

LIVER ABSCESS IN CHILDREN: A REVIEW OF CASES AT PHILIPPINE GENERAL HOSPITAL

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ABSTRACT

A review of pediatric liver abscesses during a 7 yr. period (Jan. 1987-July 1994) at UP-PGH was done. Twenty five out of 45 cases were available for review. Mean age was 6.35 years with a M:F ratio of 2:1. Most common symptoms were fever (84%) and abdominal pain (72%). Other prominent symptoms were anorexia (52%), abdominal distention (52%), diarrhea (40%), weight loss (36%). High grade fever, RUQ tenderness, hepatomegaly, mass, anemia, were the most common signs. Normal were prothrombin time in 60% and total bilirubin (mean = 20.72 $\mu\text{mol/L}$) in 30%. Alkaline phosphatase (mean = 150.61 U/L) in 59% and ALT (mean = 26 U/L) in 61% were elevated. Eighty percent were diagnosed by ultrasonography. Solitary abscess was found in 65%. Of the 10 single isolates from the liver aspirates, 9 (90%) were *Staphylococcus*, 1 (10%) *E. coli*. Two cases were mixed isolates: *Pseudomonas aeruginosa* and *Salmonella* group C, *Proteus retigeris* and *E. coli*. Treatment was by ultrasound-guided aspiration (88%), exploratory laparotomy with debridement and drainage (12%) combined with broad-spectrum antibiotics for 4-6 weeks, 36% were on medical therapy alone. Eighty percent were discharged improved with an ave. length of hospitalization of 3.4 weeks. There were 4 mortalities, 3 were diagnosed only at autopsy while 1 died due to multiple liver abscesses, perinephric abscess, pericardial effusion.

INTRODUCTION

Liver abscess in children is generally regarded as an uncommon condition¹ but it is a life-threatening disease.^{2,3} Manalo in 1992 at Philippine General Hospital showed that there were only 9 pediatric cases with liver abscess out of a total of 87 diagnosed cases, adults and children combined, between 1985-1991.⁴ No other recent series on Filipino pediatric cases with liver abscess has been published. In 1978, in a study by Chusid, this condition was shown to occur in about 3 per 100,000 hospital admissions at Milwaukee Children's Hospital between 1977-1987.⁵ In Philippine General Hospital and in other hospitals, its actual incidence has not been determined.

Presenting symptoms may be minimal and lack specificity,⁶ but frequently include fever, nausea, vomiting, weakness, fatigue, weight loss, and abdominal

pain.⁷ Because of its impact on morbidity, prompt diagnosis and treatment is necessary.² The most important factor, therefore, in making the diagnosis of liver abscess is a high index of suspicion. This is brought about only if there is an awareness and knowledge of this illness.⁴ Hence, this study was done to present the clinical manifestations, methods of diagnostic procedures used, etiologic agents, management, and outcome of liver abscess affecting pediatric patients at Philippine General Hospital.

MATERIALS AND METHODS

This study is retrospective and descriptive in design. It involves the review of records of all diagnosed cases of liver abscess in children 18 years old and below, whether solitary or multiple, pyogenic or amebic, and who were admitted to Philippine General Hospital from January 1987 and July 1994. The diagnosis of liver abscess was confirmed either on ultrasonography or on exploratory laparotomy. Those diagnosed at autopsy were also included in the study. The historical records and physical examination findings of all these patients were reviewed as to initial symptoms and clinical signs. Laboratory data, imaging studies, and results of treatment were also obtained. Complications of the disease were also noted.

RESULTS

There were 45 cases of liver abscess admitted during the 7 year period between January 1987 and July 1994, of which, 6 cases were diagnosed only by autopsy. Only 25 charts, however, were available for review.

Clinical Features

Mean age of the patients was 6.35 years (range, 3 days to 18 years), with majority (48%) occurring in those who were 3 years and below. There were 17 males (68%) and 8 females (32%) with a male to female ratio 2:1. More than half of the subjects (56%) were of normal nutritional status. Only 20% were mildly wasted, while one was moderately wasted and another was severely wasted. For the rest of the 4 subjects, their nutritional status were not assessed.

The presenting symptoms and physical examination findings in Table 1 were noted at a mean duration of

6.35 weeks (range, 2 days to 5 months) before admission. High grade fever ($> 39^{\circ}\text{C}$), abdominal pain, abdominal distention, anorexia, and diarrhea were the most common presenting symptoms, while the most common presenting signs were fever ($\geq 39^{\circ}\text{C}$), RUQ tenderness, hepatomegaly, and abdominal mass.

Diagnostic Procedures

• Radiologic Imaging

Non-invasive imaging studies using ultrasonography were done on 20 (80%) patients on admission. Abscess of the liver was identified in all

Table 1. Presenting Symptoms and Signs

SYMPTOMS	NO.	%	SIGNS	NO.	%
Fever	21	84	Temp. $\geq 39^{\circ}\text{C}$	21	84
Abdominal pain	18	72	Tenderness (RUQ)	19	76
Abdominal distention	13	52	Hepatomegaly	18	72
Anorexia	13	52	Mass	12	48
Diarrhea/Dysentery	10	40	Anemia	10	40
Weight loss	9	36	Jaundice	8	32
Chest pain	2	8	Splenomegaly	1	4
Edema	2	8			

Laboratory Results

Eighteen patients (72%) had leucocytosis ($\geq 10,000$) with a mean of $17.7 \times 10^9/\text{L}$ with neutrophilia in 71%. Hemoglobin was less than 120 g/L (mean, 98 g/L) in 84%. Total protein (mean, 53.67 g/L) was normal in about half (53%) of the patients. Hypoalbuminemia (mean, 28.04 g/L) was noted in 68%. Serum globulin (mean, 28.04 g/L) was elevated in 53%. Since the subjects were all growing children, serum alkaline phosphatase levels were expected to be higher, thus, the reference values from Nelson's Textbook of Pediatrics of 20-150 U/L was used.⁸ However, despite the higher reference value for alkaline phosphatase level, it was noted to be elevated in 59% (mean, 150.61 U/L). Liver transaminases, ALT (mean, 26.00 U/L) was elevated in 61% while AST (mean, 40.75 U/L) was normal in 77%. Total bilirubin (mean, 20.72 $\mu\text{mol/L}$) was normal in 70%. These results are presented in Table 2. Prothrombin time was normal in 60% of patients. Amebic titers were done in only 2 patients and these were both negative.

Table 2. Laboratory Findings at Presentation

LABORATORY FINDINGS	MEAN	STANDARD DEVIATION
Hemoglobin (g/L)	98	26.47
WBC (10×10^9)	17.7	9.89
Segmenters (%)	65	22.23
Total Protein (g/L)	53.67	36.86
Serum Albumin (g/L)	28.04	16.59
Serum Globulin (g/L)	28.06	20.97
Alkaline Phosphatase (U/L)	150.61	101.43
Aspartate Aminotransferase (U/L)	40.75	40.49
Alanine Aminotransferase (U/L)	26	18.62
Total Bilirubin ($\mu\text{mol/L}$)	20.72	40.13
Direct Bilirubin ($\mu\text{mol/L}$)	6.52	9.53
Indirect Bilirubin ($\mu\text{mol/L}$)	37.31	120.14

20 patients (sensitivity, 100%). No computed tomography was done (Table 3). In the 5 patients where no ultrasonography was done, 2 were diagnosed by exploratory laparotomy because one presented with acute surgical abdomen while the other was suspected of having post-operative complications from a previous abdominal surgery for liver trauma. The other 3 were diagnosed on autopsy.

The right lobe of the liver was involved in 70% while the left lobe in 18%. Both lobes of the liver were affected in 12%. Majority (65%) were solitary abscesses while about 35% were multiple (Table 4).

Table 3. Diagnostic Procedures

PROCEDURE	NO.	%
Ultrasonography	20	80
Exploratory Laparotomy	2	8
Autopsy	3	12

Table 4. Lobe Involvement and No. of Abscesses

LOBE INVOLVEMENT	NO.	%
Right	12	70
Left	3	18
Both	2	12
NO. of ABSCESSSES	NO.	%
Single	13	65
Multiple	7	35

• Bacteriologic Studies

Drainage of the liver abscess, either by ultrasound-guided percutaneous aspiration or on exploratory laparotomy was done in 16 cases (64%). Fourteen (88%) out of the 16 cases underwent ultrasound-guided percutaneous aspiration, while the other 2 cases (12%) were drained during exploratory laparotomy. In 9 cases (36%), no drainage nor aspiration was done. Gram staining was done in 14 cases out of 16 patients.

All aspirates were sent for bacteriologic studies; out of which, 12 cases (75%) had positive yield, while 4 cases (25%) were negative. Ten single isolates (83%) with 2 mixed isolates (17%) were obtained. The single isolates were *E. coli* (10%), *S. epidermidis* (20%), *S. aureus* (70%). In 2 cases, mixed organisms were isolated and these were *P. aeruginosa* and *Salmonella group C* while another was *Proteus retigeris* and *E. coli* (Table 5).

Table 5. Organisms Isolated from Liver Aspirates

ORGANISMS	NO.	%
Single Isolates	10	83
<i>S. epidermidis</i>	2	
<i>S. aureus</i>	7	
<i>E. coli</i>	1	
Mixed Isolates	2	17
<i>P. aeruginosa</i> and <i>Salmonella group C</i>	1	
<i>Proteus retigeris</i> and <i>E. coli</i>	1	

Blood cultures were done in only 13 cases (59%). Out of 25, there were 7 (44%) positive cases while 6 cases (46%) were negative. No blood cultures were done on the rest of the 12 cases (Table 6).

Out of the 7 positive blood cultures, 5 (71%) were single isolates and 2 (29%) were mixed (Table 7).

Table 6. Yield of Abscess Aspirate and Blood Culture

CULTURES	NO.
Abscess (+) Blood (+)	2
Abscess (+) Blood (-)	3
Abscess (+) Blood not Cultured	7
Abscess (-) Blood (+)	2
Abscess (-) Blood (-)	1
Abscess (-) Blood not Cultured	1
Abscess not aspirated Blood (+)	3
Abscess not aspirated Blood (-)	2
Abscess and blood not cultured	4
TOTAL	25

Only in one case was there concordance in the blood and abscess cultures wherein *Salmonella group C* was obtained. In the rest of the cases, the isolates of the blood cultures were different from the organisms isolated from cultures of aspirates.

Table 7. Organisms Isolated from Blood

ORGANISMS	NO.	%
Single Isolates	5	71
Diphtheria sp.	1	
<i>Salmonella group C</i>	1	
<i>S. aureus</i>	1	
<i>K. pneumoniae</i>	1	
<i>P. aeruginosa</i>	1	
Mixed Isolates	2	29
<i>Achromobacter</i> , <i>Proteus</i> <i>mirabilis</i> , and <i>S. saprophyticus</i>	1	
<i>Klebsiella sp.</i> and <i>P. putida</i>	1	

Table 8. Drainage Procedures

PROCEDURE	NO.	%
Drainage	16	64
Ultrasound-guided percutaneous aspiration	14	
Exploratory Laparotomy with debridement and drainage	2	
No Drainage	9	36

Treatment

Antibiotic coverage plus drainage of the abscess cavity was done in 16 (64%) out of 25. Nine cases (36%) out of 25 had pure medical therapy (Table 8).

Empirically, all cases were started on broad-spectrum parenteral antibiotic therapy to treat for aerobic and anaerobic bacteria and for a possible amebic abscess. The usual drugs were Oxacillin at 100-200 mg/kg/day, Gentamicin or another Aminoglycoside at 5-7 mg/kg/day, and Metronidazole at 30-50 mg/kg/day. Triple antibiotic coverage was given in 17 cases (68%) out of 25, double antibiotic coverage in 4 cases (16%) out of 25, and single antibiotic coverage in 1 case (4%) out of 25. Three (12%) were covered with quadruple antibiotics such as in the following combinations: Oxacillin, Gentamicin, Metronidazole, and Chloramphenicol; Oxacillin, Gentamicin, Metronidazole, and Ceftazidime; and also Oxacillin, Gentamicin, Metronidazole, and Ampicillin.

At the time of confirmed diagnosis, based on

ultrasonography, gram-staining results and yield of cultures from liver aspirates, 4 cases (40%) were positive for *Staphylococcus*. They were given monotherapy using Oxacillin until discharged. For the other cases, the initial drugs started were continued despite culture results. These drugs were usually given for several weeks, with a mean duration of 2.9 weeks (range, 4 days-5 weeks).

Outcome of Patients

Out of the 25 cases, there were 4 mortalities (16%). Three were diagnosed only at autopsy with liver abscess not entertained on admission. These were: a 4-month old male with severe bronchopneumonia and malnutrition, a 2-month old male with suspected sepsis and lastly, a 6-day old male with necrotizing enterocolitis Stage 1B with sepsis. The fourth mortality was a case who died of septic shock due to multiple liver abscesses with complications of pericardial effusion and perinephric abscess. The rest were discharged either as cured or improved. Cured were 9 (36%) when there was absence of fever, abdominal pain, and other signs and symptoms with resolution of the abscess cavity on repeat ultrasonography. Improved were 11 (44%) who showed on repeat ultrasonography a decrease in the size of the abscess cavity and absence of signs and symptoms. Repeat ultrasonography was done usually after a mean of 1.9 weeks from the first ultrasonography. The mean length of hospital stay was 3.4 weeks (Table 9).

Ten complications were noted from the cases of liver abscess reviewed. Common were pleural effusion, perinephric abscess, and abdominal muscular wall abscess (Table 10).

Table 10. Complications from Liver Abscess

COMPLICATIONS	NO.
Pleural effusion and Right Retroperitoneal Abscess	1
Pleural effusion and Subdiaphragmatic Abscess	2
Subdiaphragmatic Abscess	1
Abdominal Muscular Wall Abscess	1
Pericardial Effusion and Pleural Effusion	1
Perinephric Abscess	2
Pleural Effusion	1

DISCUSSION

In infancy and childhood, pyogenic hepatic abscess is predominantly a lesion of the first 5 years of life.⁹ Almost half of the patients (48%) in this series fall into this age group. Moreover, in our study, 68% of hepatic abscess affected boys. This is the same as in other studies done by Dehner and Kissane⁹ and also by Oschner and associates¹⁰, wherein boys were affected in 59% and 67% of cases, respectively. This is also consistent with Manalo's study in 1989 at University of the Philippines-Philippine General Hospital in which the male to female ratio was 3:1.⁴ Similar studies involving adult patients also showed predominance of males being affected with the disease.⁴

Among the important symptoms, fever associated with right upper quadrant (RUQ) abdominal pain were most commonly observed while severe systemic manifestations were less frequent. Consistent clinical signs were high fever, hepatomegaly, and RUQ tenderness. These findings have also been observed in studies by other workers.^{1,3,6,9,11} Jaundice was mild or absent. Patients usually present with a prodrome of symptoms lasting several weeks. In one study, symptoms were present for approximately 2 weeks.⁶ In our study, the symptoms of the majority of the patients were present for approximately 6 weeks prior to consult. This is probably because of the insidious onset and the non-specific signs and symptoms of this disease.¹¹

The laboratory findings were of limited value. The common observations were anemia and leucocytosis with neutrophilia (shift to the left).^{1,3,4,6,11} Moreover, hypoalbuminemia was commonly observed among the patients with hepatic abscess even if they were of normal nutritional status. In patients with symptoms of long duration, such as liver abscess, hypoalbuminemia is a frequent feature.¹¹ Another observation was that liver enzymes, ALT and AST, were elevated. Alkaline phosphatase levels were also elevated to about twice the normal value for growing children.⁸ According to Silverman and Roy, there are non-specific alterations in

Table 9. Outcome of Patients

OUTCOME	NO.	%
Cured Absence of cavity	9	36
Improved Decrease in the size of cavity	11	44
Died	4	16
Unknown	1	4

liver function that occur in 1/2 of cases including mild elevation of transaminases, serum alkaline phosphatase or gamma glutamyl transpeptidases.¹¹ Elevated liver enzymes indicate both parenchymal and cholestatic involvement.³ In another study, abnormalities of liver enzymes, particularly alkaline phosphatase were invariably present.⁶ Prothrombin time was normal in the majority of cases. Anemia, leucocytosis with granulocytosis, hypoalbuminemia, elevated serum globulin and serum alkaline phosphatase are characteristics of pyogenic liver abscess¹² and these are consistent with the findings in our study.

Ultrasonography was found to be very sensitive in identifying liver abscess. In our study, the sensitivity of the procedure was 100%. It is not only non-invasive but also accurate in localizing the site for aspiration of the abscess with no radiation exposure to the patient. It has an added value in following the course of the disease after treatment. According to one study, ultrasonography is the preferred initial diagnostic test.^{1,6} It is cost effective and remarkably accurate. Ultrasonography can help in distinguishing pyogenic from amebic abscess. The former often appear hypochoic with irregular margins, while the latter are more homogeneous, oval or round, with well defined margins.⁶ Aside from ultrasound, computed tomography (CT scan) was also noted to be very sensitive to the abnormality (100%).^{2,10} In our study, no CT scan was done.

The right lobe the liver was most commonly involved and single abscesses were more common in this study. According to Silverman and Roy, the right lobe of the liver is the site of amebic abscess in over 90% of their cases.¹¹ In our series, all cases were pyogenic abscesses and the right lobe was most commonly involved. This was also observed by other workers.^{1,4}

Pyogenic abscess of the liver is more common in the West while amebic liver abscess in the tropical and subtropical countries.¹ However, our study showed that pyogenic hepatic abscess is common in the tropical countries like the Philippines. No amebic abscesses were found, although, no cultures nor amebic titers were obtained except in 2 patients which were both negative. The indirect hemagglutination assay has been the mainstay of serologic diagnosis for many years.¹¹

On microbiologic evaluation, abscess cultures were found to yield a positive result in 75% of cases, whereas blood cultures in 44% of cases. However, organisms isolated from blood were not the same organisms seen from the abscess. Aspirates of the abscess cavity are more accurate than blood cultures in identifying the bacteria involved.⁶ Many patients do not have bacteremia, and in those with bacteremia, many of the underlying abscess pathogens will not be present in the blood.⁶

Microbiologic analysis of hepatic abscess in our study suggested that the most frequently encountered organisms are the Staphylococcus species, especially S. aureus (58%) and S. epidermidis (16%). Additional pathogens include E. coli (16%), P. aeruginosa (8%), Salmonella gr. C (8%) and Proteus retigeris (8%). Staph. aureus remains the single most common cause of pyogenic liver abscess.^{2,4,9} However, in many parts of the world, amebic abscess is a far more frequent diagnosis than pyogenic liver abscess.² The presence of an elevated amebic antibody titer in the setting of a hepatic abscess is diagnostic of an amebic etiology.

Initial conservative management with combination of broad-spectrum antibiotics plus Metronidazole were tried in all cases. When hepatic abscess was documented by ultrasonography, drainage of the abscess was done. Antibiotics, as well as, Metronidazole were continued for 2 weeks or more in the hospital. However, even when the responsible organisms causing the abscess were identified, either by gram-staining or by culture, the majority of the patients were treated continuously with the regimen initially started.

Only 4 patients with Staphylococcus aureus on culture were given monotherapy using Oxacillin. Even if blood cultures were not accurate in identifying the causative bacteria, parenteral antibiotic therapy should be continued until the patient is afebrile, asymptomatic, and without leucocytosis for at least 48 hours.⁶ The majority of our patients were treated with oral antibiotics for an additional 2 weeks.

However, antibiotic therapy is believed to be merely adjunctive to drainage of the abscess. In 1953, there was already a report describing patients successfully treated with diagnostic aspiration and antibiotics without drainage.⁶ These reports went relatively unheeded; open surgical drainage continued. As recently as 1990, open surgical drainage continued to be advocated.⁶ In our retrospective review of hepatic abscess, the patients benefited much from aspiration of the abscess percutaneously and antibiotic therapy so that from 25 cases, 20 cases (80%) were discharged as cured or as improved. Percutaneous aspiration with concomitant drainage should be used as a primary modality of treatment whenever possible because it has proven to be superior to aspiration alone.¹⁵

The complications that were noted were mostly pleural effusion, perinephric abscess and subdiaphragmatic abscesses which eventually resolved with antibiotic coverage except for one mortality who had multiple liver abscesses who later developed pericardial effusion and pleural effusion. Out of the 25 cases, 21 cases improved as evidenced by the absence of fever as early as 3 days of antibiotic therapy alone and who later became asymptomatic. Likewise, on repeat ultrasonography, there was resolution of the abscess or a decrease in the size of the abscess cavity.

These patients were discharged after a mean of 3.4 weeks of hospitalization. This was similar to the study by Stain, et. al., in which the mean duration of hospital stay was 23 days (range, 6-49 days).

Continuous improvement in diagnosis and treatment has significantly decreased the mortality of liver abscess from as high as 80% before 1965 to 16-48% in the 1970's.⁷ Much of the mortality is attributable to patients with severe underlying disease. In our study, 4 cases (16%) died and indeed had severe underlying disease like severe bronchopneumonia, malnutrition, necrotizing enterocolitis. Since hepatic abscess in the neonatal period is a rare but serious disorder,¹⁴ this condition is usually diagnosed at autopsy.¹⁴ In neonates, organisms are acquired through virtually any orifice but there is a special risk of liver infection along the portal vein through the umbilical vein.¹⁴ Since the liver is a highly vascular organ and is most vulnerable to hematogeneously disseminated infection,¹⁴ liver abscess is therefore an expected problem.

CONCLUSION

Indeed, liver abscess is a serious clinical problem. In addition to producing signs and symptoms of systemic infection, it can directly lead to death. However, contributing to the mortality is the nature of the underlying disease but this information was lacking in this research. From our results, we conclude that liver abscess in children is most commonly due to Staphylococcus species, especially Staphylococcus aureus and is therefore amenable to antibiotics, like oxacillin. However, not enough studies were done to determine etiologic agents of liver abscess in children because anaerobic as well as amebic cultures were lacking.

Among the many possible diagnostic approaches, ultrasonography has proven remarkably sensitive in the localization of lesions.

We also conclude that the etiologic organisms are oftentimes difficult to eradicate in their lush environment so that it is vital to resort to drainage when the lesions are sufficiently large and not too numerous.

SUMMARY AND RECOMMENDATION

Pyogenic liver abscess should be suspected especially in a child 5 years old and below with unexplained, persistent high grade fever, and abdominal pain especially at the right upper quadrant. If a cystic cavity is found within the liver parenchyma by ultrasonography or by computed tomography scan, aspiration of the lesion should be considered to confirm the diagnosis. Laboratory findings such as leucocytosis with predominant shift to the left, anemia, and altered liver function tests will help point to a possible liver

abscess. Microscopic examination of the aspirate with culture immediately after aspiration seems to be an excellent technique for identification of the causative organism. The most frequently encountered organism is Staphylococcus aureus. Excellent results can be expected if an early diagnosis is made with prompt drainage of the abscess and precise antibiotic therapy. The optimal duration of parenteral antibiotic therapy is not known, but most authors recommend 4-6 weeks. Careful attention should also be given to the isolation of anaerobic organisms from the cystic cavity of the liver. Amebic abscess is another important diagnosis to exclude using the immunofluorescent antibody titers for *E. histolytica*. Early diagnosis before onset of complications can affect outcome significantly and shortens the duration of stay in the hospital.

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