27	pain 95%	NM	45%	NM
Overbosch (1983)	25	hepatomegaly 96%	NM	NM	NM
Maltz (1991)	50	hepatomegaly 90.7%	NM	40%	6%
Pehrson (1983)	10	fever 100%	NM	56%	NM
Lapierre (1982)	86	fever 100%	4.7%	32%	NM

NM: not mentioned.

In this study, fever was the only sign in 14.7%. In other series this is less frequent (1.9%, 4.7%) (11, 12). Jaundice and a history of dysentery were observed with a similar frequency as reported by most authors.

In this study the sensitivity of the classical triad (fever, hepatomegaly and pain) is only 13.9%. Earlier studies all give a much higher sensitivity: Condat reported 68% (6), Laverdant 74.9%, (12) and Peters 75% (20). Apparently, clinical symptoms and signs became insufficient to establish an early diagnosis with certainty. We can not draw the conclusion that the symptomatology of this disease as such is changing. A more likely explanation may be found in the fact that our patients presented with a less advanced stage of disease as diagnosis is made earlier thanks to ultrasound and/or serum immunofluorescence.

An increased sedimentation rate (> 20 mm/h) was present in 94.4%, and a hyperleucocytosis ($> 10 \times 10^9/l$) in 88.5% of our patients. This is similar to other studies (4, 12, 17, 19, 20) (table 6).

TABLE 6
Comparison of the laboratory results in different series

	Sed. rate (> 50 mm/h)	Leukocytes ($> 10 \times 10^9/l$)	Amoebae in stools	Alkaline phosphatase (> 170 U/l)
Our series	94.4%	88.5%	3.3%	93.3%
Laverdant (1986)	88%	NM	3.3%	32%
Maltz (1991)	NM	64%	18%	76%
Overbosch (1983)	92%	76%	52%	28%
Pehrson (1983)	NM	70%	60%	NM
Peters (1979)	NM	70%	20%	46%

NM: not mentioned.

In liver amoebiasis liver tests are often abnormal. Gammaglutamyl transpeptidase was increased in 88.2% of the patients, but was not mentioned in other studies. Alkaline phosphatase was elevated in 93.3% of our patients, which is more than in other studies (12, 16, 17, 20).

Amoebae were found in the stools of only one patient (1/30, 3.3%). This is similar to the 3.3% observed by Laverdant (12), but much lower than the 60% found by Pehrson (19). This variety of results questions the value of the results of direct coprologic examination for the diagnosis of liver amoebiasis. A much higher sensitivity can be obtained by culture (72%) (9). Circulating antigen and antibodies of proteinase histolysin reach also a sensitivity of 72.7% (14). Monoclonal antibodies to galactose-specific antigen are reported as sensitive as culture in random stool-specimens (7).

The reliability of the indirect immunofluorescence has been proven in the diagnosis of liver amoebiasis (1, 2, 3, 5, 18, 23, 24, 25). It is attributed a sensitivity of more than 95-100% and a specificity of more than 90% on world-wide studies (2, 3, 8, 22, 23, 24, 25).

In this study all patients developed a positive serology as this is one of the inclusion criteria. In one patient the test was initially negative, but became positive after repeated testing. In case of a clinical or ultrasonographic suspicion of liver amoebiasis and an initial negative serologic result, repeated testing should be advised and therapy should not be postponed.

The liquid obtained by puncture does not contain amoebae and cannot be used to prove amoebic infection (20). The amoebae are found in the surrounding tissue but not in the liquefied mass. The colour of the pus was brown or chocolate-brown in 11/18 (61%) of cases where the colour after aspiration is reported. In contrast of what is traditionally mentioned (Manson-Bahr), the sensitivity of chocolate coloured pus is moderate in this series.

An elevation of the right diaphragm was seen in 28%, a pleural effusion in 14% and a pulmonary infiltration in 17% of the patients. These numbers are slightly inferior compared to other studies (4, 8, 16, 20).

The three classical ultrasonographic images: a well circumscribed fluid collection, an infiltration resembling metastasis and an ill defined infiltra-

tion (12, 20), were also observed in this study. The mean diameter of the fluid collection in this study was 7.1 cm which is slightly more than 5.8 cm and 6.5 cm reported by Peters and Laverdant (12, 20). This suggests that the diagnosis of liver amoebiasis is not made earlier in our series than in older comparable studies or that the size of the ultrasonographic image is not related to its time of existence, that abscesses do not grow over time. The largest diameter in our series was 13 cm, whereas Bourgeade mentions one of 20 cm (4).

Since an early diagnosis of liver amoebiasis cannot be established by clinical, haematological and biological means alone and since the clinical presentation is frequently aspecific, all patients who develop unexplained fever during the year after a stay in tropical countries should undergo an abdominal ultrasound examination and serological testing for *E. histolytica*.

Diagnostic de l'amibiase hépatique: à propos de 36 cas.

Résumé — Le tableau classique d'amibiase hépatique consiste en fièvre, douleur dans l'hypochondre droit et hépatomégalie. Ces dernières années, le développement de l'échographie et de tests sérologiques ont permis un diagnostic précoce, ce qui a résulté en un tableau clinique moins spécifique.

Nous avons analysé les dossiers de 36 cas d'amibiase hépatique, observés à Anvers entre 1985 et 1992. Trois patients ont acquis leur infection en Belgique. Pour les autres patients, le délai moyen entre leur arrivée en Belgique et les premiers symptômes est de 5,64 mois. La triade classique (fièvre, douleur dans l'hypochondre droit et hépatomégalie) n'est observée que dans 13,9% des patients, alors que cette triade était beaucoup plus fréquente dans des études antérieures (68-75%). Le lobe droit est atteint plus fréquemment que le lobe gauche (94%). Le liquide de ponction est brun dans 61% des patients chez qui la couleur est rapportée. Des kystes d'amibes sont retrouvés dans les selles d'un seul patient. La sérologie ambiante initiale est négative chez un seul patient, mais elle devient positive au second test. La radiographie du thorax est anormale chez 34% des patients.

Nous concluons que tous les patients qui développent une fièvre inexpliquée durant l'année qui suit un séjour en pays tropical, doivent subir une échographie abdominale et un test sérologique pour *Entamoeba histolytica*.

Diagnose van leveramoebiasis: analyse van 36 gevallen.

Samenvatting — De klassieke klinische manifestatie van leveramoebiasis bestaat uit koorts, pijn in het rechter hypochonder en hepatomegalie. De laatste jaren is een vroegtijdige diagnose mogelijk door de grotere toegankelijkheid van echografie en serologie, wat kan leiden tot een minder prominent klinisch beeld.

Wij bestudeerden zesendertig dossiers van patiënten bij wie de diagnose leveramoebiasis werd gesteld in Antwerpen tussen 1985 en 1992. Drie patiënten werden besmet in België. Voor de andere patiënten was de gemiddelde duur tussen aankomst in België en de eerste symptomen 5,64 maanden. De klassieke klinische triade (koorts, pijn in het rechter hypochonder en hepatomegalie), is enkel bij 13,9% van de patiënten waargenomen. Daarentegen was deze triade in oudere studies veel frequenter (68-75%). De rechter leverlob was het frequentst aangetast (94%). Het puntievocht was bruin in 61% van de patiënten bij wie de kleur werd gerapporteerd. Kysten van *Entamoeba histolytica* werden gevonden in de stoelgang van slechts 1 patiënt. De amoebenserologie was aanvankelijk negatief bij één patiënt, doch werd bij een tweede test positief. De radiografie van de thorax was abnormaal in 34%.

Alle patiënten die onverklaarde koorts ontwikkelden tijdens het jaar na een verblijf in de tropen, dienen onderzocht te worden met een abdominale echografie en serologie voor *Entamoeba histolytica*.

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