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Gigantic amoebic liver abscess in pregnancy: A case report

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Abstract. Amoebic liver abscess in pregnancy is genuinely rare in its presentation. Yet, the main issue surrounding this agenda is the diagnostic challenge that it poses especially when symptomatology is vague and clues are subtle which altogether evades the diagnosis proper. We would like to dwell mainly on these issues in hopes of enlightening clinicians towards these diagnostic dilemmas. We report an extremely rare case of amoebic liver abscess occurring in the third trimester of pregnancy in a 29-year-old lady living in an interior village in Sabah. It was a combination of biochemical, radiographic and molecular investigations that ultimately led to the final diagnosis. In lieu of the high risk of mortality amongst pregnant mothers afflicted with amoebic liver abscess, the inherent need for early diagnosis requiring a high index of suspicion is vital. Elevated alkaline phosphatase alongside neutrophilia appears to be the most consistent liver parameters in guiding clinicians towards the presence of liver abscess.

INTRODUCTION

Amoebic liver abscess (ALA) is one of the commonest sequelae of invasive amoebiasis, which is caused by an intestinal protozoa, *Entamoeba histolytica*. Prevalence tends to vary, but a local study reported that as high as 44.1% of liver abscess in patients were caused by ALA (Goh *et al.*, 1987). However data of ALA occurring in pregnancy, are confined to case reports from endemic regions due to its paucity of incidence and none has been reported from Malaysia. In addition to this lack of information, ALA in pregnancy poses diagnostic and treatment dilemmas (Read *et al.*, 2001).

CASE REPORT

A 29-year-old pregnant woman gravida 6 para 4 + 1 at 30-weeks gestation came to the hospital with complains of four days of fever, lethargy and flu like symptoms. There were no known comorbidities. She was initially given a course of Amoxicillin by her General Practitioner but to no avail and was subsequently admitted to the hospital. Upon presentation to the hospital, she was referred to the Internal Medicine Unit by the Obstetrics and Gynaecology team; whereupon she was treated for pneumonia. She appeared pale, mildly tachypneic with a blood pressure of 107/63 mmHg, heart rate of 120-140 bpm, temperature of 37.5°C and a SpO2 of 98% on nasal prong 2 L/min. Examination of her cardiovascular system was unremarkable. Respiratory examination revealed mild bibasal fine inspiratory crepitation's attributed to over-hydration. Abdominal examination revealed mild upper abdominal tenderness. Organomegalies were difficult to appreciate in view of the gravid uterus.

Laboratory investigations showed an elevated erythrocyte sedimentation rate at 140 mm/hr, total white count of 30-40 x 10^9/L,

elevated alkaline phosphatase at 346 U/L with borderline increment in alanine transaminase at 40-50 IU/L, raised lactate dehydrogenase at 1200-1300 U/L with persistently low albumin at 18 g/L. Bilirubin was normal. Her blood cultures, tuberculosis workup and viral hepatitis were negative. Likewise, her transthoracic echocardiography was normal while her Chest X-ray revealed interstitial edema in keeping with the clinical findings of over-hydration. The possibility of liver pathology was given due consideration and a subsequent abdominal ultrasonography revealed a huge non-liquefied abscess at the right lobe of liver measuring 13.6 cm x 15.9 cm x 20.2 cm in dimension. Antibiotics were changed to intravenous Meropenem 500 mg 8 hourly alongside intravenous Metronidazole 500 mg 8 hourly to cover for potential pyogenic and amoebic liver abscess.

Upon further questioning she revealed factors of poor personal hygiene and sanitation coupled with overcrowded living conditions. There was no history of dysentery, no history to suggest immunosuppression and her HIV screen was negative. Her travel history was insignificant. Ultrasound guided percutaneous liver abscess drainage was done upon transfer to a subspecialized tertiary center in which 2.3 liters of odorless brownish pus (anchovy sauce pus) was drained over time (Figure 1).

Subsequently, pus from the abscess, blood serum and stool samples from the patient were sent to the Department of Parasitology, Faculty of Medicine, University of Malaya for further confirmatory diagnosis.

The patient's serum was analysed for IgG antibody against *E. histolytica* using a commercial enzyme linked immunosorbent assay (ELISA) kit (Diagnostic Automation, Inc., USA). Briefly, a 1:64 dilution of patient serum was made using a dilution buffer and added into the microwells coated with *E. histolytica* antigen as in accordance to the manufacturer's instructions. The microwells were then finally read at 450 nm with a reference filter of 620 nm. An absorbance reading greater than 0.4 O.D unit was obtained in which indicated that the patient may be infected by *E. histolytica*. Given that the positive ELISA reactions would not unequivocally prove current active infection and could rather result from a persisting level of antibody from a past infection, subsequent confirmation using a nested polymerase chain reaction (PCR) was carried out.

Briefly, total genomic DNA was extracted from the pus drained from the liver abscess using Tissue DNA Isolation kit (Macherey-Nagel, Neumann-Neander, Duren, Germany) following the manufacturer's guideline and used as template DNA for further specific-species confirmation. The pus digested and incubated at 56°C overnight in an incubator shaker with proteinase K for complete cell lysis followed by genomic DNA extraction. The extracted DNA was subjected to a nested PCR targeting the 16S-like ribosomal RNA gene of *Entamoeba* genus (i.e., *E. histolytica*, *E. dispar* and *E. moshkovskii*) according to previously published protocol with some modifications (Khairnar *et al.*, 2007). The first PCR was carried for the detection of *Entamoeba* genus. Subsequently, the primary PCR product was then subjected to secondary

Figure 1. Anchovy sauce-like pus being drained from the liver abscess.

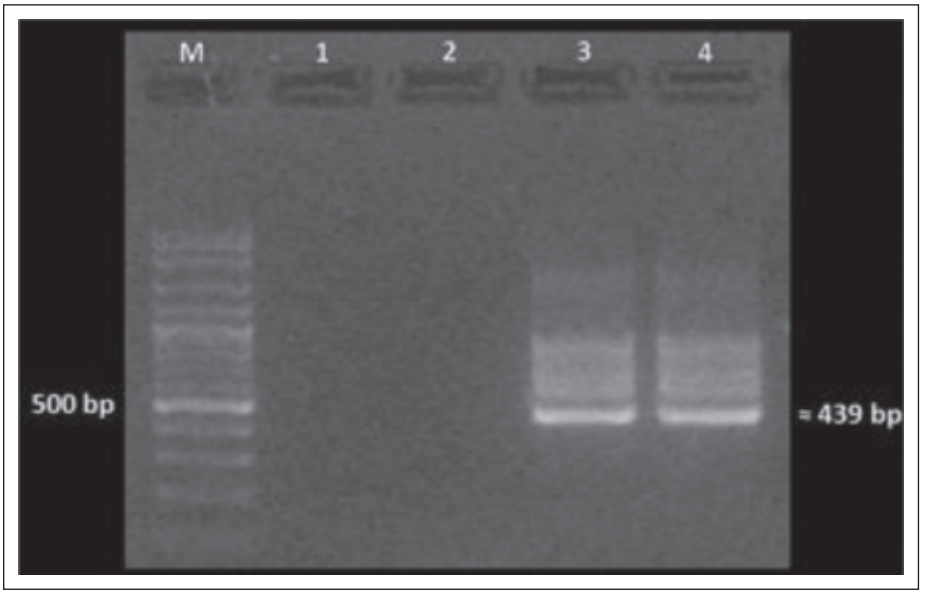

Figure 2. The PCR results. Lane M: 100 marker; Lanes 1-2: No template (negative controls); Lane 3: *E. histolytica* DNA (positive control); Lane 4: Patient's sample.

PCR for *Entamoeba* species-specific characterization. Control samples without DNA (negative control) and with *E. histolytica* as template DNA were included in each PCR run. DNA amplification produced an approximately 439 bp specific amplicon which corresponded to the specific PCR product of *E. histolytica* (Figure 2). Clinicoserological and molecular finding suggested the final diagnosis of *E. histolytica* infection occurring in this third trimester pregnant woman.

In addition, faecal sample was examined via microscopy for the presence of *E. histolytica*. However, it was negative for both *E. histolytica* cysts and trophozoites.

Meanwhile, she completed two weeks of intravenous Metronidazole with no untoward complications and the pregnancy progressed normally to term. She delivered a healthy baby girl weighing 3.0 kg at 38th week of gestation. Unfortunately, luminal amoebicide was not available locally. She remained well and was last followed up a week after her delivery. Repeated ultrasonography showed progressive size reduction of the liver abscess cavity.

DISCUSSION

Amoebic liver abscess is a disease of tropical and sub-tropical countries. It is relatively uncommon in women and is a rare complication of pregnancy (de Silva *et al.*, 1990; Mabina *et al.*, 1998). ALA previously reported in Malaysia were from males and non-pregnant females (Jamaiah & Shekhar, 1999). We believe this patient to be the first reported case in pregnancy in Malaysia. Amoebiasis occurs in people from the lower socio-economic groups. It is associated with poverty, improper sanitation, contaminated food and water. This patient came from a poor socio-economic background and she is exposed to the associated factors for amoebiasis including poor sanitation and over crowding living condition.

ALA carries significant morbidity if diagnosis is delayed. Clinicians in endemic countries need to be aware of its possibility when pregnant women present with fever, abdominal pain, and upper abdominal tenderness even if they have no bowel related symptoms. Not all of the classic features of hepatic amoebiasis were present as in our

case. Pregnancy increases the susceptibility to amoebiasis due to a defective immune response and to raised progesterone levels and thus patients with sub-clinical infections may develop clinical symptoms during pregnancy (Cowan & Houltan, 1978; Constantine *et al.*, 1987).

Fever, right upper quadrant pain and hepatomegaly are the commonest presenting features of ALA. The difficulties and the delay in diagnosing this patient was due to the vague symptomatology and the gravid uterus, which obscured clinical findings. With literature documenting 60-80% of ALA patients developing abnormally high alkaline phosphatase levels; this finding together with leukocytosis help in guiding towards the diagnosis of liver abscess (Petri & Singh, 1999; Mathur *et al.*, 2002). Though serum bilirubin was normal in this patient, it should be noted that hyperbilirubinaemia is associated with a grave outcome (Mathur *et al.*, 2002).

Abdominal ultrasonography carried out in this patient revealed a huge liver abscess in the right lobe which could either be pyogenic or ALA. Serological test carried out for this patient was positive for amoebiasis. Serological tests are positive in about 90–95% of patients with an ALA. Antibody titers can confirm *E. histolytica* infection but may persist for 6 months or more making it impossible to differentiate acute from past infections in residents from areas with a high prevalence of infection. This report also highlighted the usefulness of advanced molecular technique such as polymerase chain reaction in the diagnosis by detecting the presence of the DNA of *E. histolytica* in the pus from the liver abscess. Similarly, this has been reported in North India by Khan (2006).

In the treatment of amoebic liver abscess; antibiotics remain the cornerstone of therapy. Metronidazole is highly effective against invasive amoebiasis. When ultrasonography confirms a liver abscess and while awaiting serologic and molecular confirmation of an amoebic etiology as in this case, treatment with Metronidazole should be initiated. However drainage of liver abscess measuring more than 10 cm has been recommended to prevent its potential rupture. Such complementary management aids in preventing rupture of the abscess and expedites recovery (Mathur *et al.*, 2002). There have been cases reported of intraperitoneal rupture, rupture after birth and rupture during birth (Jamaiah & Shekhar, 1999). ALA may extend and /or rupture into the abdomen or chest. Ultrasonography is helpful in the long term follow-up of patients. It is assessed by patterns of resolution of the abscess cavity. Liver abscesses usually disappear within 8 months to 2 years after drainage.

Control of amoebiasis is via adequate sanitation, safe food and water and good personal hygiene of the population.

CONCLUSION

A high index of suspicion in the presence of confounding symptoms is vital to come to the likely diagnosis. Serum alkaline phosphatase is probably the most common and consistent biochemical indicator of amoebic liver abscess. Laboratory tests should include molecular techniques. This case serves to illustrate the importance of combining and interpreting the relevant laboratory and molecular investigations in order to clinch the diagnosis early and prevent fatal complications.

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