Liver Abscess in a Child with Fever of Unknown Origin: A Case Report with Literature Review

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Case Report

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Abstract
Fever of unknown origin (FUO) with its long list of differential diagnosis including infections, neoplasms and collagen vascular diseases, remains a challenge to all clinicians. We report a case of an infant who presented with fever of one month duration with physical finding of hepatomegaly only. Extensive work up of laboratory and imaging investigations revealed a final diagnosis of liver abscess. Despite the existence of many developed diagnostic tools for such cases, good clinical judgment can lead to the definitive diagnosis saving the patients and their physicians from this dilemma. Although controversy exists on whether to treat liver abscess medically or by percutaneous or surgical drainage, our patient was treated with broad spectrum antibiotics for a total of 6 weeks duration and showed full resolution

Introduction
Fever of unknown origin (FUO) is considered a diagnostic challenge. It is defined as temperature greater than 38.3°C (101°F) on several occasions, with more than 3 weeks' duration of illness. Most cases are caused by common problems including Infections (40%) neoplasms (20%) and collagen vascular diseases (15%) [1].

Liver abscesses are the most common type of visceral abscesses and are frequently observed in pediatric clinical practice in the tropics and subtropics especially in developing countries [2]. They continue to pose diagnostic and therapeutic challenges to physicians. Most of these abscesses are easily treatable but at the same time they fatal if left untreated. Children have a unique set of predisposing causes for liver abscesses. The classical clinical presentation is fever and abdominal pain, though, other symptoms including nausea, vomiting, anorexia, weight loss, and malaise can also occur.

We report a case of an infant who presented with fever of one month

duration, which had been worked up thoroughly as a case of Fever of Unknown Origin where extensive laboratory investigations led to a diagnostic dilemma and parental anxiety but finally proved to be caused by liver abscess. The patient was then treated with broad spectrum antibiotics and showed full resolution.

Case Presentation

Eleven months old boy with unremarkable perinatal history presented to Accident & Emergency Department at Sultan Qaboos University Hospital, Oman, with persistent high grade fever of one month duration, during which he received 4 courses of co-amoxiclav (amoxicillin and clavulanate). Systemic enquiry was negative, with no history of neurological, respiratory, gastrointest-inal, genitourinary symptoms and no abnormalities at the joints. There was no history of travel or contact with animals and family history was unremarkable. Physical examination revealed a sick looking, febrile, pale, but well thriving infant, with all growth parameters on 50^{th} centile. There was hepatomegaly (3 cm below costal margin with liver span of 10 cm), but no splenomegaly or lymphadenopathy. Other systemic examination was normal.

He was admitted for further workup and management. The initial investigations revealed microcytic hypochromic anemia with leucocytosis, mainly neutrophilia. Peripheral blood smear showed no blast cells. The inflammatory markers were also elevated (C-reactive protein CRP 152 mg/L, and erythrocyte sedimentation rate ESR 98 mm/h). Apart from minimal hypoalbuminemia (serum albumin of 32 g/L), his serum urea, creatinine, electrolytes, as well as liver enzymes, and alkaline phosphatase were all within the reference ranges. Chest X-ray was unremarkable. Blood and urine cultures were send, and the infants was started on empirical antibiotic (intravenous ceftriaxone), after which, fever spikes became less but continued to appear intermittently.

Ultrasound of the abdomen revealed hypoechoic lesion in the right lobe of liver, measuring 49 x 27 mm in size (Figure 1), with no increase in vascularity by Doppler study, suggestive of pyogenic liver abscess. Computed tomography (CT) of the abdomen showed contrast enhanced large hypodense liver lesion at segments VI and VII, measuring 50 x 43 x 48 mm in size (Figure 2). US guided aspiration and biopsy revealed necrotic tissue with inflammatory cells mainly neutrophils. The family was informed for considering percutaneous drainage of the abscess, but they refused. After prolonged counseling, they agreed to start IV antibiotic alone. The infant showed good clinical response. The biopsy bacteriology showed light growth of staphylococcus aureus sensitive to flucloxacillin and metronidazole. The antibiotics were adjusted accordingly and continued for total of 4 weeks. Work up for Immunodeficiency states including HIV serology, immunoglobulins, neutrophil and complement function were all normal. The infant showed good clinical response to treatment and became afebrile and active. The inflammatory markers have also improved gradually (table 1).

Repeat abdominal US on day 10 showed significant reduction in size of lesion (from 49 x 28 mm earlier, to 19 x 15 mm). Repeat US on day 21 showed further reduction to 11 x 8 mm. After a

month of hospital stay, the child was discharged home in a good condition, with oral cloxacillin for 2 more weeks. Follow up abdominal US after 5 weeks showed complete resolution of the liver abscess (Figure 3)

Discussion

Thorough work up and investigation of FUO should be implemented according to the clinical presentation and physical findings pointing towards one of the long listed differential diagnosis , as in our patient who had only hepatomegally as a positive physical finding, that helped in reaching the etiology of his fever.

Pyogenic liver abscess (PLA) is a cause of significant morbidity and mortality with increasing frequency in the developing world [3]. PLA has been described to be rare in infancy and childhood, but it still remains a major cause of high mortality in children [2]. Untreated PLA remains uniformly fatal. With timely administration of antibiotics and drainage procedures, the mortality occurs in 5-30% of cases. The most common causes of death include sepsis, multi-organ failure, and hepatic failure [4] The predisposing causes include parasitic infestations, skin infections, protein calorie malnutrition, and trauma [5]. Immune deficiency syndromes are important risk factors in children, such as chronic granulomatous disease (CGD), C1 complement deficiency and hyper Immunoglobulin E syndrome [1].

Hematogenous spread occurs from seeding of bacteria into the liver in cases of systemic bacteremia from bacterial endocarditis or urinary sepsis [6]. Transmission may also occur through the portal route as in appendicitis, diverticulitis, inflammatory bowel disease, or through biliary route mainly in adults, in conditions like extrahepatic biliary obstruction, choledocholithiasis, tumors, or postsurgical strictures [4]. Other co-morbid conditions associated with the risk of PLA including liver transplantation, diabetes mellitus, and malignancy [7]. It has been documented that the majority of patients with PLA were healthy. This might be attributed to the high rate of environmental infection in developing countries [8].

The clinical presentation of liver abscess is insidious with many patients have symptoms for weeks prior to presentation. Fever and right upper quadrant pain are the most common complaints. Fever occurs in 67-100% of patients and is usually associated with chills and malaise. Pain is reported in 67-100% of patients and may be associated with pleuritic chest pain or right shoulder pain [9]. Physical examination findings might be normal in as high as 38% of cases, however, right upper quadrant tenderness, hepatomegaly, liver mass, and jaundice are common findings [9].

Increased serum alkaline phosphatase activity and low albumin concentration have been reported as the most common abnormal laboratory findings [10]. However, leukocytosis, elevated levels of billirubin and aminotransferases are also common in PLA [10]. Other laboratory findings include anemia, leucocytosis, raised ESR and C-reactive protein.

For diagnosing PLA, abdominal ultrasonography is 80-100% sensitive. The finding of a round or oval hypoechoic mass is usually consistent with pyogenic abscess which was the case in our patient. Other imaging modalities include MRI and CT scanning which have become the imaging studies of choice for detecting

liver lesions. A hypodense lesion with low attenuation areas and an enhancing rim is a classical CT scan image [11]. Also, in PLA the blood cultures are positive in roughly 50% of cases and culture of abscess fluid should be the goal in establishing microbiologic diagnosis [12].

Most liver abscesses in children are pyogenic that is usually polymicrobial with Staphylococcus is the most commonly encountered organism. Other organisms include anaerobes, streptococci, klebsiella, tuberculosis, and candida species. Amoebic abscesses are less common constituting 21-30% of all cases of liver abscesses and should be considered as a cause of primary liver abscess [13].

A significant reduction in the mortality has occurred for all PLA since 1950, possibly related to the advent of percutaneous drainage and the use of broad spectrum antibiotics [14]. There is no definite consensus about the management of liver abscesses. Although some authors have emphasized the importance of percutaneous and surgical drainage of pyogenic abscess [15]; others recommended drainage when the abscess is large or seems to rupture on US examination, or not responding to antibiotic therapy after 72 h, or if the patient is septicemic [16]. A course of six weeks antibiotic therapy alone, including two weeks intravenously, followed by four weeks orally is recommended by some authors, especially when multiple or small abscesses exist [15]. In our case, the decision not to drain the abscess was based on parental refusal of the procedure. However, the dramatic response to antibiotics was supportive to our decision of treatment with broad spectrum antibiotics intravenously that resulted in complete resolution of the abscess.

Conclusion

FUO in children is considered to be a diagnostic challenge. Thourough history and clinical examination can lead to the definitive diagnosis and save the patients and their physicians from this dilemma. Visceral abscesses are to be considered as a possible differential diagnosis, among which, liver abscess is the most common. Although there is no definite consensus about the management of liver abscesses, medical treatment with prolonged broad spectrum antibiotics is an acceptable option.

References

1. M.P. Sharma and Arvind Kumar. Liver abscess in children. Symposium on Hepatology and Gastroenterolgy- II, Indian Journal of Pediatrics, Volume 73- September, 2006.
2. Chen SC, Huang CC, Tsai SJ, et al. Severity of disease as main predictor for mortality in patients with pyogenic liver abscess. Am J Surg. Aug 2009;198(2):164-72.
3. Seeto RK, Rockey DC. Pyogenic liver abscess. Changes in etiology, management, and outcome. Medicine (Baltimore). Mar 1996;75(2):99-113.
4. Rintoul R, O'Riordain MG, Laurenson IF, et al. Changing management of pyogenic liver abscess. Br J Surg. Sep 1996;83(9):1215-8.
5. Kaplan, GG, Gregson, DB, Laupland, KB. Population-based study of the epidemiology of and the risk factors for pyogenic liver abscess. Clin Gastroenterol Hepatol 2004; 2:1032.
6. Giorgio A, de Stefano G, Di Sarno A, et al. Percutaneous needle aspiration of multiple pyogenic abscesses of the

liver: 13-year single-center experience. AJR Am J Roentgenol. Dec 2006;187(6):1585-90.
7. Israeli R, Jule JR, Hom J. Pediatric pyogenic liver abscess. Pediatric Emergency Care. 2009;25:107–8.
8. Benedetti NJ, Desser TS, Jeffrey RB. Imaging of hepatic infections. Ultrasound Q. Dec 2008;24(4):267-78.
9. Muorah M, Hinds R, Verma A, Yu D, Samyn M, Mieli-Vergani G, et al. Liver abscesses in children: A single center experience in the developed world. J Pediatr Gastroenterol Nutr. 2006;42:201–6.
10. Lok, KH, Li, KF, Li, KK, Szeto, ML. Pyogenic liver abscess: clinical profile, microbiological characteristics, and management in a Hong Kong hospital. J Microbiol Immunol Infect 2008; 41:483.
11. Lederman ER, Crum NF: Pyogenic liver abscess with a focus on Klebsiella pneumoniae as a primary pathogen: an emerging disease with unique clinical characteristics. Am J Gastroenterol 2005, 100:322-331.
12. Cheng HP, Siu LK, Chang FY: Extended-spectrum cephalosporin compared to cefazolin for treatment of Klebsiella pneumoniae-caused liver abscess. Antimicrob Agents Chemother 2003, 47:2088-2092 .
13. Bari S, Sheikh KA, Malik AA, Wani RA, Naqash SH. Percutaneous aspiration versus open drainage of liver abscess in children. Pediatr Surg Int. 2007;23:69–74.

Table 1 Result of inflammatory markers during the course of admission.

Day of admission	D2	D8	D16	D30
WBC ($X10^9$/L)	18.4	7.3	13.4	5.4
CRP (mg/L)	152	84	9	3
ESR (mm/hr)	98	114	47	NA

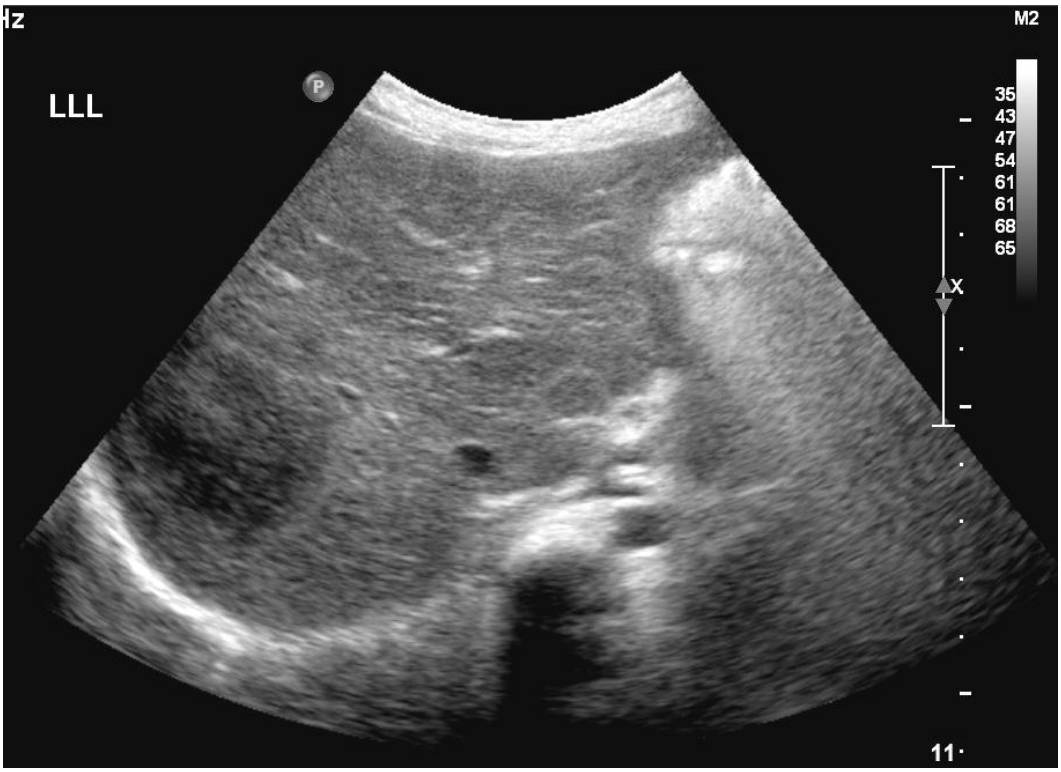

Figure 1 Ultrasound abdomen showing the liver lesion (black arrow) at the level of segment 7. It is hyper-echoic in the centre and hypo-echoic at the periphery. It measures 4.9 x 2.7 cm in size.

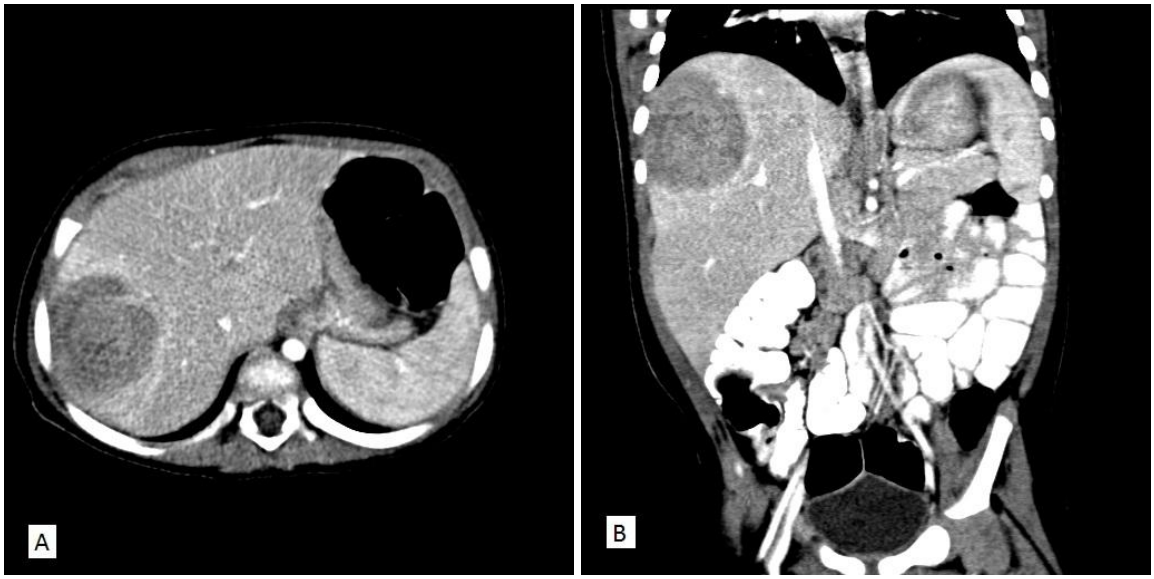

Figure 2 Contrast enhanced CT scan of the liver (A: cross section. B: sagital section) showing hepatomegally with large hypodense lesion seen at segments VI and VII, measuring 50 x 43 x 48 mm in size. This lesion shows contrast enhancement within the lesion and there is perilesional enhancement.

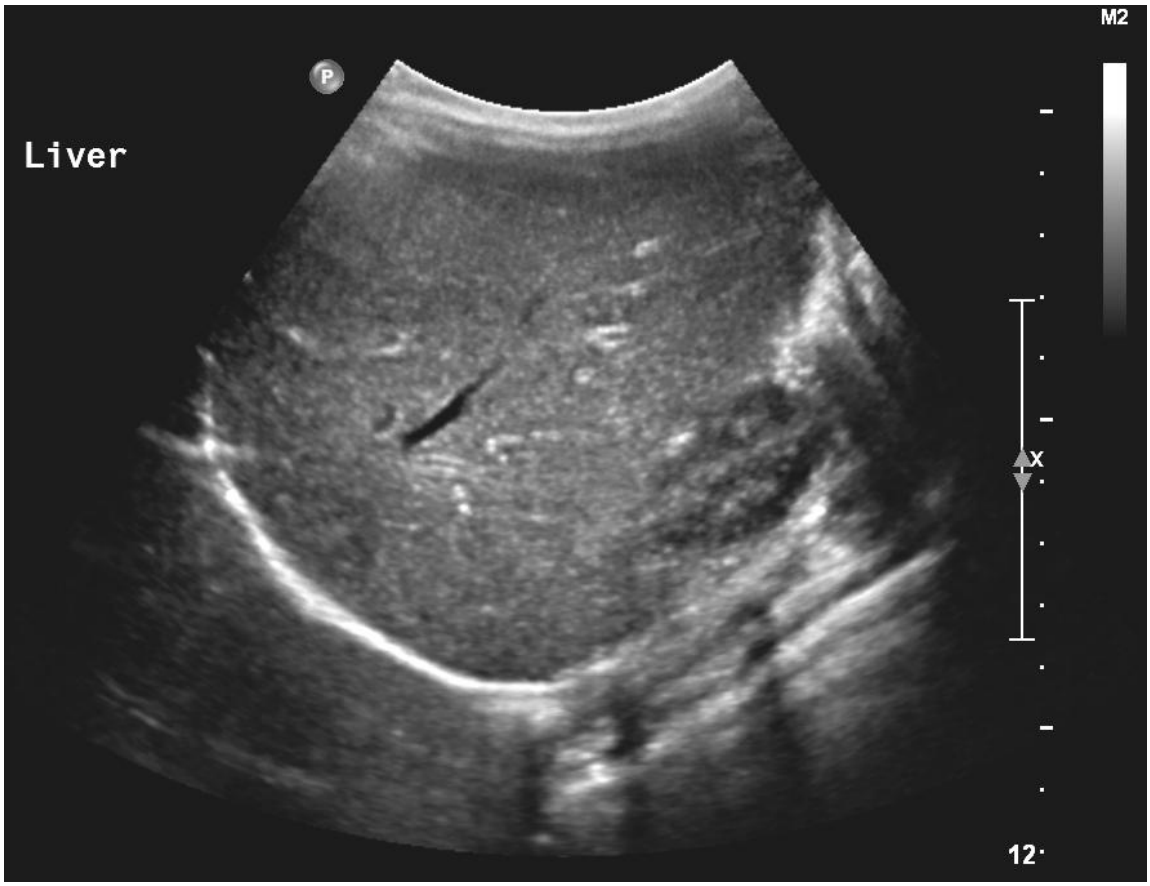

Figure 3 Post treatment Ultrasound Showing total resolution of the liver lesion.