A case of acute cholecystitis caused by methicillin-resistant *Staphylococcus aureus* in an immunocompromised patient

Joseph Kim MD FRCPC[1], Daniel B Gregson MD FRCPC[1,2,3], Deirdre L Church MD PhD FRCPC[1,2,3]

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Although infections with *Staphylococcus aureus* can implicate multiple organ systems, involvement of the biliary tract is rare. A case of acute cholecystitis and bacteremia with methicillin-resistant *S aureus* (MRSA) in a patient with HIV infection is presented. The MRSA isolate was found to be a community-associated strain. The present case highlights the invasive nature of staphylococcal infections and the emerging importance of community-associated MRSA strains.

Key Words: *Cholecystitis; Hematogenous seeding; HIV; Methicillin-resistant* Staphylococcus aureus

Un cas de cholécystite aiguë causée par un *Staphylococcus aureus* résistant à la méthicilline chez un patient immunocompromis

Même si les infections par le *Staphylococcus aureus* peuvent toucher de multiples systèmes organiques, l'atteinte du tractus biliaire est rare. Un cas de cholécystite aiguë et de bactériémie causé par un *S aureus* résistant à la méthicilline (SARM) chez un patient ayant une infection par le VIH est présenté. Il a été établi que l'isolat du SARM était de souche non nosocomiale. Le présent cas souligne la nature envahissante des infections staphylococciques et l'importance émergente des souches non nosocomiales du SARM.

The spectrum of diseases caused by *Staphylococcus aureus*, an invasive Gram-positive pathogen, is wide. While metastatic infections leading to suppurative complications in bones, joints and lungs are common, staphylococcal infections of the biliary tract are rare (1). Recently, the rapid emergence of community-associated methicillin-resistant *S aureus* (CA-MRSA), a genetically distinct epidemic strain, has raised a serious concern (2,3). We report a case of acute cholecystitis caused by CA-MRSA in a patient with HIV infection.

CASE PRESENTATION

A 36-year-old Aboriginal woman presented with a four-day history of right upper quadrant abdominal pain and fever. Other symptoms included productive cough, nausea, vomiting, nonbloody diarrhea and anorexia. Her medical history was remarkable for longstanding HIV infection and untreated hepatitis C infection. According to the patient, her usual antiretroviral treatment consisting of zidovudine, lamivudine and ritonavir-boosted lopinavir was discontinued for two months due to gastrointestinal side effects. She had not been assessed at the Southern Alberta HIV Clinic for more than five years before this presentation because she had relocated to a different city. Previously, she had a history of noncompliance with treatment and clinic appointments. Her historical CD4 cell count and viral load results were not available since her last visit to the regional HIV clinic. She admitted to alcohol use and active intravenous drug use with crack cocaine.

On initial physical examination, she appeared diaphoretic with the following vital signs: blood pressure of 124/86 mmHg, pulse of 114 beats/min, respiratory rate of 24 breaths/min, temperature of 38.5°C and oxygen saturation of 98% on ambient air. The rest of her physical examination was remarkable for right upper quadrant tenderness with voluntary guarding and rebound tenderness. Bronchial breath sounds at the right lung base were also appreciated on auscultation. Laboratory investigations in the emergency department noted the following abnormalities: total leukocyte count of 18.8×10^9/L (range 4.0×10^9/L to 11.0×10^9/L), platelet count of 127×10^9/L (range 150×10^9/L to 400×10^9/L) and alkaline phosphatase level of 146 U/L (range 30 U/L to 145 U/L). The remainder of the blood chemistry tests and liver enzyme levels were within normal limits. Blood and urine cultures were obtained. Chest roentogram showed chronic scarring and a pulmonary nodule in the right middle lobe area. Abdominal ultrasound revealed a distended gallbladder containing sludge and a solitary stone measuring 1.2 cm in diameter. The gallbladder distention and presence of pericholecystic fluid suggested acute inflammation of the gallbladder. Subsequent enhanced computed tomography confirmed the ultrasound findings (Figure 1) and showed multiple cavitary pulmonary lesions bilaterally, suggestive of septic emboli. Empirical intravenous antimicrobial therapy with 1 g of vancomycin (15 mg/kg) every 12 h, 3.375 g of piperacillin/tazobactam every 6 h, and 350 mg of gentamicin daily, was started. The patient was admitted to the general surgery service with a diagnosis of acute cholecystitis. She underwent urgent percutaneous cholecystostomy for decompression and drainage.

Two days after the admission, *S aureus* was isolated from blood and bile fluid cultures. Methicillin resistance in the clinical isolate was identified on VITEK Gram-positive susceptibility card (bioMerieux Inc, USA) and confirmed with growth on agar screen plates supplemented with oxacillin (6 mg/L) and detection of the *mec*A gene.

[1]*Division of Infectious Diseases, Department of Medicine;* [2]*Department of Pathology and Laboratory Medicine, University of Calgary;* [3]*Calgary Laboratory Services, Calgary, Alberta*

Correspondence and reprints: Dr Joseph Kim, Division of Infectious Diseases, Department of Medicine, University of Calgary, 3A151-7007, 14 Street Southwest, Calgary, Alberta T2V 1P9. Telephone 403-943-8823, e-mail joskim@ucalgary.ca

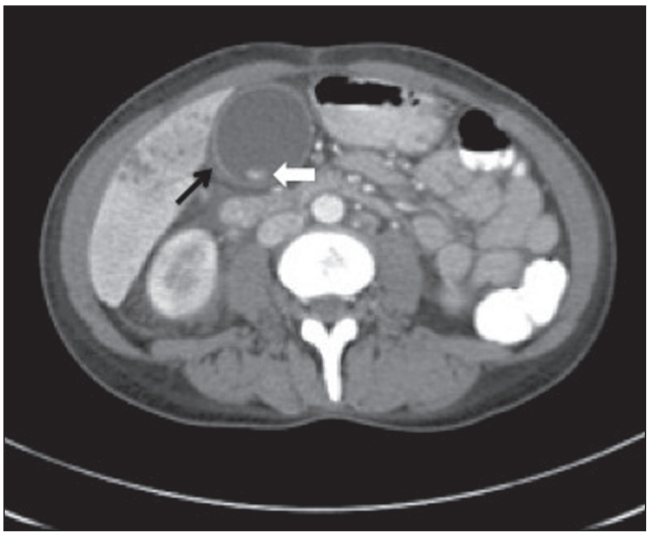

Figure 1) *Enhanced computed tomography of the abdomen showing an enlarged gallbladder with sludge and a solitary stone measuring 1.2 cm (white arrow). Pericholecystic fluid is also present (black arrow)*

Susceptibility testing was performed with VITEK or Kirby Bauer methods, plus a D test for clindamycin susceptibility (4). The MRSA isolate was susceptible to vancomycin, trimethoprim-sulfamethoxazole, doxycycline, rifampin, clindamycin and linezolid, but resistant to oxacillin, cefazolin, erythromycin and levofloxacin. Strain typing was performed with pulsed-field gel electrophoresis after DNA extraction and digestion with *Sma*1 according to standard protocol (5). Identification of MRSA isolates matching the CMRSA10 strain was based on the similarity of pulsed-field gel electrophoresis patterns to control strains provided by the National Microbiology Laboratory of the Public Health Agency of Canada.

Transesophageal echocardiography did not reveal any evidence of valvular vegetation. The antimicrobial therapy was narrowed to intravenous vancomycin (1 g every 12 h) and oral trimethoprim-sulfamethoxazole (10 mg/kg divided every 12 h). Repeat blood cultures at 48 h were still positive for MRSA and eventually became negative at five days after the initiation of antibiotic therapy. Because the patient developed a significant rash and neutropenia while on the antimicrobial therapy, the regimen was modified to 600 mg of oral linezolid every 12 h.

The duration of her hospitalization was four weeks and was complicated by intolerance to antimicrobial therapy, acute renal failure and chronic abdominal pain. Absolute CD4 lymphocyte count during the hospitalization was 137 cells/mm^3. She was discharged from the hospital with a cholecystostomy tube, and a follow-up was arranged with the attending surgeon for consideration of cholecystectomy. Prophylaxis for *Pneumocystis jiroveci* infection with dapsone was also prescribed. One week after discharge from the hospital, the patient was readmitted with abdominal pain – secondary to a suspected blocked cholecystostomy tube. She had eventual resolution of symptoms once a new drain was inserted. A repeat computed tomography scan of the chest showed smaller pulmonary nodules compared with five weeks earlier, suggesting resolving septic emboli. The patient completed a six-week course of anti-MRSA therapy in hospital.

DISCUSSION

Acute cholecystitis starts with an obstruction of the cystic duct, which leads to ischemia and inflammation. Infection may complicate 20% to 50% of cases (6). Members of the Enterobacteriaceae family, *Enterococcus* species and anaerobes are the most common organisms found in infected bile fluid (7). In contrast, isolation of *S aureus* is rare, accounting for 0.8% to 5.6% of organisms cultured from cholecystectomy specimens (7-9). Merchant and Falsey (10) reported three cases of *S aureus* acute cholecystitis associated with bacteremia. The authors concluded that *S aureus* cholecystitis with bacteremia, while rare, should prompt an investigation for an endovascular source. Interestingly, two of three patients in their series had MRSA with one fatal outcome. In another report, a 75-year-old vascular surgery patient died of MRSA gall bladder empyema following a previous episode of MRSA bacteremia (11).

Similar to the cases reported in the literature, our patient had concomitant bacteremia. It was unclear whether the gallbladder represented a metastatic focus or the source. Hematogenous cholecystitis has been described in other infections including typhoid fever (12,13). Given her risk factors, hematogenous seeding of the gallbladder was thought to be likely and, despite a negative transesophageal echocardiography result, the presence of multiple pulmonary septic emboli was highly suspicious for tricuspid valve bacterial endocarditis. Consequently, the patient was treated with a prolonged course (six weeks) of anti-MRSA therapy.

The overall prevalence of MRSA is increasing (14,15). More alarming has been the rapid dissemination of CA-MRSA strains, of which CMRSA10 is the predominant prototype (16,17). For instance, CA-MRSA strains now account for the majority of skin and soft tissue infections, as well as a significant proportion of bacteremias in the United States (18,19). CA-MRSA strains are genetically and phenotypically distinct from health care-associated strains (17), which may explain their propensity to spread readily and cause invasive diseases including necrotizing fasciitis and pneumonia (20,21).

To our knowledge, this is the first reported case of MRSA cholecystitis occurring in an HIV-infected patient. There are several unique features to the current case presentation. Using molecular techniques, we were able to determine that the strain was CMRSA10. This reflects the changing local epidemiology of *S aureus* because approximately 20% of all *S aureus* isolates are methicillin resistant, and CMRSA10 accounts for more than one-half of all MRSA strains in our health region (unpublished data from Calgary Laboratory Services and Provincial Laboratory for Public Health). Another feature is the host factor. Cholecystitis in HIV-infected patients typically implicates viral and protozoan agents (8). In 1990, Yao and Scialdone (22) reported a single case of gallbladder empyema in an AIDS patient in whom *S aureus* was isolated. Unfortunately, the antimicrobial susceptibility profile was not available. Although the authors speculated that such patients were more susceptible to bacterial infections, it is unclear whether staphylococcal infections are more common in this patient population.

Our case highlights the importance of being cognizant of local microbiological epidemiology. Physicians should also be aware that hematogenous seeding can be a cause of acute cholecystitis, and *S aureus*, including MRSA, should be considered in the differential diagnosis, particularly in high-risk patients. In areas where MRSA is endemic, unusual infectious presentations may warrant anti-MRSA antimicrobials, such as vancomycin, in the initial empirical therapy until culture results are available.

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