Neonatal Hepatic Abscess in Preterm Infants: A Rare Entity?

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Abstract

Introduction and Objective: Neonatal pyogenic hepatic abscess in preterm infants is a rare entity. We present 6 cases of neonatal liver abscesses diagnosed in our hospital as well as an approach that will facilitate the early diagnosis and management of neonatal pyogenic liver abscess based on our case series and review of the literature. Materials and Methods: Retrospective review of case records of all 6 patients diagnosed with neonatal liver abscess from January 2000 to December 2002 in KK Women’s and Children’s Hospital, Singapore. Results: All neonates were premature with gestational ages between 24 and 34 weeks. Persistence of positive blood culture despite appropriate antibiotic treatment in 67% of the cases prompted use of hepatobiliary ultrasounds to detect liver abscess. Surgical drainage of liver abscess was performed in 33% of the cases, with the remainder treated conservatively with appropriate intravenous antibiotics. Half of the infants recovered with resolution of their liver abscess on serial hepatobiliary ultrasound. The other half died of fulminant sepsis. Conclusions: Neonatal pyogenic liver abscess, though rare, is associated with good outcome if diagnosed promptly and appropriate treatment instituted. In a preterm infant with sepsis, a high index of suspicion is required if there is persistence of positive blood culture despite appropriate antibiotic treatment, and hepatobiliary ultrasound should be done to detect and monitor neonatal liver abscess.

Key words: Liver abscess, Outcome, Preterm, Ultrasonography

Introduction

Liver abscess has been recognised since the time of Hippocrates. The first report on liver abscess was published by Bright in 1836. However, reports pertaining to liver abscess in the neonatal period have been published only since the 1930s. Neonatal liver abscess is a rare entity. To our knowledge, fewer than 100 cases have been reported in the literature. We present 6 additional cases and a review of the current literature pertaining to the latest techniques in diagnosis and management of neonatal liver abscess.

Materials and Methods

Information on the diagnosis of neonatal liver abscess was obtained from the neonatal intensive care unit and surgical log books in KK Women’s and Children’s Hospital, Singapore from January 2000 to December 2002. There were 6 infants diagnosed with neonatal liver abscess in this period. Their case records were analysed for demographic data, age of diagnosis, possible risk factors, clinical presentation, diagnostic methods, treatment and outcome.

Results

Table 1 shows the individual characteristics, treatment and outcome of the 6 cases of neonatal liver abscess in our series. Four of the 6 babies (67%) were males. All the neonates were premature, with a median gestational age of 24.5 weeks and birth weight of 743 g. The median age of diagnosis of neonatal liver abscess was 17.5 days. Figures 1 to 3 show the hepatobiliary ultrasound findings of 3 babies. Figure 4 gives an overall outline of the management of all the infants in the case series.
## Table 1. Characteristics, Treatment and Outcome of the 6 Neonates in the Case Series

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Sex</th>
<th>Gestation (weeks)</th>
<th>Birth weight (g)</th>
<th>Age of diagnosis (days)</th>
<th>Possible risk factors</th>
<th>Clinical presentation</th>
<th>Radiological finding/Operative finding</th>
<th>Aetiological agent</th>
<th>Other abscesses</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>24</td>
<td>745</td>
<td>16</td>
<td>Septis: <em>Chryseobacterium gleum</em></td>
<td>Clinically well</td>
<td>U/S HBS: 1.5 x 2.0 x 1.7cm liver abscess in right lobe superiorly located. (Fig. 1)</td>
<td>Most likely <em>Chryseobacterium gleum</em></td>
<td>NA</td>
<td>IV ceftazidime for 42 days</td>
<td>Discharged well. Complete resolution of liver abscess on follow-up.</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>24</td>
<td>960</td>
<td>19</td>
<td>Septis: <em>Candida sp.</em>, <em>Acinetobacter baumanii</em></td>
<td>Septic with hypotension</td>
<td>U/S HBS: Multiple microabscesses in the liver. (Fig. 2)</td>
<td>Most likely <em>Candida sp.</em>, <em>Acinetobacter baumanii</em></td>
<td>Several cerebral abscesses on day 36</td>
<td>IV fluocytosine for 28 days, and IV amphotericin for 28 days, IV ampicillin-sulbactam for 42 days</td>
<td>Last U/S HBS: Liver enlarged but microabscesses much less and distinct. In view of cerebral abscesses, sepsis with multiorgan failure, parents opted for withdrawal of care on day 59 and the infant died.</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>27</td>
<td>481</td>
<td>60</td>
<td>1) Septis: MRSA 2) NEC (Bell Stage I)</td>
<td>Septic with hypotension; hepatomegaly and abdominal distention</td>
<td>U/S HBS: Enlarged liver with possibly several microabscesses. (Fig. 3)</td>
<td>Most likely MRSA</td>
<td>NA</td>
<td>IV vancomycin for 29 days (expired before 6 weeks of therapy)</td>
<td>Last U/S HBS: Echogenic foci possibly microabscesses still present in mainly segment 4 of left lobe – no change in size. Died of sepsis and fulminant hepatic failure on day 76.</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>34</td>
<td>1900</td>
<td>33</td>
<td>Surgery for tracheoesophageal fistula and duodenal atresia</td>
<td>Symptomatic adhesions</td>
<td>Operative finding on laparotomy for adhesiolysis: Small liver abscesses on inferior surface of right lobe discharging into peri toneal cavity.</td>
<td><em>Candida glabrata</em>, MRSA on liver abscess culture</td>
<td>NA</td>
<td>1) Open drainage of liver abscess 2) IV amphotericin for 42 days</td>
<td>Last U/S HBS: No obvious residual/recurrent liver abscess. Discharged well.</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>25</td>
<td>740</td>
<td>9</td>
<td><em>Haemophilus influenzae</em>, <em>chorioamnionitis</em></td>
<td>Bile stained aspirate, abdominal distention</td>
<td>Abdominal X-ray showed 2 unusual gas shadows at the hepatic region. U/S HBS: Large 4.0-cm liver abscess in mainly anterior segment of right lobe and also medial segment of left lobe.</td>
<td>Unknown: Blood and liver abscess cultures negative. U/V tip: MRSE Ear swab: <em>Haemophilus influenzae</em> NPA: <em>Ureaplasma</em></td>
<td>NA</td>
<td>1) Open drainage of liver abscess 2) IV cefotaxime for 13 days, IV erythromycin for 9 days, IV metronidazole for 13 days and IV vancomycin for 5 days.</td>
<td>Last U/S HBS: Liver normal configuration and homogeneous echogenicity. This baby later developed NEC and MRSE sepsis but was eventually discharged well.</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>24</td>
<td>660</td>
<td>11</td>
<td>1) Septis: <em>Candida albicans</em>, <em>Klebsiella sp.</em>, 2) NEC (Bell Stage I)</td>
<td>Septic with hypotension, abdominal distention and acidosis</td>
<td>Chest X-ray showed right pleural effusion. U/S HBS: scattered tiny echogenic foci suspicious of liver microabscesses.</td>
<td>Most likely <em>Candida albicans</em>, <em>Klebsiella sp.</em> (on blood culture) Pleural fluid culture: <em>Candida sp.</em></td>
<td>Multiple cerebral abscesses on d7, right empyema thoracis on d10</td>
<td>IV ampicillin for 6 days, IV gentamicin for 8 days, IV cefotaxime for 5 days and IV amikacin for 4 days*</td>
<td>In view of multiple cerebral abscesses, sepsis with multiorgan failure, parents opted for withdrawal of care on day 11 and the infant died.</td>
</tr>
</tbody>
</table>

MRSA: methicillin-resistant *Staphylococcus aureus*; MRSE: methicillin-resistant *Staphylococcus epidermidis*; NEC: necrotising enterocolitis; NPA: nasopharyngeal aspirate; TPN: total parenteral nutrition; UAC: umbilical arterial catheter; U/S HBS: ultrasound of hepatobiliary system; UVC: umbilical venous catheter.

*Results of *Candida* in blood and pleural fluid cultures came back after the patient expired.*
Discussion

Possible Risk Factors

Previous reports in the literature have identified blood culture-proven sepsis, umbilical catheterisation, central parenteral nutrition catheters, necrotising enterocolitis, surgery and prematurity as risk factors for the development of neonatal pyogenic liver abscess. All these factors were found in our case series. Newborn very-low-birth-weight preterm infants are at greater risk of liver abscess due to the decreased adherence and chemotaxis of their neutrophils. In addition, they often undergo aggressive treatment such as umbilical catheterisation. Their risk is further accentuated by being nursed in neonatal intensive care units where there is increased chance of being colonised with nosocomial bacteria and by the frequent need for surgical intervention due to necrotising enterocolitis. Immunodeficiency in the form of chronic granulomatous disease has also been found to cause liver abscesses in a 15-day-old male infant with concomitant Serratia sepsis and pulmonary Aspergillosis.

Enteric organisms may reach the liver of the newborn by several pathways – via the systemic circulation, hepatic artery, portal circulation draining the gastrointestinal system or via direct invasion from contiguous structures. Another route of acquiring liver abscess in neonates is through breast milk – Guillois et al. have reported neonatal Staphylococcal sepsis, liver abscess and pleuropulmonary infection transmitted via breastfeeding when there is lymphangitis of the breast in the mother.

Clinical, Radiological and Operative Findings

While patients in previous reports commonly manifested fever, lethargy, vomiting and hepatomegaly as their major signs, the diagnosis of pyogenic liver abscess in the neonate is difficult to establish from the clinical picture alone, as the signs and symptoms are non-specific and related to sepsis. While only 3 patients were clinically septic, all the patients in our series showed at least 1 positive haematological marker of sepsis (raised total white blood cell count, raised immature: total ratio, low platelet count or raised C-reactive protein).

Liver function tests may or may not be abnormal. In our study, all of the babies had low albumin levels and 67% had at least one raised liver enzyme.

Radiologically, a combination of an elevated right hemidiaphragm, right pleural effusion and air in an abscess cavity on the abdominal radiograph may suggest the diagnosis of liver abscess in the neonate. Radiological signs were seen in only 2 neonates in our series. One neonate had a right pleural effusion on chest X-ray and another had 2 unusual gas shadows at the hepatic region.
Fig. 4. Outline of the diagnosis and management of the 6 cases of neonatal liver abscess in the case series.

Fig. 5. Recommended approach to neonatal pyogenic liver abscess based on our case series and review of the literature.
visually rectum and amebic colon. In a patient with a history of presentation of abdominal pain and fever. In our study, liver abscess was found to be the right lobe in all 3 cases. On the other hand, liver abscess can also be multiple in nature and may involve other organs as well. In our case series, 3 babies had multiple liver abscesses (microabscesses), and 2 also had co-existing cerebral abscesses and 1 had right empyema thoracis.

Pyogenic abscesses can be found in any part of the liver. The majority are found in the posterior portion of the right lobe for reasons not clearly established, but are thought to be caused by the pattern of portal venous flow. In our study, solitary liver abscess was found to involve the right lobe in all 3 cases. On the other hand, liver abscess can also be multiple in nature and may involve other organs as well. In our case series, 3 babies had multiple liver abscesses (microabscesses), and 2 also had co-existing cerebral abscesses and 1 had right empyema thoracis.

Whenever possible, liver abscess culture should be obtained for microbiologic diagnosis. The aetiological agent of neonatal pyogenic liver abscess in the literature is variable. Review of reports of neonatal pyogenic liver abscess prior to 1972 indicated that *Staphylococcus* was the most common aetiological agent. However in recent cases,9,10 gram-positive cocci like *Staphylococcus aureus*,15,22,26 methicillin-resistant *Staphylococcus aureus* (MRSA),12 coagulase-negative *Staphylococcus*,13,27 Group A *Streptococcus*,28,29 gram-negative bacilli like *Escherichia coli*,5,11,13 *Klebsiella* species,6,7 *Stenotrophomonas (Xanthomonas) maltophilia*,13 *Haemophilus paras- influenzae*,30 *Enterobacter liquefaciens*,16 *Enterobacter cloacae*,7 *Serratia* species,14 anaerobic organisms11 and fungal pathogens like *Candida* species.15 Neonatal liver abscess has also been reported in listeriosis, congenital tuberculosis and congenital syphilis.32,34 In our case series, MRSA, *Chryseobacterium gleum, Acinetobacter baumannii, Klebsiella* species and *Candida* were isolated from blood or liver abscess cultures. Compared to other case reports, there is a higher incidence of fungal liver abscesses in our study (*Candida*species was isolated in 50% of the neonates). Fungal liver abscesses usually occur in individuals with prolonged antibiotic exposure or compromised immune systems. *Candida albicans* is the most common fungal organism isolated.34

Amebic liver abscess in neonates is extremely uncommon. Recently, there have been 2 case reports in the literature of amebic liver abscess in a 3-week-old35,36 and a 20-day-old neonate.37 Although amoebiasis is endemic in tropical and subtropical countries with poor sanitation and malnutrition, industrialised countries have recently experienced an increase in the incidence of amebic liver abscess due to immigration, reduced standards of living and overcrowding.35 Amebic liver abscess presents with high fever and tender hepatomegaly. Diagnosis of amebic liver abscess requires a high index of suspicion and is confirmed with elevated indirect haemagglutination titres and ultrasonography of the liver.36

**Treatment**

Based on the classic work by Oshsner and associates in 1938, open surgical drainage of pyogenic liver abscess had been the recommended treatment. McFadzean and coworkers demonstrated some 40 years ago that percutaneous drainage by aspiration with antibiotics was a safe and effective non-surgical approach, but their results were largely disregarded until the advent of newer diagnostic imaging, when it was shown again that therapeutic percutaneous catheter drainage and/or needle aspiration was a safe and effective procedure.38 Since then, the procedures of open surgical drainage, percutaneous needle aspiration/catheter drainage have been adapted for use in neonates with liver abscess.

As the lesions of pyogenic neonatal liver abscess are often multiple and diffuse, surgical drainage is usually not possible and medical therapy is the only option.31 This is especially so in the case of diffuse pyogenic or fungal microabscesses of the liver which cannot be completely drained individually. In our case series, all 3 cases with multiple microabscesses of the liver were treated conservatively.

In single pyogenic abscesses of the liver, early recognition and prompt surgical evacuation or percutaneous drainage31 would conceivably be life-saving. In our series, of the 3 neonates with solitary liver abscess, 2 underwent open drainage with good results.

Primary surgical intervention is recommended for patients...
with abscess rupture on presentation, multiloculated abscesses, presence of biliary communication, incomplete percutaneous drainage and a known surgical pathology in the abdomen. Apart from drainage, it may be necessary to carry out surgical exploration to remove the underlying pathology. Pre-existing lesions of the liver such as cysts sometimes become infected and give rise to abscesses. Contraindications to surgery as the initial intervention include shock with multi-system organ failure and septic shock.

An alternative to surgical open drainage of liver abscess is percutaneous drainage, which offers a reduced risk compared with surgical drainage, without the need for general anaesthesia. It has been reported in adults to allow prolonged drainage for advanced abscesses and may aid more complete cavity evacuation. Relative contraindications to percutaneous drainage include coagulopathy, limited access path to the abscess cavity or the presence of a multiloculated, non-communicating abscess.

We report 1 neonate whose solitary pyogenic liver abscess was treated successfully with intravenous antibiotics alone. Successful conservative treatment of a solitary liver abscess in a premature baby was also reported by Nars et al. Whether the neonatal pyogenic abscesses are single or multiple, or whether localised to the liver or diffuse, vigorous antibiotic therapy is crucial; the specific antibiotic selection depends on the causative organism, even with drainage of the abscess. The duration of antibiotic therapy would depend on the number of abscesses, clinical response and radiographic progress and potential toxicity of the chosen regimen. It is generally accepted that the duration of antibiotic therapy for pyogenic liver abscess in childhood is between 3 and 6 weeks. It is recommended that the duration of parenteral antibiotic therapy after drainage of the liver abscess should be at least 2 weeks. In our study, 3 patients completed 6 weeks of intravenous antibiotics, 1 of whom also underwent open surgical drainage. Two other patients died before completing antibiotic treatment. The last patient was treated with a maximum of 13 days of antibiotics after surgical open drainage in view of negative blood and liver abscess cultures.

As for amoebic liver abscess, early institution of treatment with metronidazole (duration of therapy ranging from 2 to 5 weeks) and timely percutaneous aspiration of amoebic abscesses with potential for rupture have been found to obviate the need for surgery.

Follow-up

Serial ultrasounds are required to document adequate progress of therapy and resolution in neonatal liver abscess. In our study, all the patients who survived beyond 2 weeks had serial ultrasounds of the hepatobiliary system done every fortnightly on average to monitor the size of the liver abscess with treatment.

Outcome

Pyogenic neonatal liver abscess is a serious disorder. This infection remains uniformly fatal if untreated. Complications include bacteraemia and rupture of the abscess into the peritoneal cavity. In our case series, 1 neonate had a small liver abscess on the inferior surface of the right lobe discharging into peritoneal cavity, discovered incidentally at surgery for adhesiolysis, requiring open drainage and peritoneal washout. Metastatic septic emboli to the brain is another complication. Two of the neonates in our study had concomitant cerebral abscesses. Liver abscess rupturing into the pleural space can result in empyema. One infant in our study had concomitant empyema thoracis on the right side. Other rare complications reported in the literature include acute glomerulonephritis and portal vein thrombosis.

The prognosis for pyogenic liver abscess has improved dramatically due to more rapid diagnosis as a result of better radiological imaging, improvement in microbiologic identification, more effective antibiotic therapy and the development of better drainage procedures. However, when complications set in, the prognosis remains poor. In our study, mortality rate was 50%. All 3 infants who expired had multiple microabscesses of the liver. Other factors associated with mortality in our case series were extreme prematurity, extremely low birth weights and fulminant sepsis. In addition, 2 babies had concomitant cerebral abscesses and 1 infant also had right empyema thoracis.

Figure 5 shows the recommended approach to neonatal pyogenic liver abscess based on our case series and review of the literature.

Limitations

Our study was limited mainly by not having confirmatory gross or histopathological diagnosis of liver abscess and microbiological liver abscess cultures in 4 neonates. In 1 neonate, the liver abscess was treated successfully with conservative management. In the 3 neonates who expired, the parents declined postmortem examination because of religious reasons.

Conclusion

In conclusion, neonatal pyogenic liver abscess is rare; if untreated, the outcome remains uniformly fatal. However, good outcome is possible with prompt diagnosis and the institution of appropriate treatment. A strong index of suspicion for neonatal liver abscess is required if there is persistence of positive blood culture despite appropriate antibiotic treatment. Ultrasound of the hepatobiliary system
is a good bedside diagnostic tool for diagnosing neonatal liver abscess. Serial ultrasounds are also useful for monitoring the progress of therapy and to document resolution of the liver abscess.

REFERENCES


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