

Pyogenic Liver Abscess: Recent Trends in Etiology and Mortality

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Background. Pyogenic liver abscess, a potentially life-threatening disease, has undergone significant changes in epidemiology, management, and mortality over the past several decades.

Methods. We reviewed the data for patients admitted to Bellevue Hospital and New York University Downtown Hospital (New York, New York) over a 10-year period.

Results. Of 79 cases reviewed, 43% occurred in patients with underlying biliary disease. The most common symptoms were fever, chills, and right upper quadrant pain or tenderness. The most common laboratory abnormalities were an elevated white blood cell count (in 68% of cases), temperature $\geq 38.1^{\circ}\text{C}$ (90%), a low albumin level (70.2%), and an elevated alkaline phosphatase level (67%). Seventy percent of the abscesses were in the right lobe, and 77% were solitary. *Klebsiella pneumoniae* was identified in 41% of cases in which a pathogen was recovered. Eighteen (50%) of 36 Asian patients had *K. pneumoniae* isolated, in contrast to 6 (27.3%) of 22 non-Asian patients (not statistically significant). Fifty-six percent of cases involved treatment with percutaneous drainage. Although prior reports noted mortality of 11%–31%, we observed only 2 deaths (mortality, 2.5%).

Conclusions. The data suggest that *K. pneumoniae* has become the predominant etiology of pyogenic liver abscess and that mortality from this disease has decreased substantially.

Pyogenic liver abscess (PLA) was reported in the writings of Hippocrates, who based prognosis on the type of fluid recovered from the abscess [1]. In 1938, Och-sner and DeBakey [2] described the treatment and mortality of patients with PLA and recommended surgical treatment as the primary treatment modality. At that time, PLA was most commonly a complication of acute appendicitis, occurred predominantly in young men, and was associated with high mortality. Surgery remained the therapy of choice until the mid 1980s, when percutaneous drainage was shown to be a safer alternative in many cases [3–6].

Mortality rates have decreased substantially over the past several decades, with recent studies reporting rates of 11%–31%. The mean age of patients with PLA has increased, and the most common cause reported in recent series has shifted to biliary disease [5–10].

In reports from the United States, the most common organism recovered from patients in the United States has been *Escherichia coli* [4–6, 11], although one study found *Klebsiella pneumoniae* to be predominant [7, 12]. Recent reports from Taiwan have described an increase in the rate of PLA due to *K. pneumoniae*, which, in one series, was recovered from 82% of patients [13]. Because such experiences have not yet been reported in the United States, we reviewed the cases of PLA seen at our institutions over the past decade.

METHODS

Bellevue Hospital is a 900-bed municipal hospital in Manhattan (New York). New York University (NYU) Downtown Hospital is a 140-bed community hospital, also located in Manhattan (New York), near to New York's Chinatown district. This study was approved by the institutional review boards of the participating hospitals.

All 171 cases involving inpatients who received a discharge diagnosis of PLA from January 1993 through December 2003 from either Bellevue Hospital or NYU Downtown Hospital were eligible for inclusion. Cases were included if the abscess was confirmed by imaging as well as by either documentation of an organism re-

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covered from the abscess site or resolution of symptoms and signs after antibiotic treatment. Of the 171 patients, 66 had miscoded charts. The most common diseases among patients with miscoded charts were amebic liver abscess (13 cases) and tuberculosis of the liver (13 cases). Twenty-one charts could not be retrieved, and 5 charts had incomplete data. The charts for the remaining 79 cases were reviewed.

Charts were abstracted to a data collection form. Information recorded included age, sex, ethnicity, year of admission, country of origin, and underlying medical conditions (including biliary disease, inflammatory bowel disease, appendicitis, diverticulitis, cholecystitis, diabetes, other intra-abdominal infection, malignancy, hypertension, alcohol abuse, cardiovascular disease, abdominal trauma, and cirrhosis). The presence of these conditions was determined on the basis of their documentation in the medical history from the first admission for PLA. Presenting signs and symptoms were recorded, including decreased appetite, fever, chills, right upper quadrant pain, nausea, vomiting, weight loss, myalgias, headache, diarrhea, jaundice, hepatomegaly, and abnormal chest radiograph findings. Initial laboratory values were recorded, including WBC count, presence of an elevated platelet count, lactose dehydrogenase level, liver function test results, amylase level, and lipase level. Initial values

were considered to be the first value obtained within the first 24 h after the presentation of PLA. Microbiological results of blood and abscess cavity cultures were assessed. Cultures were isolated for aerobic and anaerobic organisms using the standard diagnostic techniques of the institutions' clinical laboratories. Organisms recovered from the abscess were assumed to be the etiologic organisms. Charts were reviewed for evidence of serological testing for HIV infection, hepatitis A, hepatitis B, hepatitis C, and amebic disease, and they were reviewed for examination of stool for fecal occult blood and parasites. The cause of PLA was ascribed to the process that, in the opinion of the reviewer, was most likely to account for the abscess. If no clear cause was identified, the case was described as cryptogenic.

Radiographic reports were reviewed to determine the location and number of abscesses. Charts were also reviewed for evidence that other forms of imaging and visualization were performed, such as upper gastrointestinal series, colonoscopy, and endoscopic retrograde cholangiopancreatography (ERCP).

The primary therapeutic modality was defined by whether percutaneous drainage or open surgery was first therapeutic procedure done. If neither of these procedures were performed, cases were classified as medically managed. All patients received antibiotic therapy for their abscesses, and the name, duration,

Table. 1. Clinical characteristic and initial laboratory values for patients with pyogenic liver abscesses.

Characteristic	Mean (range)	Cases with abnormal values, ^a %
Age, years (<i>n</i> = 79)	56.4 (25–90)	...
Duration of fever after admission, days (<i>n</i> = 74)	4.6 (0–21)	...
Duration of hospitalization, days		
All treatments (<i>n</i> = 76)	19.6 (1–58)	...
Open surgery (<i>n</i> = 20)	20.8 (4–58)	...
Percutaneous drainage (<i>n</i> = 43)	19.4 (4–48)	...
Medical management (<i>n</i> = 13)	18.7 (1–52)	...
Duration of antibiotic therapy, days		
Intravenous therapy (<i>n</i> = 73)	17.5 (0–45)	...
Oral therapy (<i>n</i> = 73)	13.6 (0–56)	...
Initial laboratory value		
Albumin level (<i>n</i> = 74)	3.1 (1.3–4.9)	70.2
WBC count (<i>n</i> = 75)	15.4 (3.8–65.3)	68.0
Alkaline phosphatase level (<i>n</i> = 78)	206.8 (57–1271)	66.7
Alanine aminotransferase level (<i>n</i> = 78)	93.4 (8–1215)	53.8
Direct bilirubin (<i>n</i> = 66)	0.8 (0.0–5.6)	53.0
Aspartate aminotransferase level (<i>n</i> = 78)	86.1 (13–1237)	46.2
Total bilirubin level (<i>n</i> = 77)	1.9 (0.2–15.8)	41.6
Lactic dehydrogenase level (<i>n</i> = 29)	249.2 (33–551)	17.2
Lipase level (<i>n</i> = 32)	26.7 (4–193)	6.3
Amylase level (<i>n</i> = 52)	52.1 (14–446)	5.8

^a For all laboratory values except albumin level, the value shown is the percentage of cases with values above normal. For albumin level, the value shown is the percentage of cases with values below normal.

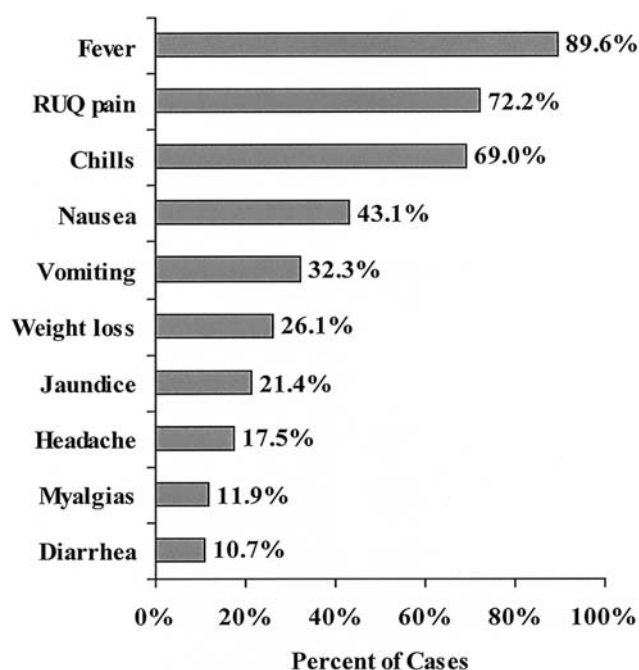


Figure 1. Presenting symptoms in cases of pyogenic liver abscess. RUQ, right upper quadrant.

and mode of administration were recorded for each case. Mortality and recurrence were assessed on the basis of documentation in the chart, including any available information on subsequent admissions or outpatient visits. Time to defervescence and duration of hospitalization were also recorded.

All collected data were transcribed into an Microsoft Excel spreadsheet and analyzed using SPSS software, version 11 (SPSS). Continuous variables were compared using analysis of variance, and categorical variables were compared with the χ^2 test, applying Yates correction when dichotomous variables were tested.

RESULTS

Forty-seven patients from Bellevue Hospital and 32 from NYU Downtown Hospital were included in our study. The mean age was 56.4 years. Fifty-five (69.6%) of the patients were male. Forty-five patients (56.9%) were Asian, 15 (18.9%) were white, 11 (13.9%) were Hispanic, and 6 (7.6%) were black. Two patients (2.5%) had unspecified ethnicity. Asian patients represented 25 (78.1%) of the 32 patients from NYU Downtown Hospital but only 20 (36.4%) of the 55 Bellevue patients ($\chi^2 = 12.51$; $df = 1$; $P < .001$). Compared with the proportion of Asian patients admitted for all causes, Asian patients were overrepresented among cases of PLA at both institutions. The overrepresentation was statistically significant at Bellevue, where 44.1% of PLA admissions were Asian patients, in contrast with 12.8% of all admissions ($\chi^2 = 16.2$; $df = 1$; $P < .001$).

The mean duration of fever was 4.6 days (table 1). Twenty-

two patients (28.6%) were febrile for ≥ 7 days, and 4 patients (5.2%) were febrile for >14 days. All 4 patients survived. The mean duration of hospitalization was 19.6 days, and there was no significant difference in length of stay between patients who received different treatment modalities (1-way analysis of variance, $F_{2,75} < 1$; P , not significant).

The most common laboratory abnormalities noted were decreased albumin levels, increased WBC counts, and elevated alkaline phosphatase levels (table 1). Chest radiographs were obtained for 65 patients, and 24 (36.9%) had abnormal findings. Fourteen patients (21.5%) had radiographs that showed abnormalities in the right lower lung field, of which 7 were pleural effusions, 5 were atelectasis or infiltrates, and 1 was an elevated right hemidiaphragm.

The most frequent presenting symptoms and signs are shown in figure 1. Fever (oral temperature, $>38.1^\circ\text{C}$) was seen in 89.6% of patients, chills in 69.0%, and right upper quadrant pain or tenderness in 72.2%. The triad of fever, right upper quadrant pain or tenderness, and an elevated alkaline phosphatase level was present in 32 (43%) of 74 patients who had data recorded for all 3 findings, and 86% had ≥ 2 of these symptoms and signs on initial evaluation.

Sixty (77%) of 78 evaluable abscesses were solitary. Fifty-four (70.5%) were right sided, 11 (14.1%) were left sided, and 4 (5.1%) were bilateral. In 9 patients, the location of the abscess was not documented.

The most common underlying or concomitant conditions were biliary disease (in 34 [43%] of the patients), hypertension (14 [17.7%]), intra-abdominal infection (14 [17.7%]), and diabetes (12 [15.2%]). Other underlying diseases included malignancy (12.7%), cardiovascular disease (12.7%), alcohol abuse (2.5%), and cirrhosis, diverticulitis, and inflammatory disease (1.3% each).

Fifty-four patients had ≥ 1 organism recovered from the abscess. Eighteen (33.3%) of the infections were polymicrobial; 6 of these included anaerobes. In 2 cases, anaerobes were the

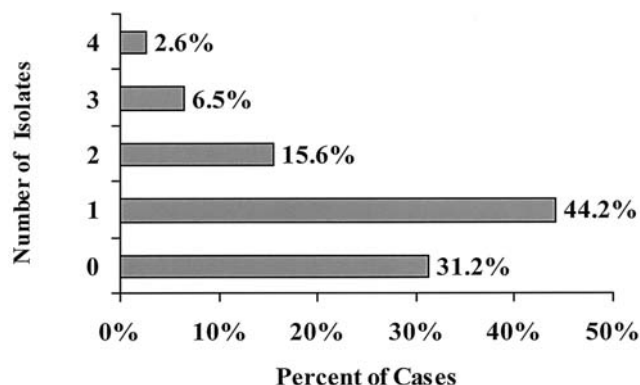


Figure 2. Number of bacterial isolates recovered per case in patients with pyogenic liver abscesses.

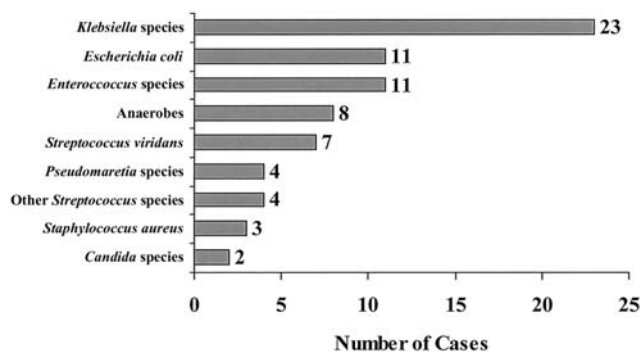


Figure 3. Identity of organisms recovered from patients with pyogenic liver abscesses.

only bacterial isolate. The number of bacterial species isolated from the abscess cavity for each case is shown in figure 2. Most often, only a single organism was identified (44.2% of cases).

The species of bacteria that were isolated are summarized in figure 3. *K. pneumoniae* was the species most commonly isolated and was found in 41% of the 54 cases in which an organism was recovered. *E. coli* and *Enterococcus* species were tied as the second most commonly isolated organisms (11 cases each). *Klebsiella* isolates were more common among Asian patients than other patients, and they were only isolated from Asian and Hispanic patients (figure 4). Eighteen (50%) of 36 Asian patients had *K. pneumoniae* isolated, in contrast with 6 (27%) of 22 non-Asian patients, a difference that was not statistically significant ($P = .075$).

In the 23 cases in which *K. pneumoniae* was recovered, it was most often the only pathogen. Only 5 of the 23 infections were polymicrobial. *K. pneumoniae* was recovered in 22 (46.8%) of 47 cases in which there was no extrahepatic intra-abdominal infection, but it was recovered in only 1 of 11 cases in which such an infection was present. The percentage of *K. pneumoniae* isolates recovered was similar in cases from Bellevue Hospital and NYU Downtown Hospital (42.4% and 40.0%, respectively).

Twenty-one of the 23 *K. pneumoniae* isolates were tested for antimicrobial susceptibility. Almost all of the isolates were highly susceptible, with only 3 isolates showing resistance to any drug tested other than ampicillin. Only 1 isolate was an extended-spectrum β -lactamase (ESBL) producer.

There was no significant difference in the number of febrile days or days hospitalized between patients with and patients without *K. pneumoniae* isolates, nor was there any significant difference between *K. pneumoniae* and non-*K. pneumoniae* cases in terms of the initial laboratory parameters. Only 1 patient was noted to have a *Klebsiella* species isolated other than *K. pneumoniae* (*Klebsiella oxytoca*), but it was found in conjunction with *K. pneumoniae*.

Twenty-nine patients had bacteremia. Of these patients, 17 (58.6%) had concordant results of blood and abscess cultures,

6 had additional organisms isolated from the abscess, 6 had an entirely different organism or organisms isolated from the abscess, and 6 had bacteremia in the absence of any bacteria isolated from the abscess. One patient had more organisms recovered from blood samples than from the abscess. There were 10 patients with *K. pneumoniae* bacteremia. In all 10 cases, *K. pneumoniae* was the only organism recovered in the blood samples, and in 7 patients, *K. pneumoniae* was also isolated from the abscess. None of these infections were polymicrobial. There was no significant difference between the frequency of bacteremia among patients with abscesses due to *K. pneumoniae* (34.8%) and its frequency among patients with abscesses caused by other bacteria (48.4%). Most cases were considered cryptogenic in origin (38 patients). The most commonly identified underlying cause was biliary disease (in 23 cases), followed by cancer (8), surgery (6), pancreatitis (2), diverticulitis (1), and appendicitis (1). Only 4 patients were tested for HIV infection, all of whom were HIV negative. There were no patients admitted with a prior diagnosis of HIV infection. The most common method of diagnosis was CT, which was used in 78 cases. Twenty-one patients had an abdominal ultrasound examination.

The most common primary treatment modality was percutaneous drainage, which was done in 44 patients (55.7%). Twenty patients (25.3%) were treated surgically, and 14 (17.7%) were treated medically. Treatment patterns differed significantly between the 2 hospitals. At Bellevue Hospital, 67.4% of the patients were treated primarily with percutaneous drainage, 19.6% received medical management, and 13.0% received surgical management. At NYU Downtown Hospital, 43.8% were treated surgically, 40.6% were treated with percutaneous drainage, and 15.6% received medical management ($\chi^2 = 9.50$; $df = 2$; $P = .009$). This difference was attributed to the lack of on-site interventional radiology at NYU Downtown Hospital.

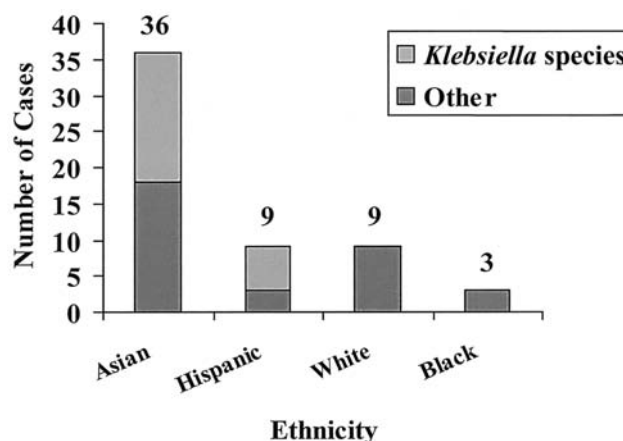


Figure 4. Isolation of *Klebsiella* species from pyogenic liver abscesses, by ethnic group.

Four patients (5.0%) required surgery after an initial treatment modality failed (3 had initial percutaneous drainage, and 1 had initial surgery). All patients were afebrile at the time of discharge. There were only 2 documented cases of recurrence after discharge (2.5%). In both cases, the primary treatment modality had been percutaneous drainage.

The antibiotics most commonly used were ESBLs (29 cases), followed by cephalosporins with or without metronidazole (27), fluoroquinolones with or without metronidazole (14), ampicillin and gentamicin (4), carbapenems (2), and vancomycin and gentamicin (2). The overall mortality rate was 2.5%. Two patients died, both of whom had been treated surgically. However, assessment of mortality is limited in that the mean duration of follow-up after discharge was 11.7 days, and 51 patients (65.4%) had no documented follow-up once discharged from the hospital.

DISCUSSION

The epidemiology, treatment, and mortality rate for cases of PLA have changed remarkably from the initial case descriptions. The average age of patients has increased substantially. In our study, the mean age was 56.4 years, and most recent studies have also reported mean ages of 55–60 years [5–10, 12–17]. Our finding of a predominance of right-side abscesses (in 70% of cases) is also consistent with prior reports, in which right-side lesions occurred in 56%–71% of patients [5–9, 12, 13, 17]. Most studies have also been consistent in finding either a slight predominance of male patients or an equal ratio of male to female patients [5, 6, 9, 10, 12, 15, 17]. These observations contrast with the findings of Ochsner and DeBakey [2], in which there was a far larger percentage of male patients.

These changes are likely to be caused by changes in the prevailing causes of PLA. Recent studies have noted an increase in the proportion of cases with underlying biliary disease, which is more prevalent in women. In our study, as in other recent reports [5–8, 10, 14], biliary disease was the most common identifiable cause of PLA. Most of our cases were considered cryptogenic, although colonoscopy and ERCP were only done in 3.8% and 8.9% of our patients, respectively. Therefore, some cases of colonic or biliary disease may have gone undetected.

Our observations are also consistent with prior reports in several other ways. We noted similar frequencies of low albumin levels, elevated alkaline phosphatase levels, elevated WBC counts, and bacteremia [6, 8–10, 18, 19].

One important new finding in this study is that 41% of our cases were due to *K. pneumoniae*. In contrast, the recovery rates in other reports from the United States have previously been noted to be 7%–27% [4–7, 10–12, 17, 18]. One report from the United States showed a higher rate of *K. pneumoniae* recovery, but unlike our experience, most of the cases from that report were polymicrobial [9]. The higher rate of *K. pneumoniae*

monomicrobial cases that we observed may reflect an evolution in the United States of changes in the etiology of liver abscess noted over the past 15 years in reports from Taiwan. In that country, *K. pneumoniae* has become by far the most common organism recovered (in up to 82.1% of cases) [13, 14, 19, 20]. The reason for the increase in cases of *Klebsiella* infection may simply be a reflection of the increase in the Asian population at our institutions, or it may suggest that a different strain of *K. pneumoniae* with an increased propensity for causing liver abscesses is now being seen in the United States. It is also possible that the relative increase is a result of as-yet-unidentified risk factors in an older patient population. It remains to be seen whether this epidemiological change is also occurring at other institutions and whether this trend will continue.

In our study, we did not note endophthalmitis, meningitis, or other serious metastatic infections associated with *K. pneumoniae*, as has been reported from Taiwan [14, 21, 22]. A majority of the reported cases from Taiwan (up to 67.5%) have occurred in patients with diabetes. In contrast, the prevalence of diabetes was only 15.2% in our study. Our rate is similar to that noted in prior US reports, in which the prevalence ranged from 10% to 27% [6, 9–11]. However, this number may be an underestimation, because it reflects only patients with a documented history of diabetes on the chart and does not include patients who may have had undiagnosed disease or abnormal glucose tolerance.

Only 1 patient was found to have an ESBL-producing *K. pneumoniae* isolate. This is consistent with reports from Taiwan, where isolates of *K. pneumoniae* causing PLA have all been highly susceptible [19]. The cases from Taiwan involving *Klebsiella* species were also mostly monomicrobial, which agrees with the findings of our report.

Our study has one of the lowest reported mortality rates for PLA. Other studies have also demonstrated a progressive decrease in mortality rates [6, 9, 12]. This may be due in part to improved imaging and diagnostic techniques, as well as to increased use of percutaneous drainage. Also, the high degree of antimicrobial susceptibility of the *K. pneumoniae* strains currently associated with PLA may account for the reported decrease in mortality. A similar phenomenon has been noted in Taiwan [14].

Twelve (41%) of the patients with bacteremia had organisms recovered from abscess cultures that were different from or in addition to those recovered in blood cultures. Therefore, blood culture alone does not accurately reflect the microbiology of PLA in many cases. Although there did not appear to be a higher rate of mortality in those cases that were managed medically, only 14 patients had cases that were in this category. Medical management has previously been noted to be associated with a higher mortality rate, compared with invasive therapy [5].

Percutaneous drainage has been shown to be safe in multiple prior studies and is now considered by many to be the standard treatment modality, along with antibiotics. Several prior studies show a similar or decreased mortality rate, compared with open surgery, without significant differences in recurrence rates [5–7, 17]. We did not distinguish between cases involving percutaneous insertion of an indwelling drainage catheter and those involving percutaneous aspiration, which has also been reported to be a reasonable option for treatment [4].

Although few have treated PLA with <2 weeks of intravenous antibiotic therapy, the optimal duration intravenous therapy—as well as the duration of subsequent oral therapy—remains unclear. In Taiwan, therapy has become somewhat standardized, with 3 weeks of intravenous therapy followed by 1 or 2 months of oral therapy [14]. Some US studies have also used a longer period of intravenous therapy [6]. Our mean durations of intravenous therapy (17.5 days) and oral therapy (13.6 days) were shorter than those in some prior reports. This shorter course was associated with extremely low mortality, suggesting that longer courses of antibiotic therapy may be unnecessary. There was no significant difference in the duration of antibiotic use or time to defervescence among patients who were treated with medical management, compared with those who were treated with percutaneous drainage or surgery.

A recent report from Taiwan has demonstrated a novel virulence gene in *K. pneumoniae* strains causing PLA [23]. Organisms with the *magA* gene were highly resistant to killing by human serum or phagocytosis. The presence of this gene in US isolates has not yet been assessed.

In summary, PLA was once considered to be a highly fatal disease but has recently been associated with low mortality. *K. pneumoniae* appears to be becoming a more common cause of PLA in New York City, paralleling changes in etiology seen in Taiwan over the past 15 years.

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