



Case Report

Livestock-associated methicillin-resistant *Staphylococcus aureus* (clonal complex 398) causing bacteremia and epidural abscessM. Murra^{a,*}, K.L. Mortensen^b, M. Wang^a^a Department of Clinical Microbiology, Aarhus University Hospital, Aarhus, Denmark^b Department of Infectious Diseases, Aarhus University Hospital, Aarhus, Denmark

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) clonal complex (CC) 398 has spread from pigs to humans, but rarely from person to person. This strain of MRSA has been considered less virulent than others. Livestock-associated MRSA CC398 (LA-MRSA CC398) is particularly known to colonize pig farmers. Recent studies have shown an increasing number of people colonized with LA-MRSA CC398 and invasive infections caused by LA-MRSA CC398. The case of a previously healthy, 61-year-old woman admitted to a Danish regional hospital is reported here. She presented with fever, severe back pain, and bilateral hyperreflexia of patellar and Achilles reflexes. Blood tests revealed leukocytosis and elevated C-reactive protein. Empiric antimicrobial therapy with intravenous piperacillin–tazobactam was initiated, but blood cultures grew MRSA and antimicrobial therapy was changed to intravenous vancomycin. Whole-genome sequencing showed that the MRSA strain belonged to LA-MRSA CC398 spa type t011 and was Pantón–Valentine leukocidin-negative. Magnetic resonance imaging revealed an epidural abscess at the level of L1–L4. Surgery was performed and pus from the abscess grew MRSA. The duration of antimicrobial therapy was 12 weeks. This case report describes bacteremia with LA-MRSA CC398 in a previously healthy patient without exposure to livestock or previous admission to a hospital. This highlights the risk of person-to-person transmission of LA-MRSA CC398 and brings into question whether LA-MRSA CC398 may have a greater pathogenic potential than previously assumed.

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Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) clonal complex (CC) 398 is associated with livestock and is known for colonizing farmers working on pig farms. Livestock-associated MRSA CC398 (LA-MRSA CC398) has been isolated from various types of livestock (cattle, chicken, and horses), but pigs remain the primary host (Fitzgerald, 2012). For a long time, LA-MRSA CC398 has been known to spread from pigs to humans, but rarely from person to person. LA-MRSA CC398 is reckoned to be less virulent than human MRSA strains (van Cleef et al., 2010; Vekade and Kluytmans, 2014; Smith and Pearson, 2011; van Rijen et al., 2008; Wassenberg et al., 2011).

Several studies have shown that there has been a rapid increase in the number of people colonized with LA-MRSA CC398 in recent years. Not all of the colonized people have had livestock exposure (Larsen et al., 2015; Lekkerkerk et al., 2015). The incidence of

invasive infections caused by LA-MRSA CC398 has likewise increased and peaked in 2014 in Denmark (Larsen et al., 2017).

A severe case of infection with LA-MRSA CC398 presenting with bacteremia and an epidural abscess is presented here.

Case report

A previously healthy, 61-year-old woman was admitted to a Danish regional hospital in August 2016. She presented with severe back pain located to the lumbar region and radicular pain in both legs. On admission she was febrile with a rectal temperature of 38.1 °C and had bilateral hyperreflexia of the patellar and Achilles reflexes. The knee and ankle reflexes were unaffected, while strength over the hip joints was decreased. Blood tests revealed leukocytosis and elevated C-reactive protein of 425 mg/l. Infectious spondylitis was suspected.

A computed tomography scan of thorax and abdomen performed on the night of admission did not reveal a site of infection. Empiric antimicrobial treatment with intravenous piperacillin–tazobactam 4 g three times daily was initiated.

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Two days later, blood cultures grew MRSA and the antimicrobial treatment was changed to intravenous vancomycin 1 g twice daily. The following day the patient was transferred to the department of neurosurgery. Magnetic resonance imaging (MRI) showed an epidural abscess at level L1–L4 (Figure 1, arrows). A hemilaminectomy and drainage of the abscess was performed. Pus from the abscess grew MRSA similar to the blood culture isolates.

On the fifth day of hospitalization, the patient was transferred to the department of infectious diseases for continued antimicrobial treatment. Further investigation revealed that the patient had been colonized with LA-MRSA CC398 since October 2015 and that the MRSA strain had been found in a leg wound at that time. She did not have direct contact with livestock, but her husband had contact with cattle. However her husband was found to be negative for MRSA in surveillance cultures from the nose, throat, and perineum and was therefore not considered the source of MRSA transmission. The patient reported having close friends with occupational contact with pigs; however these friends were not household contacts.

A repeat MRI 10 days after admission showed regression of the abscess, but there was inflammation related to the bone structures. Therefore moxifloxacin 400 mg once daily was added. In total she received vancomycin for 4 weeks and moxifloxacin for 12 weeks. There has been no evidence of ongoing MRSA colonization at follow-up visits. However, the patient suffered from several complications including neuropathic pain, ataxia, and bladder and fecal incontinence. She has subsequently received an ileostomy.

Whole-genome sequencing (WGS) performed at Statens Serum Institute (SSI) showed that the blood culture strain belonged to LA-MRSA CC398 spa type t011 and was Pantón–Valentine leukocidin-negative. The strain was positive for the virulence factors gamma-hemolysin A (hlgA), hlgC, hlgB, and hemolysin B. WGS was also performed on the initial MRSA strain isolated from the patient's leg wound. This isolate was identical to the blood culture isolate.

In the Department of Clinical Microbiology at the authors' institution, only MRSA suspected to be a part of an outbreak is investigated by WGS. Only 72 MRSA isolates out of 3760 MRSA isolates obtained during the years 2010–2017 were examined by WGS, and 20 out of the 72 MRSA belonged to CC398. Comparison was performed using a constructed phylogenetic tree from single nucleotide polymorphism differences in genome sequences. This

comparison showed no similarity between the patient's LA-MRSA CC398 and the LA-MRSA CC398 in the institutional collection.

Discussion

This case report describes a severe infection with LA-MRSA CC398 causing an epidural abscess and bacteremia in a previously healthy 61-year-old woman. The patient received antimicrobial treatment for 12 weeks, and she sustained sequelae in the form of incontinence and decreased sensitivity and strength in both legs.

Colonization with LA-MRSA CC398 is strongly associated with direct exposure to livestock, especially contact with pigs. However, the patient had not had any occupational exposure to livestock. The patient's husband had contact with cattle, but he was negative for MRSA in surveillance cultures. She did have close friends with occupational contact with pigs; however, as these friends were not household contacts, they would not be considered a risk factor for LA-MRSA acquisition.

It is suspected that in this case LA-MRSA CC398 was transmitted from person to person. As the patient's husband was found negative for MRSA, the MRSA transmission may have occurred outside the household.

Recent studies have shown that LA-MRSA CC398 is increasingly isolated from people without exposure to livestock. Larsen et al. reported that 148 of 416 LA-MRSA CC398 isolated between 1999 and 2011 were from patients with infections, and that 51 of the 148 patients (34%) with an infection did not have exposure to livestock (Larsen et al., 2015). Another recent Danish study investigated LA-MRSA CC398 in bloodstream infections (BSI) and skin and soft tissue infections (SSTI) in 2010–2015. The study found that 32% of patients with LA-MRSA CC398 SSTI and 59% of patients with LA-MRSA CC398 BSI did not have exposure to livestock. Furthermore, six fatal cases of LA-MRSA CC398 bacteremia were reported in that study, which underlines the pathogenic potential of LA-MRSA CC398. None of the patients who died had been exposed to livestock (Larsen et al., 2017).

In this case, LA-MRSA CC398 caused an epidural abscess and bacteremia in a previously healthy patient without direct livestock exposure. The case highlights the risk of person-to-person transmission of LA-MRSA CC398 and raises concerns about the possibility of LA-MRSA CC398 causing invasive infections in the general population. LA-MRSA CC398 may have a greater pathogenic potential than previously assumed and is not limited to at-risk people due to livestock exposure or predisposing disease.

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Consent

Informed consent was obtained from the patient.

Conflict of interest

The authors of this paper have no conflicts of interest.

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Figure 1. Arrows showing the epidural abscess from L1–L4.

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