Analysis of Factors Associated to Failure of Medical Treatment of Amoebic Liver Abscess

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Summary

Introduction. To identify the laboratory and ultrasound factors that could predict the response to medical treatment of amoebic liver abscess.

Material and method. Retrospective study of patients with diagnosis of amoebic liver abscess in Hospital Central in San Luis Potosí, Mexico. We included patients greater than 15 years of both sexes. We excluded those with probable pyogenic abscess, immunosuppression, history of abdominal, or biliary surgery, abdominal neoplasm abdominal or sepsis. We identified patients with good response to medical treatment and patients who needed the abscess drained. We studied the ultrasound findings, plasma levels of albumin, alkaline phosphatase, and bilirubin.

Results. We analysed 45 patients, 31 had a good response (controls) and 14 needed drainage (cases). The medians of the variables with statistical significance in bivariate analysis were: albumin 2.65 g/dL and 1.7 g/dL (p < 0.001); alkaline phosphatase 133 U and 259 U (p = 0.02) and diameter of abscesses 5.9 cm and 9.95 cm (p < 0.001), controls and cases respectively. By logistic regression the diameter of the abscess showed a determination coefficient of 0.447 (p < 0.05) and OR = 14.85 (95% CI, 2.11-104.9) for drain if it was > 8 cm.

Conclusions. A diameter bigger than 8 cm in hepatic amoebic abscess is associated with failure of medical treatment. Low albumin could be related to malnutrition and increased alkaline phosphatase with extrinsic compression of extrahepatic conducts due to big abscesses.

Key words: Abscess. Amebic. Liver. Diameter. Prognosis.

ANÁLISIS DE FACTORES ASOCIADOS AL FRACASO DEL TRATAMIENTO MÉDICO DEL ABSCESO HEPÁTICO AMEBIANO

Introducción. Identificar los factores de laboratorio y ultrasonográficos que pudieran predecir la respuesta al tratamiento médico del absceso hepático amebiano.

Material y método. Se realizó un estudio retrospectivo de pacientes con diagnóstico de absceso hepático amebiano en el Hospital Central de San Luis Potosí, México. Se incluyó a los pacientes mayores de 15 años de ambos sexos. Se excluyó a los sujetos con sospecha clínica de absceso piógeno, inmunosupresión o con antecedentes de cirugía abdominal o biliar o neoplasia abdominal. Se identificó a los pacientes que respondieron favorablemente al tratamiento médico y aquellos que requirieron de intervención para el drenaje del absceso. Se estudiaron los hallazgos ultrasonográficos, concentraciones séricas de albumina, fosfatasa alcalina y bilirrubinas.

Resultados. Se analizó a 45 pacientes, 31 respondieron al tratamiento (controles) y 14 requirieron intervención (casos). Las medianas de las variables con significación estadística en el análisis bivariable fueron: concentraciones de albumina de 2.65 g/dL y 1.7 g/dL (p < 0.001); fosfatasa alcalina de 133 U y 259 U (p = 0.02) y diámetro mayor del absceso de 5.9 y 9.95 cm (p < 0.001), en controles y casos, respectivamente. Mediante regresión logística el diámetro mayor del absceso mostró un coeficiente de determinación de 0.447 (p < 0.05) y odds ratio = 14,85 (intervalo de confianza del 95%, 2.11-104.9) de requerir drenaje a un valor de corte > 8 cm.

Conclusiones. Un diámetro > 8 cm del absceso hepático amebiano se relacionó con fracaso del tratamiento médico. La asociación con hipoalbuminemia probablemente se relaciona con desnutrición, mientras que valores elevados de fosfatasa alcalina pueden deberse a compresión extrínseca de los conductos extrahepáticos por abscesos de gran tamaño.

Introduction

Amebiasis is an infectious disease caused by *Entamoeba histolytica*, a protozoan transmitted by the fecal-oral route as a result of poor hygienic conditions. It is estimated that 10% of the world population is infested, though 90% of those infected are asymptomatic. It possibly has the second highest mortality rate of any parasitic disease. Its prevalence in Mexico varies by geographic zone and socioeconomic level, generally predominant in the south-southeast, and the central region (San Luis Potosí state and surrounding states) is considered to be an endemic zone for the disease.

Amebiasis shows a high variety of clinical forms which go from acute or chronic intestinal disease to severe forms of amebic dysentery, fulminant colitis, or toxic colitis. It can also be present as amebic appendicitis or, rarely, as an ameboma. Extraintestinal presentation can manifest as hepatic abscess or rare cutaneous, genital, pulmonary, and cerebral forms. The most frequent extraintestinal form of amebiasis is amebic hepatic abscess which results from virulent *E histolytica* trophozoite migration from the colon to the liver through the mesenteric veins and the portal system. It is more common in children under 1 year of age and adults over 45 years of age. It is 3 to 4 times more frequent in men than in women. It usually presents as a single large abscess.

SeroLOGY studies such as ELISA and PCR have high sensitivity and specificity (>90%) in the diagnosis of amebic hepatic abscess. Ultrasound also allows us to know the location, number, and volume of abscesses. Initial treatment of amebic hepatic abscess is medical; nevertheless, cases that are resistant to medical treatment require drainage of the abscess either through ultrasound guided percutaneous aspiration or by open surgery. There is evidence that serum bilirubin concentrations >3.5 mg/dL, encephalopathy, abscess volume, hypoalbuminemia (<2 g/dL), and the number of abscesses are all independent risk factors for mortality. However, the risk factors that determine a lack of response to treatment, indicative of early complications related to the abscess such as rupture to the thoracic or abdominal cavity were considered. The controls were those patients with amebic hepatic abscess that responded favorably to medical treatment alone (metronidazole). Fifty nine charts that made up the total population of patients with a discharge diagnosis of amebic hepatic abscess in 1999 were reviewed. Five paediatric charts were excluded. Of the remaining 54, 9 were excluded: 2 for suspected pyogenic hepatic abscess, 3 due to lack of an ultrasound report, and 4 cases couldn't be followed-up due to voluntary discharge. Of the 45 cases analyzed, 31 responded to medical treatment and 14 required drainage (10 percutaneous and 4 surgeries).

Serum concentrations of alkaline phosphatase (U), direct and indirect bilirubin (mg/dL), albumin (g/dL), and total leukocytes (cells/µL) on admission were studied as possible predictors of failure of medical treatment. The greatest diameter of the abscess and the number of abscesses from the first ultrasound study were measured; in cases of multiple abscesses, the diameter of the largest abscess was measured. Ultrasound was performed using a Phillips Sterling 110V, 50/60 Hz device with 3.5-7.5 Hz transducers.

### Material and Method

A study of cases and controls was performed, based on the charts of patients who were admitted in 1999 to the Dr Ignacio Morones Prieto Central Hospital in the city of San Luis Potosí, Mexico, and who were diagnosed with amebic hepatic abscess on admission and confirmed with ultrasound. All cases were confirmed by histopathology studies or by an adequate response to treatment with metronidazole. All patients over 15 years of age of both genders were included. Patients with a clinically suspected pyogenic hepatic abscess were excluded, as were patients who were immunodeficient, had a history of abdominal or biliary surgery, or a history of abdominal neoplasms. Cases of patients with amebic abscess that required drainage by percutaneous hepatic aspiration or surgery due to persistent symptoms despite 3-4 days of antiparasitic treatment, or those cases that presented complications related to the abscess such as rupture to the thoracic or abdominal cavity were considered. The controls were those patients with amebic hepatic abscess that responded favorably to medical treatment alone (metronidazole). Fifty nine charts that made up the total population of patients with a discharge diagnosis of amebic hepatic abscess in 1999 were reviewed. Five paediatric charts were excluded. Of the remaining 54, 9 were excluded: 2 for suspected pyogenic hepatic abscess, 3 due to lack of a discharge diagnosis of amebic hepatic abscess. Medical treatment was considered a failure when there was a lack of response to treatment, indicative of early complications related to the abscess such as rupture to the thoracic or abdominal cavity.

### Results

Table shows the comparison of the different variables studied. The serum albumin, alkaline phosphatase, and greatest diameter of the abscess had a statistically significant difference (Figure). Hospitalization period was 9.19 (range, 7.35-11.03) days in the medical treatment group and 13.79 (range, 10.99-16.58) days in the surgical group, with a statistically significant difference (P=.006).

Upon applying logistical regression, the only variable that maintained statistical significance was the abscess size, with a coefficient of determination of 0.44 (P<.001). Several cutoff levels for this variable were analyzed and we found that 8 cm represented a point of greater clinical significance. Eight patients with a diameter >8 cm responded favorably, while 13 required surgery. When less than 8 cm was used as a reference, we found that 23 patients responded to medical treatment while 1 required surgery. Therefore, it had an OR of 2.51 (95% confidence interval [CI], 1.44-4.36) for a diameter <8 cm; meaning abscesses with a diameter of less than 8 cm have twice the possibility of responding...
to medical treatment as larger abscesses do; meanwhile, when the diameter is greater than 8 cm, the possibility of requiring surgery is 14 times greater (OR=14.85; 95% CI, 2.11-104.9).

Discussion

Treatment for amebic hepatic abscess may be pharmacological or surgical.\textsuperscript{12,13} The former has been widely accepted since hepatic amebiasis can be cured with just metronidazole.\textsuperscript{7,13} Surgical treatment has been divided into percutaneous aspiration or surgical drainage. The indications for percutaneous aspiration are not well defined; however, in general, abscesses that are punctured are usually larger than 150 mL, in the case of less than 3 abscesses, with failure of medical treatment for 3-5 days, location in the left lobe, imminence of rupture, or accessibility for puncture.\textsuperscript{13-18}

Laparotomy is prescribed when the aspiration puncture fails, in very large abscesses, in those that have a high risk of pericardial rupture, when there is bacterial contamination, or intra-abdominal sepsis. In general, patients that require surgical treatment have higher mortality and more complications since they can present with lung infection, ileus, bleeding, and biliary fistula.

The usefulness of primary drainage of the hepatic abscess has been described in the medical literature and there have also been reports of factors that can influence mortality.\textsuperscript{7,11} Nevertheless, there are no studies that have evaluated the factors that lead to the decision to carry out an early drainage, and thereby avoid the appearance of complications. According to our results, we can conclude that the size of the abscess (at the greatest diameter) is a predictor of the need to drain the amebic hepatic abscess. Based on this, the physician can decide whether to drain the large abscess in order to avoid complications (such as rupture) or to accelerate the recovery process and reduce the patient's hospital stay. The usefulness of abscess size as a predictor of medical treatment failure should be evaluated prospectively, and it should be determined whether the combination of other variables allows it to have a higher predictive ability that is more useful in clinical practice. By using 8 cm as the cut off value, the risk of requiring drainage is 14 times higher, which can be used as a predictor of the possibility of resolving with medical treatment of not.

The purpose of this study was to determine the tendency of variables and to consider those that, because of their association with the response, should be analyzed in a prospective study. Also, in addition to the diameter, we find that the poor response to treatment is related hypoalbuminemia, which is probably associated with malnutrition and an elevation of alkaline phosphatase, which in turn may be caused by extrinsic compression of the extrahepatic ducts by large abscesses.

References