



ELSEVIER



<http://intl.elsevierhealth.com/journals/ijid>

Cryptogenic invasive *Klebsiella pneumoniae* liver abscess syndrome

Fadi Braiteh^{a,*}, Marjorie P. Golden^b

^a Phase I Program, Division of Cancer Medicine, The University of Texas M.D. Anderson Cancer Center and The University of Texas Graduate School of Biomedical Sciences at Houston, 1515 Holcombe Blvd, Unit 422, Houston, TX 77030-4009, USA

^b Division of Infectious Diseases, The Hospital of Saint Raphael and Yale University School of Medicine, New Haven, Connecticut, USA

Received 12 August 2005; received in revised form 20 October 2005; accepted 26 October 2005

Corresponding Editor: Michael Whitby, Brisbane, Australia

KEYWORDS

Pyogenic liver abscess;
Bacterial meningitis;
Klebsiella pneumoniae;
Thrombocytopenia;
Lung abscess;
Bacteremia;
Diabetes mellitus;
Taiwan

Summary

Background: *Klebsiella pneumoniae*-associated liver abscesses have distinct clinical and epidemiologic features.

Methods: We report the unusual case of an American patient with a *K. pneumoniae*-associated liver abscess and septic spread to other organs. We additionally present a comprehensive review of *K. pneumoniae*-associated liver abscess syndromes in adults.

Results: We identified three distinct *K. pneumoniae* liver abscess syndromes: the polymicrobial liver abscess, the monomicrobial cryptogenic noninvasive liver abscess, and the monomicrobial cryptogenic invasive *K. pneumoniae*-associated liver abscess (CIKPLA) syndromes, with distinct clinical, epidemiologic and outcome features. CIKPLA syndrome typically affects diabetic patients, mainly in Southeast Asia, and is complicated by septic spread to other organs.

Conclusions: The community-acquired, monomicrobial, *K. pneumoniae*-associated liver abscess syndromes that typically occur in the USA are mainly noninvasive and affect Asian or Hispanic persons. However, this report provides an alert that CIKPLA syndrome can occur in North America, and physicians need to be aware of it.

© 2006 International Society for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

Introduction

Klebsiella pneumoniae is a common pathogen responsible for diverse nosocomial and community-acquired infections, and is the third most common pathogen (10%) found in cases of

nosocomial bacteremia, after *Escherichia coli* (20%) and *Staphylococcus aureus* (16.5%).¹ About 72%² to 88%³ of *K. pneumoniae* nosocomial bacteremias are monomicrobial. The proportion of community-acquired versus nosocomial *K. pneumoniae* infections has increased markedly during the past two decades. In the USA, 41% of all *K. pneumoniae* infections are now community-acquired;^{4,5} the incidence is even higher in Taiwan, where it has been reported to be as high as 68%.^{6,7} In contrast to the 55% mortality associated

* Corresponding author. Tel.: +1 713 794 5188; fax: +1 713 563 4001.
E-mail address: fbraiteh@mdanderson.org (F. Braiteh).

with nosocomial *K. pneumoniae* bacteremia, the mortality rate with community-acquired *K. pneumoniae* bacteremia varies between 14% and 22% (Table 1).^{8,9}

K. pneumoniae is occasionally the cause of some liver abscesses. In the USA, liver abscesses are commonly polymicrobial,¹⁰ and *K. pneumoniae* has been isolated in 7–27% of cases. Interestingly, Rahimian et al.¹¹ recently identified in New York a series of distinctive *K. pneumoniae*-associated liver abscesses, which are mostly monomicrobial and uncomplicated. A distinct clinical syndrome of invasive monomicrobial *K. pneumoniae*-associated liver abscesses frequently associated with complications such as meningitis, endophthalmitis, lung abscess, or fasciitis has been repeatedly reported. Endemic in Taiwan,¹² mostly in patients with diabetes mellitus, this syndrome is anecdotally reported in western countries and almost never described in the USA (Table 1).

We present an unusual case of an American patient with *K. pneumoniae*-associated cryptogenic liver abscess and bacterial meningitis. We also discuss the reported cases of the cryptogenic invasive *K. pneumoniae* liver abscess (CIK-PLA) syndrome, identifying its clinical and epidemiologic features.

Case report

Patient symptoms and history

A 42-year-old man of Filipino descent residing in Connecticut and working as a mechanic, who immigrated to the USA at age 22, reported to his primary care physician with a 4-day history of fever (40 °C (104 °F)), severe headache, malaise, and anorexia. His medical history was unremarkable, and negative for diabetes mellitus or corticosteroid treatment. The patient, his wife, and their children had just returned from a one-week vacation at a Rhode Island beach resort. The patient denied any recent travel to Southeast Asia, and did not recall any contact with anyone who had recently returned from that area. His last visit to the Philippines had been four years previously.

Evaluation and treatment

A physical examination revealed lethargy, irritability, confusion, and neck stiffness. Results of an ophthalmologic exam were normal. Peripheral blood counts were unremarkable (leukocyte count = $8.7 \times 10^9/L$ (88% neutrophils and 8% lymphocytes) and hemoglobin = 15.5 mg/dL), and results of liver function tests were within normal limits. He had mild hyponatremia ($Na^+ = 130$ mEq/L (normal, 135–147 mEq/L)) and severe thrombocytopenia (platelet count = $19 \times 10^9/L$) (Figure 1). Results of computed tomography (CT) of the head were unremarkable.

A lumbar puncture was performed in the emergency department, after which the patient was started on 2 g ceftriaxone given intravenously (IV). A subsequent analysis of the cerebrospinal fluid (CSF) revealed pleocytosis (leukocyte count = $1.7 \times 10^9/\mu L$ (81% segmented neutrophils, 6% lymphocytes, and 13% monocytes)), an elevated protein level (400 mg/dL (normal, 20–45 mg/dL)), and a decreased glucose level (0 mg/dL (normal, 50–80 mg/dL)); these findings

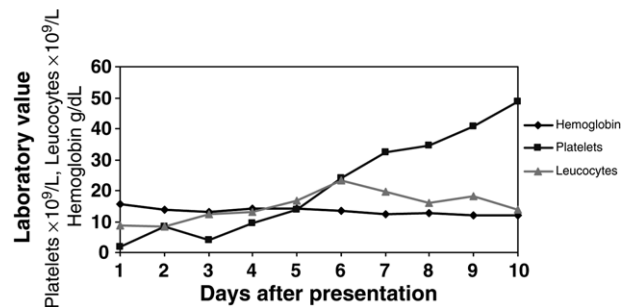


Figure 1 Leukocyte count ($\times 10^9/L$), hemoglobin levels (g/dL), and platelet count ($\times 10^9/L$) over time since the patient first presented. The initial thrombocytopenia (platelets = $19 \times 10^9/L$) subsided after the initiation of antibiotic therapy and clinical improvement occurred (platelets = $500 \times 10^9/L$). Despite the thrombocytopenia, which usually indicates a poor prognosis in this syndrome, the patient had a rapid recovery in his platelet count and an uneventful clinical outcome.

were consistent with bacterial meningitis. Serum and CSF Lyme immunoglobulin G and M levels (Specialty Labs, Santa Monica, CA, USA) ruled out Lyme disease. Results of an initial Gram stain and microscopic examination of the CSF fluid were unremarkable; however, the culture grew *K. pneumoniae* after 48 hours of incubation. Unfortunately, the isolated *K. pneumoniae* was not analyzed further to determine whether or not it was serotype K1 or K2. The isolate was resistant to ampicillin but sensitive to gentamicin, levofloxacin and cephalosporins (cefazolin, cefepime, ceftazidime, ceftriaxone). Results of an enzyme-linked immunosorbent assay for the human immunodeficiency virus were negative.

Despite being treated with high-dose ceftriaxone (2 g IV twice daily) for bacterial meningitis, the patient remained febrile. On hospital day 5, a repeat lumbar puncture showed increasing pleocytosis. Because of his persistent fever, magnetic resonance imaging (MRI) of the brain was performed on hospital day 7, and it revealed multiple small ring-enhancing lesions consistent with septic emboli (Figure 2). Transthoracic and transesophageal echocardiograms showed normal valve anatomy and no patency of the foramen ovale. CT of the chest revealed a nodule suggestive of an abscess (Figure 3).

The patient next developed right upper quadrant tenderness and an elevation of his liver enzyme levels (serum aspartate aminotransferase = 39 U/L, serum alanine aminotransferase = 74 U/L, serum alkaline phosphatase = 237 U/L, and total serum bilirubin = 1.0 mg/dL). CT of the abdomen revealed a 4 × 3.5-cm multicystic abscess in the right liver lobe (Figure 4). Aspiration of the liver abscess returned frankly purulent material that subsequently grew *K. pneumoniae* with an identical antibiogram to that of the strain isolated from the CSF. Metronidazole, 500 mg IV three times daily, was added to the ceftriaxone regimen.

One week later, repeat MRI showed increasing edema of the brain lesions and apparent development of new lesions. Over the next two weeks, however, the patient's fever abated, the liver and lung lesions decreased in size, and MRI showed gradual resolution of the brain lesions. On follow-up three years later, the patient maintains a full recovery without developing any new health problems.

Table 1 *Klebsiella pneumoniae*-associated infectious syndromes in adults

Syndrome	Bacteremia	Metastatic infection	Geographical cluster	Diabetes mellitus	Hepatobiliary or GI anomalies	Comments and notes	Mortality
<i>K. pneumoniae</i> bacteremia	N/A	N/A	USA: mainly nosocomial (60%)	(2%) +/-	(21%) ++	Associated malignancy: 53% +	36–55% ^a ++++
			Taiwan: mainly community-acquired (60–70%)	(49%) +++++	(31%) +++	Associated malignancy: 14% +++	14–22% +
Community-acquired <i>K. pneumoniae</i> pneumonia	+/-	Unusual	Taiwan: 62% South Africa and Singapore: 15% USA: 1%	+/-	-	Frequently associated with alcohol intake in Taiwan and South Africa (++++) Rarely associated with alcohol intake in USA (-)	65% ^b ++++ 55% ^b ++++
Community-acquired <i>K. pneumoniae</i> meningitis	+/-	Unusual	Taiwan and Singapore: 18–33% USA: 1.2%	(49–65%) +++++	-	Occasionally associated with liver cirrhosis or thalassemia	43–66% ^c ++++
Polymicrobial liver abscess	+	Rare	USA: 7–27% cases Taiwan: 82% cases	(10–25%) ++	(95%) +++++	Frequent relapse: 41% (++++)	31–41% ++++
Cryptogenic noninvasive monomicrobial <i>K. pneumoniae</i> liver abscess	+	Rare/absent	Western countries (only among Asian or Hispanic persons)	(15%) +	(0.6%) -	Mainly community-acquired No relapse ESBL (+) strains are rare ^d	<2.5% +/-
Cryptogenic invasive monomicrobial <i>K. pneumoniae</i> liver abscess (CIKPLA)	++++	Endophthalmitis (60%) Lung abscess (40%) Meningitis (25%) Necrotizing fasciitis (4%) Osteomyelitis, prostatitis, muscle abscess, septic arthritis (exceptionally)	Taiwan (endemic) Japan, Hong Kong, China, Singapore, India, Thailand, Trinidad (cases reported) Spain, Ireland, Belgium, Canada, USA and Australia (exceptionally) ^e	(70%) +++++	-	Mainly community-acquired Rare relapse: 4% (+/-) ESBL (+) strains are rare	11% +

Abbreviations: ESBL, extended spectrum beta-lactamase; GI, gastrointestinal.

Signaling: absent or anecdotal (-); very rare (+/-); rare (+); occasional (++); frequent (+++); very frequent (++++); almost always (+++++).

^a With early adequate appropriate antibiotherapy (at least one cephalosporin), associated mortality is 38%, compared to 88% when delayed or inappropriate. Nosocomial *K. pneumoniae* is more frequently resistant to aminoglycosides, antipseudomonal penicillin, and all three generations of cephalosporins than community-acquired strains.

^b Mortality in patients admitted to the intensive care units in France, USA, and Taiwan were 43%, 55%, and 63%, respectively.

^c The highest mortality is in Taiwan.

^d As reported in one series in New York by Rahimian et al.¹¹

^e In Western countries, many of these cases were reported in patients of Southeast Asian origin and/or after returning from Southeast Asia.

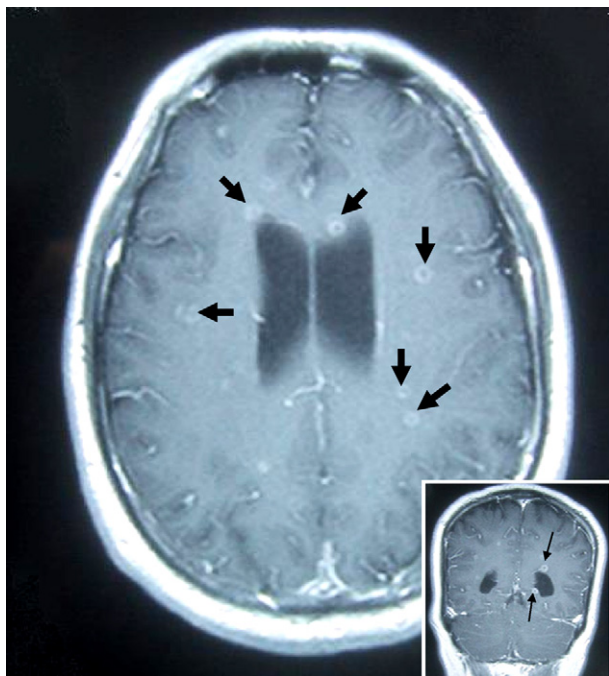


Figure 2 Magnetic resonance imaging scan of the head performed two days after presentation revealed multiple 5-mm ring-enhancing lesions, both supratentorial and infratentorial, throughout the cerebral hemispheres, compatible with septic emboli and microabscesses (arrows).

We postulated that our patient had a *K. pneumoniae*-associated cryptogenic liver abscess which, because of its large size (4–11 cm), was likely the original lesion, and that his *K. pneumoniae* bacteremia had seeded to his lungs, brain, and meninges.

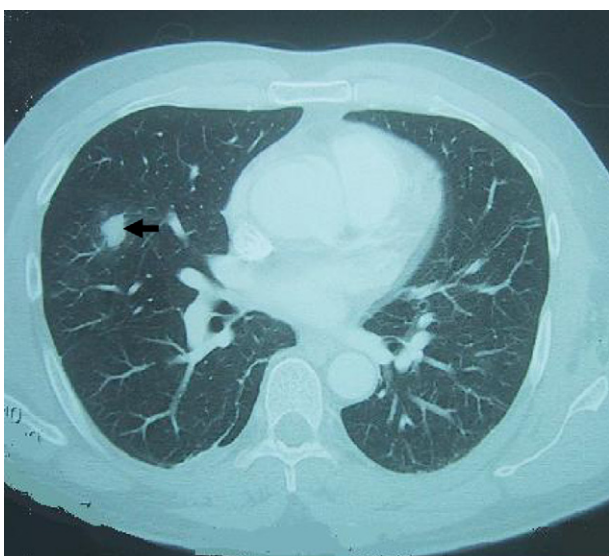


Figure 3 Contrast computed tomography scan of the chest showing a nodule (arrow) suggestive of an interstitial pulmonary abscess.

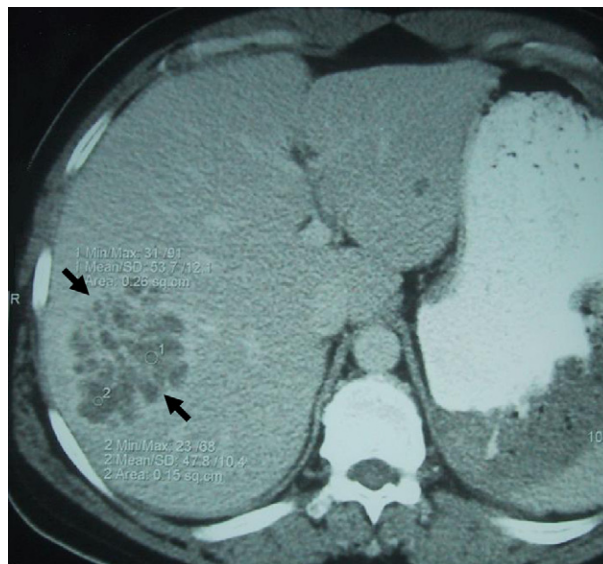


Figure 4 Abdominal computed tomography scan with iodine intravenous contrast clearly identified a large polylobar right lobe hypodense lesion (arrows) with peripheral enhancement suggestive of a hepatic abscess. CT-guided fine needle aspiration returned frank purulent material in which Gram-negative rods were seen on microscopic examination; these rods were identified as *Klebsiella pneumoniae* after 48-hour culture in aerobic media.

Discussion

Nosocomial and community-acquired *K. pneumoniae* bacteremia typically complicates *K. pneumoniae* suppurative infections (e.g., pneumonia, urinary tract infection, intravenous catheter site infection, meningitis) or results from underlying gastrointestinal or hepatic disease with a subsequent hepatic abscess, which is usually polymicrobial. Cryptogenic *K. pneumoniae* liver abscesses can be monomicrobial, and self-limited (noninvasive) even when associated with bacteremia. Lately, an invasive type of *K. pneumoniae* monomicrobial cryptogenic liver abscess presenting with metastatic septic seeding has been described.¹²

Cryptogenic noninvasive *K. pneumoniae*-associated liver abscess syndrome

The noninvasive *K. pneumoniae*-associated liver abscess syndrome is a rare condition worldwide, with a peak incidence in Southeast Asia. It accounts for 17% of the patients with *K. pneumoniae*-associated bacteremias in Singapore.¹³ In the USA, Rahimian et al.¹¹ isolated *K. pneumoniae* from 41% of liver abscess syndromes in two major urban hospitals in New York. The microorganism was exclusively recovered from Asian and Hispanic patients. Interestingly, one of the hospitals in that review served mainly the Chinatown neighborhood. The *K. pneumoniae*-associated liver abscess syndrome was community-acquired in all cases and presented mainly as a monomicrobial abscess (in 78% of cases).¹¹ All cases involved isolated liver abscesses without the extrahepatic

bacterial meningitis, endophthalmitis, or fasciitis identified in the invasive syndrome described in Taiwanese patients. A similar *K. pneumoniae* liver abscess syndrome has been described in Mississippi, in the USA.¹⁴

Unlike polymicrobial liver abscesses, where the infection commonly originates from the biliary tract or the lower intestine, the monomicrobial *K. pneumoniae*-associated liver abscess is not associated with an identifiable gastrointestinal or hepatobiliary anomaly.¹⁰ Therefore, the liver abscesses caused by non-invasive *K. pneumoniae* infection in the USA are typically monomicrobial, community-acquired, rarely associated with diabetes mellitus, and usually uncomplicated by extrahepatic seeding, with a very good clinical outcome (Table 1).

Cryptogenic invasive *K. pneumoniae*-associated liver abscess syndrome

Cryptogenic invasive *K. pneumoniae*-associated liver abscess (CIKPLA) syndrome is also typically community-acquired⁶ and unrelated to gastrointestinal or hepatobiliary anomalies (Table 1). Unlike the cryptogenic non-invasive liver abscess syndrome, CIKPLA is highly associated with distant septic seeding and is distinguished by its geographical distribution. It is almost exclusive to Taiwan,¹⁵ where it has been endemic, although a few cases have also been described in China, Korea, Singapore, Japan, India, Thailand, Trinidad, and Jamaica.^{16–20} *K. pneumoniae* is the leading cause of cryptogenic liver abscesses in Taiwan, where it has been isolated in 30% (in the 1980s) to 80% (in the 1990s) of pyogenic abscesses.^{12,15,21}

According to Ko et al., more than 900 cases of *K. pneumoniae*-associated liver abscess syndrome have been reported from Asian countries in the last decade; fewer than 23 cases were reported from regions outside Asia.⁶ In western countries, however, anecdotal cases have recently been reported: a few cases of cryptogenic invasive liver abscesses associated with diabetes mellitus and endophthalmitis have been described in Spain,^{22–24} Belgium,²⁵ Ireland (where the patient was a Taiwanese seaman),²⁶ Italy,²⁷ and Australia.²⁸ Compared with the monomicrobial cryptogenic noninvasive *K. pneumoniae* liver abscess syndrome, CIKPLA is characterized by a 20-fold increased association with diabetes mellitus and is frequently complicated by metastatic infections.^{6,14,15,18,21,29–31} Endophthalmitis is the most common (as many as 60% of cases) and serious septic lesion of this syndrome,^{29,31,32–36} although lung abscesses (40%), meningitis (25%),³⁷ and necrotizing fasciitis (4%)^{38–41} are also encountered frequently. Additionally, prostatitis, osteomyelitis, septic arthritis, septic epidural abscesses, and muscle abscesses have occasionally been reported.^{31,42,43} Compared to the polymicrobial pyogenic liver abscess, CIKPLA has lower mortality (11.3% vs. 41%) and relapse rates (4.4% vs. 41%).¹⁵

In the USA, pyogenic liver abscesses are often polymicrobial,^{44–46} and *K. pneumoniae* accounts for 7–27% of the strains isolated.^{45–47} To our knowledge, only one case fitting the criteria for CIKPLA syndrome has thus far been reported in the USA. The patient was an African American man who presented with a community-acquired, monomicrobial, *K. pneumoniae*-associated liver abscess with meningitis and endophthalmitis.⁴⁸ The reasons for the geographic differ-

ences in the incidence of CIKPLA syndrome are unknown, but hypotheses should address differences in socioeconomic factors, possible occupational exposures (e.g., food handling),⁴⁹ defects in host defenses caused by diabetes mellitus or alcoholism, and possibly differences in genetic and immunologic susceptibilities in different ethnic groups.

Distinctive bacterial virulence is a probable contributing factor since a major cluster of *K. pneumoniae* isolates with genetic similarities was identified in Taiwanese patients with invasive liver abscesses and septic metastases,¹² including infections occurring in siblings.⁵⁰ *K. pneumoniae* serotypes isolated in Taiwanese patients with CIKPLA had a high prevalence of capsular polysaccharide serotypes K1 and K2 and an increased resistance to phagocytosis and intracellular killing.⁵¹ Resistance to phagocytosis and bacterial death in human serum observed in the invasive strains has been linked to the virulence gene *magA*, which encodes the outer membrane protein of a mucoviscous exopolysaccharide web.⁵²

There is an emerging concern about Gram-negative rods producing extended-spectrum β -lactamases (ESBLs), which are resistant to all β -lactam antibiotics except cephamycins and carbapenems, to most aminoglycosides, to trimethoprim-sulfamethoxazole, and sometimes to the fluoroquinolones.⁵³ *K. pneumoniae* is the most common species to produce ESBLs,⁵⁴ particularly in nosocomial infections (30.8% vs. 3.5% in community-acquired infections).⁶ In fact, the prevalence of ESBL-producing strains of *K. pneumoniae* varies between 18.5%⁵³ and 53%⁵⁴ in nosocomial infections. The highest rates of ESBL-producing *K. pneumoniae* are reported in Eastern Europe (approximately 50% of isolates)⁵⁵ and South America (45% of isolates), followed by the western Pacific region (25%), Europe (23%), the USA (8%), and Canada (5%).⁵⁶ Strains isolated from both invasive and noninvasive *K. pneumoniae* monomicrobial liver abscesses¹¹ are highly susceptible to antibiotics but commonly resistant only to ampicillin.²⁵ ESBL-producing *K. pneumoniae* is rarely isolated from the aspirates of monomicrobial liver abscesses (invasive or noninvasive) which are commonly community-acquired conditions (4.3%).¹¹ Therefore, the treatment of choice would be a third generation cephalosporin, preferably ceftriaxone, because it accumulates in the vitreous fluid and CSF at therapeutic concentrations.⁵⁷

CIKPLA syndrome has a relatively good outcome. Endophthalmitis, meningitis and thrombocytopenia are its most alarming findings. A retrospective study identified thrombocytopenia (platelets $<150 \times 10^9/L$) to be a predictor of a poor prognosis because it is associated with a 3-fold increased mortality rate over patients with normal platelet counts (37% vs. 11%),¹³ a finding that has been confirmed by a more recent prospective study.⁸ One half to two thirds of patients with associated meningitis die of their disease.⁵⁸ Despite his initial thrombocytopenia and central nervous involvement, the patient described in the case report had an uneventful recovery. When seen two years after his initial treatment, the patient had not developed any hepatobiliary, gastrointestinal, or metabolic disease. To our knowledge, this is only the second case of CIKPLA syndrome to be reported in the USA. A case of CIKPLA syndrome has been reported in Canada, but it involved a sailor of Indian descent who had a cryptogenic *K. pneumoniae*-associated liver abscess and necrotizing fasciitis after returning from a trip to Singapore

and South Africa.³⁹ Interestingly, our patient was of Asian descent but not diabetic.

Conclusion

CIKPLA is a community-acquired, mostly monomicrobial, solitary liver lesion frequently associated with diabetes mellitus and classically complicated by one or more septic conditions (e.g., meningitis, endophthalmitis, lung abscess, or necrotizing fasciitis). This syndrome occurs almost exclusively in Asia, possibly due to a distinctive virulent strain, but which is not particularly resistant to antibiotics, and therefore it usually has a good outcome. Although it is endemic in Taiwan, it can occur in North America, as our report shows. Therefore, physicians should be aware of this insidious syndrome and should identify early signs of meningitis or endophthalmitis because timely management remains critical for a good outcome. Physicians should recognize the risks of endogenous endophthalmitis and meningitis in complication of pyogenic liver abscesses, especially in patients with diabetes mellitus and/or of Asian descent. Of concern are whether future similar cases in North America will remain sporadic or become endemic. The identification of the serotype of *K. pneumoniae* responsible for any new CIKPLA cases, the analysis for ESBL-production and identification of virulence factors in future isolates such as the *magA* gene are warranted.

Conflict of interest: No conflict of interest to declare.

References

- Eisenstein BI, Zaleznik DF. Enterobacteriaceae. In: Mandell GL, Bennett JE, Dolin R, editors. *Principles and practice of infectious diseases*. 5th ed. Philadelphia, USA: Churchill Livingstone; 2000. p. 2294–310.
- Watanakunakorn C, Jura J. *Klebsiella* bacteremia: a review of 196 episodes during a decade (1980–1989). *Scand J Infect Dis* 1991;23:399–405.
- Garcia de la Torre M, Romero-Vivas J, Martinez-Beltran J, Guerrero A, Meseguer M, Bouza E. *Klebsiella* bacteremia: an analysis of 100 episodes. *Rev Infect Dis* 1985;7:143–50.
- Haddy RI, Lee 3rd M, Sangal SP, Walbroehl GS, Hambrick CS, Sarti GM. *Klebsiella pneumoniae* bacteremia in the community hospital. *J Fam Pract* 1989;28:686–90.
- Montgomerie JZ, Ota JK. *Klebsiella* bacteremia. *Arch Intern Med* 1980;140:525–7.
- Ko WC, Paterson DL, Sagnimeni AJ, Hansen DS, Von Gottberg A, Mohapatra S, et al. Community-acquired *Klebsiella pneumoniae* bacteremia: global differences in clinical patterns. *Emerg Infect Dis* 2002;8:160–6.
- Wang LS, Lee FY, Cheng DL, Liu CY, Hinthorn DR, Jost PM. *Klebsiella pneumoniae* bacteremia: analysis of 100 episodes. *J Formos Med Assoc* 1990;89:756–63.
- Tsay RW, Siu LK, Fung CP, Chang FY. Characteristics of bacteremia between community-acquired and nosocomial *Klebsiella pneumoniae* infection: risk factor for mortality and the impact of capsular serotypes as a herald for community-acquired infection. *Arch Intern Med* 2002;162:1021–7.
- Yang PY, Huang CC, Leu HS, Chiang PC, Wu TL, Tsao TC. *Klebsiella pneumoniae* bacteremia: community-acquired vs. nosocomial infections. *Chang Gung Med J* 2001;24:688–96.
- Seeto RK, Rockey DC. Pyogenic liver abscess. Changes in etiology, management, and outcome. *Medicine (Baltimore)* 1996;75:99–113.
- Rahimian J, Wilson T, Oram V, Holzman RS. Pyogenic liver abscess: recent trends in etiology and mortality. *Clin Infect Dis* 2004;39:1654–9.
- Lau YJ, Hu BS, Wu WL. Identification of a major cluster of *Klebsiella pneumoniae* isolates from patients with liver abscess in Taiwan. *J Clin Microbiol* 2000;38:412–4.
- Lee KH, Hui KP, Tan WC, Lim TK. *Klebsiella* bacteremia: a report of 101 cases from National University Hospital, Singapore. *J Hosp Infect* 1994;27:299–305.
- Ayinala SR, Vulpe M, Azaz M, Cohen H, Donelson SS, Lee M. Pyogenic liver abscesses due to *Klebsiella pneumoniae* in a diabetic patient. *J Miss State Med Assoc* 2001;42:67–70.
- Wang JH, Liu YC, Lee SS, Yen MY, Chen YS, Wann SR, et al. Primary liver abscess due to *Klebsiella pneumoniae* in Taiwan. *Clin Infect Dis* 1998;26:1434–8.
- Ohmori S, Shiraki K, Ito K, Inoue H, Ito T, Sakai T, et al. Septic endophthalmitis and meningitis associated with *Klebsiella pneumoniae* liver abscess. *Hepatol Res* 2002;22:307–12.
- Naito T, Kawakami T, Tsuda M, Ebe T, Sekiya S, Isonuma H, et al. A case of endophthalmitis and abscesses in the liver and the lung caused by *Klebsiella pneumoniae*. *Kansenshogaku Zasshi* 1999;73:935–8.
- Valabhji J, Robinson S, Elkeles RS. Hepatic abscess in a diabetic patient. *Postgrad Med J* 2000;76:797–8. 802.
- Barton E, Daisley H, Gilbert D, et al. Diabetes mellitus and *Klebsiella pneumoniae* liver abscess in adults. *Trop Geogr Med* 1991;43:100–4.
- Gaskin DA, Bodonaik NC, Williams NP. Hepatic abscesses at the University Hospital of the West Indies. A 24-year autopsy review. *West Indian Med J* 2003;52:37–40.
- Yang CC, Chen CY, Lin XZ, Chang TT, Shin JS, Lin CY. Pyogenic liver abscess in Taiwan: emphasis on gas-forming liver abscess in diabetics. *Am J Gastroenterol* 1993;88:1911–5.
- Casanova C, Lorente JA, Carrillo F, Perez-Rodriguez E, Nunez N. *Klebsiella pneumoniae* liver abscess associated with septic endophthalmitis. *Arch Intern Med* 1989;149:1467.
- Aguilar J, Cruz A, Ortega C. Multiple hepatic and pulmonary abscesses caused by *Klebsiella pneumoniae*. *Enferm Infecc Microbiol Clin* 1994;12:270–1.
- Torres L, Escorihuela A, Eslava A, Losada J, Avila A. Liver abscess caused by *Klebsiella pneumoniae* associated with septic endophthalmitis. *Enferm Infecc Microbiol Clin* 1989;7:173–4.
- Couez D, Libon E, Wasteels M, Derue G, Gilbeau JP. *Klebsiella pneumoniae* liver abscess with septic endophthalmitis. The role of computed tomography. *J Belge Radiol* 1991;74:41–4.
- Cahill M, Chang B, Murray A. Bilateral endogenous bacterial endophthalmitis associated with pyogenic hepatic abscess. *Br J Ophthalmol* 2000;84:1436.
- Giobbia M, Scotton PG, Carniato A, Cruciani M, Farnia A, Daniotti E, et al. Community-acquired *Klebsiella pneumoniae* bacteremia with meningitis and endophthalmitis in Italy. *Int J Infect Dis* 2003;7:234–5.
- Lindstrom ST, Healey PR, Chen SC. Metastatic septic endophthalmitis complicating pyogenic liver abscess caused by *Klebsiella pneumoniae*. *Aust N Z J Med* 1997;27:77–8.
- Han SH. Review of hepatic abscess from *Klebsiella pneumoniae*: an association with diabetes mellitus and septic endophthalmitis. *West J Med* 1995;162:220–4.
- Chang FY, Chou MY. Comparison of pyogenic liver abscesses caused by *Klebsiella pneumoniae* and non-*K. pneumoniae* pathogens. *J Formos Med Assoc* 1995;94:232–7.
- Cheng DL, Liu YC, Yen MY, Liu CY, Wang RS. Septic metastatic lesions of pyogenic liver abscess. Their association with *Klebsiella pneumoniae* bacteremia in diabetic patients. *Arch Intern Med* 1991;151:1557–9.
- Wong TY, Chiu SI. Septic metastatic endophthalmitis complicating *K. pneumoniae* liver abscess in a non-diabetic Chinese man. *Hong Kong Med J* 2001;7:303–6.

33. Chee SP, Ang CL. Endogenous *Klebsiella* endophthalmitis—a case series. *Ann Acad Med Singapore* 1995;24:473–8.
34. Liu YC, Cheng DL, Lin CL. *Klebsiella pneumoniae* liver abscess associated with septic endophthalmitis. *Arch Intern Med* 1986;146:1913–6.
35. Liao SB, Yang KJ, Lai CC, Chen TL, Lee SC. Bilateral endogenous *Klebsiella pneumoniae* endophthalmitis associated with meningitis-useful vision regained after treatment: case report. *Chang Gung Med J* 2000;23:566–71.
36. Chiu CT, Lin DY, Liaw YF. Metastatic septic endophthalmitis in pyogenic liver abscess. *J Clin Gastroenterol* 1988;10:524–7.
37. Ohmori S, Shiraki K, Ito K, Inoue H, Ito T, Sakai T, et al. Septic endophthalmitis and meningitis associated with *Klebsiella pneumoniae* liver abscess. *Hepato Res* 2002;22:307–12.
38. Hu BS, Lau YJ, Shi ZY. Necrotizing fasciitis associated with *Klebsiella pneumoniae* liver abscess. *Clin Infect Dis* 1999;29:1360–1.
39. Dylewski JS, Dylewski I. Necrotizing fasciitis with *Klebsiella* liver abscess. *Clin Infect Dis* 1998;27:1561–2.
40. Chou FF, Kou HK. Endogenous endophthalmitis associated with pyogenic hepatic abscess. *J Am Coll Surg* 1996;182:33–6.
41. Ho PL, Tang WM, Yuen KY. *Klebsiella pneumoniae* necrotizing fasciitis associated with diabetes and liver cirrhosis. *Clin Infect Dis* 2000;30:989–90.
42. Wang TK, Wong SS, Woo PC. Two cases of pyomyositis caused by *Klebsiella pneumoniae* and review of the literature. *Eur J Clin Microbiol Infect Dis* 2001;20:576–80.
43. Kuramochi G, Takei SI, Sato M, Isokawa O, Takemae T, Takahashi A. *Klebsiella pneumoniae* liver abscess associated with septic spinal epidural abscess. *Hepato Res* 2005;31:48–52.
44. McDonald MI, Corey GR, Gallis HA, Durack DT. Single and multiple pyogenic liver abscesses: natural history, diagnosis and treatment, with emphasis on percutaneous drainage. *Medicine (Baltimore)* 1984;63:291–302.
45. Branum GD, Tyson GS, Branum MA, Meyers WC. Hepatic abscess: changes in etiology, diagnosis, and management. *Ann Surg* 1990;212:655–62.
46. Huang CJ, Pitt HA, Lipsett PA, et al. Pyogenic hepatic abscess: changing trends over 42 years. *Ann Surg* 1996;223:600–9.
47. Giorgio A, Tarantino L, Mariniello N, et al. Pyogenic liver abscesses: 13 years of experience in percutaneous needle aspiration with US guidance. *Radiology* 1995;195:122–4.
48. Saccente M. *Klebsiella pneumoniae* liver abscess, endophthalmitis, and meningitis in a man with newly recognized diabetes mellitus. *Clin Infect Dis* 1999;29:1570–1.
49. Habib AG, Tambyah PA. Community-acquired *Klebsiella pneumoniae* central nervous system infections in adults in Singapore. *Eur J Clin Microbiol Infect Dis* 2003;22:486–8.
50. Chiu CH, Su LH, Wu TL, Hung IJ. Liver abscess caused by *Klebsiella pneumoniae* in sibilings. *J Clin Microbiol* 2001;39:2351–3.
51. Lin JC, Chang FY, Fung CP, Xu JZ, Cheng HP, Wang JJ, et al. High prevalence of phagocytic-resistant capsular serotypes of *Klebsiella pneumoniae* in liver abscess. *Microbes Infect* 2004;6:1191–8.
52. Fang CT, Chuang YP, Shun CT, Chang SC, Wang JT. A novel virulence gene in *Klebsiella pneumoniae* strains causing primary liver abscess and septic metastatic complications. *J Exp Med* 2004;199:697–705.
53. Paterson DL, Ko WC, Von Gottberg A, et al. International prospective study of *Klebsiella pneumoniae* bacteremia: implications of extended-spectrum beta-lactamase production in nosocomial infections. *Ann Intern Med* 2004;140:26–32.
54. Bradford PA. Extended-spectrum β -lactamases in the 21st century: characterization, epidemiology, and detection of this important resistance threat. *Clin Microbiol Rev* 2001;14:933–51.
55. Goossens H. MYSTIC program: summary of European data from 1997 to 2000. *Diagn Microbiol Infect Dis* 2001;41:183–9.
56. Winokur PL, Canton R, Casellas JM, Legakis N. Variations in the prevalence of strains expressing an extended-spectrum β -lactamase phenotype and characterization of isolates from Europe, the Americas, and the Western Pacific region. *Clin Infect Dis* 2001;32:S94–103.
57. Wang FD, Wang LS, Liu YC, Liu CY, Lin CL, Wong WW. Successful treatment of metastatic endophthalmitis. Case reports. *Ophthalmologica* 1989;198:124–8.
58. Tang LM, Chen ST, Hsu WC, Chen CM. *Klebsiella* meningitis in Taiwan: an overview. *Epidemiol Infect* 1997;119:135–42.