Pediatric Hepatic Abscess: A Ten-year Review of the Features and Outcome at the Philippine General Hospital

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ABSTRACT

Objective. Hepatic abscess is a rare childhood infection with incidence of 1 to 140 per 10^5 admissions. It has signs and symptoms that mimic other liver diseases. This study determined the clinical, biochemical, microbiologic and imaging features and outcome of children diagnosed with hepatic abscess at a tertiary hospital in Manila.

Method. We conducted a review of medical records of admitted patients aged ≤18 years diagnosed with hepatic abscess in a tertiary referral center from 2007–2018. A diagnosis was confirmed if with (1) fever; (2) imaging study of solitary or multiple hepatic focus; AND (3) at least one more sign or symptom. We computed for mean (SD) for continuous variables or n (%) for categorical variables.

Result. We included 40 patients out of 559, 583 pediatric admissions during the study period (0.007%), with a mean age of 8 years (SD 6.5), and 57% of whom were males. Thirty-seven (92%) were probable pyogenic in etiology, while three were tuberculous abscess. The most common signs and symptoms were fever (100%), abdominal mass (31%), abdominal distension (34%) and weight loss (31%). Majority had anemia (63%) and leukocytosis (89%). The most common imaging finding was a solitary mass (58%) with right lobe (80%) involvement. Nine abscess aspirates yielded *Staphylococcus aureus* (3), *Mycobacterium tuberculosis* (3), *Klebsiella pneumoniae* (1) and no growth (2). All patients were medically treated but eight also required percutaneous/surgical drainage. Majority (36) were discharged improved; four were improving but left before treatment completion.

Conclusion. Majority had pyogenic hepatic abscess, presenting with non-specific clinical and laboratory features. Most abscess were solitary and involved the right lobe. Limited abscess aspirates yielded *Staphylococcus aureus* and *Mycobacterium tuberculosis*. Prognosis is favorable with treatment.

Keywords: pyogenic liver abscess, tuberculous liver abscess, solitary hepatic mass, childhood hepatic abscess

INTRODUCTION

Hepatic abscess is a collection of purulent material in the liver parenchyma which may be secondary to a bacterial, parasitic, fungal or a mixed infection. It is potentially a life-threatening condition with pyogenic liver abscess constituting 80% of cases in children.[1,2] The disease has varied prevalence in different countries depending on the economic condition. In developed countries, it has been reported at three to 28 per 100, 000 pediatric admissions in studies done in USA, Denmark and Taiwan.[3-5] In developing countries, the prevalence is reported at 1 in 140 admissions (Brazil) and 79 per 100 000 admissions in children <12 years (India).[6,7] A review of the Philippine Pediatric Society 15-year registry of diseases (2006 to May 2021) revealed a total of 358 (0.00007%) cases of hepatic abscess out of 4,764,910

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entries, but the etiology was not reported. Local studies showed 25 cases over seven years both in our institution and 25 cases in 5 years in another children's hospital, which are both tertiary referral centers.[8,9] We decided to do this study as the previous report on pediatric hepatic abscess in our institution was done 25 years ago and it was deemed to have a serious risk of bias as only 55% of the medical records of the patients during the seven- year study period was available for review. Newer modalities in the diagnosis and treatment of hepatic abscess have also evolved.

Hepatic abscess is suspected in any child presenting with nonspecific signs and symptoms of right upper quadrant pain, fever and hepatomegaly and supported by the presence of leukocytosis, anemia, elevated transaminases and hypoalbuminemia.[8] The diagnosis is usually confirmed by imaging studies, either an ultrasound or a computer tomography (CT) scan of the liver and hepatobiliary tree. In abscesses more than 5 cm, aspiration of the lesion is done, and microbiologic studies may isolate the causative agent.

In children, signs and symptoms of hepatic abscess may mimic other chronic liver disease such as hepatitis, hepatic tumors, and biliary disorders such as cholecystitis and cholelithiasis. The objective of this paper is to present the clinical, biochemical, microbiologic, and imaging features and outcome of pediatric patients diagnosed with hepatic abscess at the Philippine General Hospital (PGH). Knowledge of this information will guide the physician in making a prompt diagnosis and initiating rationale empiric antibiotic treatment.

METHODS

This is a retrospective cohort study done among pediatric patients less than 18 years old admitted at the PGH, a tertiary referral center, from January 2007 to December 2018 with a final diagnosis of hepatic abscess. Approval from the University of the Philippines Manila Research Ethics Board was obtained before the conduct of the study and confidentiality was observed during the study period.

The names of the patients were obtained from the monthly census of the Divisions of Pediatric Gastroenterology, Hepatology and Nutrition; Infectious and Tropical Pediatrics and Diseases; and Pediatric Surgery. We reviewed the medical records of these patients. Those who fulfilled the following inclusion criteria were included in this study: presence of fever (temperature > 37.8°C), radiologic findings showing a solitary or multiple focus in the liver suggestive of an abscess AND at least: (1) one of the following symptoms (abdominal pain, abdominal distention, anorexia, weight loss, vomiting); OR (2) one of the following signs (right upper quadrant tenderness, hepatomegaly, abdominal mass, jaundice, ascites).[8,10,11] Patients who did not fulfill the inclusion criteria were excluded.

The patient's age, gender and nutritional status based on WHO criteria were noted.[12] A detailed account of the patient's onset of symptoms and the presence or absence of fever (temperature >37.8°C), jaundice, abdominal pain, abdominal distension and right upper quadrant tenderness was recorded. We also noted comorbidities of the patient and the presence of any of the reported predisposing factors that may cause hepatic abscess such as malignancy, diabetes, chronic granulomatous disorder, blunt trauma and malnutrition.[3,7] Information as to the patient's nutritional status and physical examination were documented with emphasis on the liver size and consistency, presence of superficial veins, ascites and splenomegaly. Results of the complete blood count, liver function tests, microbiologic cultures and imaging studies were verified. All blood cultures were taken before empiric antibiotic was initiated. Medical and or surgical interventions that were done and patient outcomes (improved, died) were documented. We considered patients to have a pyogenic liver abscess even without a bacterial isolate from the mass if there was a therapeutic response to antibiotic treatment. An improvement was considered in the absence of any signs and symptoms and a decrease or resolution in the size of the abscess on ultrasound.

All patients were comanaged with the Division of Infectious and Tropical Pediatrics of the department. Patients suspected with hepatic abscess were started on empiric broad spectrum amikacin and metronidazole and either oxacillin, cefuroxime or cefoxitin. All necessary blood tests including blood culture were done before starting treatment.

Data were analyzed using means and standard deviations for continuous data and described as frequencies (percentages) for categorical type.

RESULTS

During an 11 year period, 43 children had a final diagnosis of hepatic abscess out of 559, 583 (0.7%) pediatric admissions, giving an estimated prevalence of 7 to 8 per 10^5 admission in our institution. Of the 43, only 40 medical records were available for review. Table 1 presents the clinical features of the patient. The mean age of the patients was 8 (± 6.5) years. Forty two percent were less than five years and another 28% between 16 to 18 years. The youngest patient was a three-month-old who developed limb ischemia and *Acinetobacter baumannii* septicemia and during the course of illness, presented with fever and hepatomegaly. There was a slight male predominance (58%). Fever (100%) and presence of abdominal mass (30%) were the most common signs. Abdominal distension (32%) and weight loss (30%) were the most common symptoms. Eleven (28%) patients had co morbidities including pneumonia in six, intestinal parasitism in 4 and pulmonary tuberculosis in one. Anemia and leukocytosis were seen in the majority of cases (Table 2).

Imaging studies. Ultrasound examination was done in all patients (Table 3) and confirmed the diagnosis in 33 (83%) patients. In most cases, the abscess presented as a

Table 1. Demographic and clinical features of 40 children diagnosed with hepatic abscess

Features	n (%)
Mean (SD) age (years)	8 (± 6.5)
Age (years)	
<1	4 (10)
1–5	13 (32)
6–10	6 (15)
11–15	6 (15)
16–18	11 (28)
Males	23 (58)
Nutritional Status (WHO)	
No wasting	25 (62)
Moderate to severe wasting	15 (38)
Co-morbidities	
Pneumonia	6 (15)
Intestinal parasitism	4 (10)
Pulmonary tuberculosis	1 (2)
Signs	
Fever	40 (100)
Palpable abdominal mass	12 (30)
Right upper quadrant tenderness	9 (22)
Jaundice	6 (15)
Hepatomegaly	4 (10)
Ascites	5 (13)
Symptoms	
Abdominal distention	13 (32)
Weight loss	12 (30)
Vomiting	7 (18)
Anorexia	6 (15)
Abdominal pain	3 (8)

Table 2. Laboratory findings of 40 children with hepatic abscess

Findings	n (%)
Anemia (< 120 g/dl)	23 (58)
Leukocytosis (> 10,000/mm^3)	34 (85)
Hypoalbuminemia (< 35 g/dl)	12 (30)
Elevated Total Bilirubin (0.2–1.3 mg/dL)	7 (18)
Elevated Alkaline phosphatase (> 350U/L; > 126 U/L older children)	8 (20)
Elevated Aspartate aminotransferase (> 59 U/L)	1 (3)

Table 3. Imaging findings of 40 children diagnosed with hepatic abscess

		Ultrasound (n=40)	Computer Tomography (n=7)
Lobe	Left	8 (20)	2
	Right	19 (48)	3
	Both	13 (32)	2
Abscess form	Solitary	23 (58)	3
	Multiple	17 (42)	4

Table 4. Microbiologic growth of 40 children with hepatic abscess based on blood culture and hepatic abscess aspirate

Blood Culture (n=40)	n (%)
Staphylococcus epidermidis	1 (2.5)
Serratia marcescens	1 (2.5)
Klebsiella pneumoniae	1 (2.5)
Methicillin resistant *Staphylococcus aureus*	1 (2.5)
Acinetobacter baumannii	1 (2.5)
No growth	35 (87.5)
Hepatic Abscess Culture	**n (%)**
Percutaneous drainage (n=6)	
Methicillin resistant *Staphylococcus aureus*	2 (5)
Mycobacterium tuberculosis	2 (5)
Klebsiella pneumoniae	1 (2.5)
No growth	1 (2.5)
Open Surgical Drainage (n=3)	
Methicillin resistant *Staphylococcus aureus*	1 (2.5)
Mycobacterium tuberculosis	1 (2.5)
No growth	1 (2.5)

solitary mass (58%). Right lobe involvement was noted in 32 (80%) patients, either solely or with the left lobe.

Seven patients also underwent abdominal CT scan for the following indications: in three cases, the ultrasound description was an intraabdominal tumor but was a hepatic abscess on CT scan; in two, to further define the multiple hypoechoic foci located at segments V, VI and VIII that were seen on ultrasound, with the CT scan (Figure 1) demonstrating thickened intestinal bowel loops with mediastinal lymphadenopathy, indicative of intraabdominal tuberculosis; and in two, a CT scan was requested due to presence of peritoneal involvement on physical examination and confirmed to have hepatic abscess with rupture into the abdominal cavity (Figure 2).

Microbiologic studies. Of the 40 patients, only five (12%) had positive blood cultures (Table 4) and no anaerobic cultures were done. No test was done for amoebic infection. Nine liver abscess aspirates were performed in eight patients to which three were methicillin resistant *Staphylococcus aureus*, three grew *Mycobacterium tuberculosis*, one *Klebsiella pneumoniae* and two had no growth. Overall, 37 (92%) were considered to have a possible pyogenic liver abscess and three had tuberculous hepatic abscess.

Treatment

Medical. All patients were started on empiric amikacin (15mg/kg/day) and metronidazole (30mg/kg/day). A third antimicrobial was also started depending on the possible

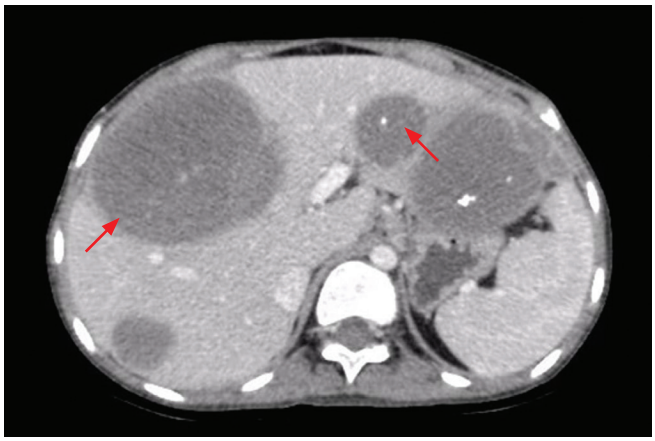

Figure 1. Computer tomography scan showing multiple hypodense peripherally enhancing foci with some calcifications at segments VIII and II.

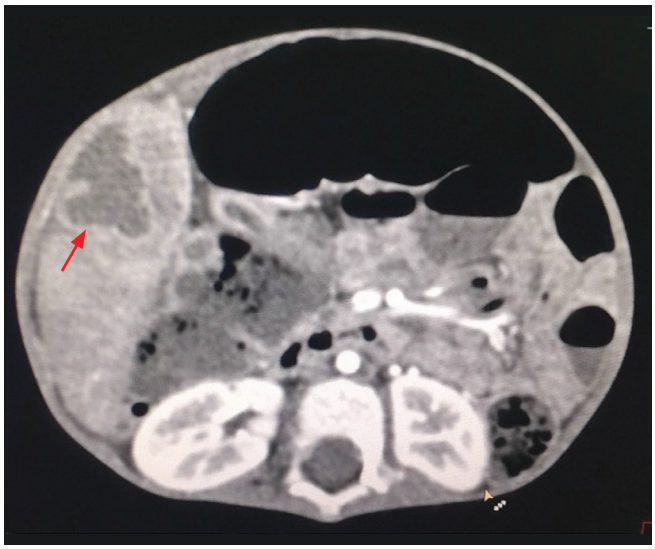

Figure 2. Computer tomography scan showing several rim enhancing hypodense lesions scattered in the right lobe especially at the peripheral and subcapsular regions with area of cluster measuring 2.9 x 1.8 x 2.6 cm noted segment IV with surrounding hypo attenuation, likely representing edema.

source of abscess either on oxacillin (23 patients), cefuroxime (nine patients) or cefoxitin (eight patients). Of the 40, sixteen patients were shifted to another antibiotic after 7 to 14 days when no clinical improvement was observed, guided by the blood culture results. These antibiotics consisted of meropenem (five patients), cefuroxime (four) ceftriaxone (three) and clindamycin (four). Two patients on clindamycin were eventually shifted to meropenem due to skin rash and dyspnea attributed to the drug. The duration of treatment for pyogenic liver abscess was a mean of 5 weeks (SD 2.16) (range, 3 to 12).

The three patients with hepatic abscess secondary to tuberculosis were treated with quadruple anti-Koch's medications for six months when the diagnosis of TB was confirmed and responded well to treatment.

Surgical. A total of nine cases (eight patients) required abscess drainage. In six, these were done percutaneously as there was persistence of febrile episodes after 7 to 14 days of intravenous antibiotics and no noted regression of hepatic abscess on repeat ultrasound. Five of these patients eventually had amelioration of symptoms and decrease in abscess size while one, a 12-year-old boy had persistence of fever and abdominal pain with increase in abscess size from 5 to 6.5 cm on ultrasound, thus, he underwent an open surgical drainage. The culture of the abscess drained percutaneously grew *Klebsiella pneumoniae* but the one aspirated during surgery yielded *Mycobacterium tuberculosis.* He responded to anti-tuberculosis drugs.

In addition, two other patients required an open surgical drainage for a 6-cm thick-walled abscess and a 5.5-cm abscess with concomitant liver hematoma. Both patients had resolution of fever and abdominal pain after drainage.

Outcome. Of the 40 patients, 36 improved and were discharged, three were clinically improving with treatment but went home against medical advice, and one was transferred to another hospital for completion of medications. Of the 36 patients who were discharged, the mean duration of hospital stay was 6 weeks (SD 1.9) (range, 3 to 12 weeks).

DISCUSSION

This study showed that hepatic abscess occurred in seven to eight cases per 10^5 in a tertiary government referral center. The prevalence is relatively low compared to that of India, also a developing country that reported 18 children in six years and with an estimate of 79 per 10^5 admissions and in 65 children in three years with 140 per 10^5 (Brazil).[7] In developed countries like Denmark and USA, the prevalence was from 1 to 25 per 10^5 admissions but data from these studies were obtained more than 30 years ago.[3,4] There are no recent reports from these countries, and it might well be that they no longer see cases of hepatic abscess.

The mean age of our patients was 8 years, mostly 1 to 5 years old. This is comparable with previous studies which reported a mean age ranging from 3 to 12 years.[7] Our youngest patient was a three-month-old who had gram negative septicemia and limb ischemia. Review of literature showed that the youngest reported case was a 6-day-old baby with lethargy, fever and hepatomegaly and was diagnosed with *Staphylococcus aureus* sepsis. The baby underwent exchange transfusion for ABO incompatibility and died nine days later.[13] Post-mortem autopsy revealed presence of multiple small hepatic abscesses and thrombophlebitis. The umbilical vein appeared to be the initial source of infection as it also contained purulent exudate. None of our patients had any of the reported predisposing factors for hepatic abscesses

including malignancy, immunodeficiency, and chronic granulomatous disease but 40% were classified as moderate to severe wasting**.** In other reports on hepatic abscess, 50 to 75% of the children were also malnourished.[1,9] Malnutrition may lead to the loss of the protective mechanisms of macrophages predisposing to infection.[10] Another factor was the presence of sepsis with five of our patients having a positive blood culture on admission. Bacteremia may infect the liver via the bile duct, hepatic artery, or portal vein and this may cause localized septic thrombophlebitis, releasing septic emboli into the portal circulation which are trapped by hepatic sinusoids and become the nidus for hepatic abscess formation.[14,15]

Both clinical and biochemical features of patients with hepatic abscess are non-specific and the diagnosis is only confirmed by imaging studies. Fever in all our patients and in 80 to 100% of other cases suggests the presence of infection.[7-11] The diagnosis was suspected in 30% in our study by the presence of an abdominal mass, which have also been noted in 48% (12 of 25 patients) in a previous report done locally.[8] Another clue was the presence of right upper quadrant tenderness in 22% in our patients and has been described from 20 to 100% of children with the disease.[7,10,11,14] Evidence of infection was supported by the presence of leukocytosis, seen in 89% in our study and described in 60 to 95% of hepatic abscess.[8,9,11] We also observed 58% of patients with anemia and noted in 50 to 90% of reported cases.[7- 11] Anemia in infection is attributed to the decrease in the release of iron by the reticuloendothelial system.

Ultrasonography confirmed the presence of hepatic abscess in 82% of our patients with majority being a solitary mass (58%) and involved the right lobe (80%), either solely or both the right and left lobes. Hepatic abscess is more common on the right lobe due to the bigger volume of blood in the right portal vein and its continuous flow in the direction of the common portal vein while the left portal vein takes a more horizontal direction. Ultrasound has a sensitivity of 96–100% for hepatic abscess and is the preferred imaging procedure because it is non-invasive, easily available and cheaper than other modalities of imaging.[8,10,14] It is, however, operator dependent. In a study of 698 adult patients in Taiwan with hepatic abscess, 175 (25%) had equivocal results on ultrasound and 14% had false negative results.[16] In instances that the ultrasound findings are inconclusive, computer tomography is requested as what we did in seven of our patients to confirm the diagnosis.

Consistent with previous studies done in children, majority (97%) of our patients had a probable pyogenic liver abscess and only three had *Mycobacterium tuberculosis* as an etiology. We considered pyogenic liver abscess even in the absence of an isolate on the mass based on signs and symptoms and therapeutic response with antimicrobial agent. Establishing the etiologic agent was challenging as only five (12%) of our patients had a positive blood culture and test for anerobic and amoebic organisms was not routinely done. Surgical drainage was also reserved for patients with a fluid filled mass more than 5 cm or those who are refractory to treatment and have developed complications, as we have observed in two patients who had a rupture of the abscess in the peritoneum. No work ups were done to exclude an amoebic hepatic abscess as the disease has not been reported locally in children in the last 30 years. Most of the referrals in our institutions are also not from regions endemic for amoeba.[17] A prevalence study of *E. histolytica* in stool samples among 2232 informal settlers in our region of Manila was reported in only eight (0.358%) subjects using PCR for detection.[18,19]

Staphylococcus aureus is the most common causative agent in childhood hepatic abscess and observed in thirty percent (27 of 93) of cultures of hepatic aspirate.[8] The organism was also seen in three of nine aspirates in our study. However, in Taiwan, out of 14 aspirates, nine grew *Klebsiella pneumoniae* and only one had *Staphylococcus aureus*.[20] One of our patients also had an abscess secondary to *Klebsiella pneumoniae* on aspirate but on surgical drainage, the culture grew *Mycobacterium tuberculosis*. With regards tuberculous hepatic abscess, several case reports with a total of four patients showed that all presented with fever and leukocytosis and three had an associated right upper quadrant tenderness.[21-23] The PPD skin test was positive in two patients. Akin to our experience, the diagnosis of tuberculosis was not suspected initially, and the patients were initially managed as pyogenic. The diagnosis was confirmed based on abscess culture and all responded with anti-tuberculosis medications. Interestingly, these case reports were from Turkey, India, and Slovakia, which, like the Philippines, are developing countries with high incidence of tuberculosis.[21-23]

Of the 40, 32 (80%) of our patients responded with medical treatment alone while eight (20%) required a percutaneous or open surgical drainage. Our results are better than the findings in India were only 10 (55%) of 18 children were treated medically while the rest necessitated drainage.[7] Patients in the India study were initially started on anti-staphylococcus and aminoglycosides and only six had anaerobic coverage. In our institution, all patients initially started on an empiric aminoglycoside (amikacin/ gentamicin), anti-anaerobic/amoebic agent (metronidazole) and an anti-staphylococcal (oxacillin) or an appropriate antibiotic depending on the possible source of infection.[7,24] The initial treatment combination we provided resulted in improvement in 60% of our cases while the rest required a change of antimicrobial treatment. However, the present National Antibiotic Guidelines for pediatric patients with hepatic abscess recommends the use of ampicillin-sulbactam or piperacillin-tazobactam or ceftriaxone and metronidazole for pediatric patients with hepatic abscess.[25] Aside from the medical treatment, the drainage procedure was considered in nine of our cases (eight patients) for the following indications: six with no response to medical treatment and two because of an abscess greater than 5 cm in size; and one patient who required both a percutaneous and open

surgical drainage as there was still no response to medical treatment after the percutaneous drainage yielded *Klebsiella pneumoniae*. The open surgical drainage grew *Mycobacterium tuberculosis* and the patient responded with anti-tuberculosis drugs. This patient probably had both *Mycobacterium tuberculosis* and a superimposed pyogenic hepatic abscess. The liver damage caused by the *Mycobacterium tuberculosis* altered the hepatic tissue and was infected by the *Klebsiella pneumoniae* during its hematogenous spread.[26] Blood culture of this patient, however, showed no growth.

All our patients improved with treatment. The outcome of hepatic abscess in children is excellent and death is usually reported in <20% of case series, mostly from sepsis and rupture of abscess in the peritoneal cavity.[3,7,8] In the previous study done in our institution 25 years ago, the clinical features of hepatic abscess of fever, abdominal distension and presence of abdominal mass and biochemical feature of leukocytosis were also observed in the present study. However, the difference in the last 10 years is the availability of diagnostic imaging which has resulted in better outcomes. In the earlier study, four of 25 (15%) patients died, three who were diagnosed only on autopsy and one who died of sepsis from multiple abscess. The only imaging modality that was used then was an ultrasound and these deaths could have probably been prevented with better and more localized images we can obtain now from CT scan. Ten of the 25 (40%) patients previously reported also developed complications including pleural and pericardial effusion and perinephric abscess probably secondary to a delay in diagnosis and treatment. In the last 10 years, the prognosis is also better as these patients are already managed at onset by a multidisciplinary team composed of a pediatric gastroenterologist, pediatric infectious disease specialist, pediatric surgeon, and interventional radiologist. At a primary care level, prompt diagnosis of hepatic abscess is made when there is a high index of suspicion in a child who presents with fever, abdominal pain, abdominal mass, or distention and an imaging study such as an ultrasound or CT scan is requested. Once the diagnosis is considered, a referral for admission is then done in an institution with specialty care to establish the causative agent, initiate empiric antibiotic therapy, periodic reassessment and when needed a referral to an interventional radiologist or a pediatric surgeon for drainage of the abscess.

CONCLUSION

In summary, the majority of our patients had probable pyogenic hepatic abscess. It presented with non-specific clinical and laboratory features. The ultrasound confirmed the diagnosis in the majority of cases and is mostly solitary and involved the right lobe. Limited abscess aspirates yielded *Staphylococcus aureus* and *Mycobacterium tuberculosis*. Most patients responded with medical treatment alone and only a fifth required drainage. The outcome of both medical and surgical treatment was favorable.

Statement of Authorship

Dr. Besa prepared the research protocol, collected the data, analyzed and wrote the paper. Dr. Gregorio conceptualized the study, assisted in the analysis and edited the manuscript. Both authors approved the final version submitted.

Author Disclosure

Both authors declared no conflicts of interest.

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