Empyema caused by MRSA ST398 with Atypical Resistance Profile, Spain

To the Editor: We report a case of empyema caused by methicillin-resistant *Staphylococcus aureus* (MRSA) sequence type ST398 in a 79-year-old man in Spain who had severe chronic obstructive pulmonary disease. In 2009, the patient was hospitalized in the intensive care unit because of decompensation of his chronic obstructive pulmonary disease, profound iliofemoral venous thrombosis, right pneumothorax, and lung carcinoma. Thoracic drainage, support measures, and intravenous levofloxacin were initiated, but no clinical improvement was seen. Purulent exudates from the thoracic drainage tube and of a tracheal aspirate were cultured. MRSA was isolated from both samples and from a nasal swab. Antimicrobial drug therapy was changed from levofloxacin to intravenous linezolid, but the patient's clinical situation rapidly worsened, and he died of multiorgan failure.

The 3 MRSA isolates were typed (multilocus sequence typing-, *spa*-, staphylococcal cassette chromosome [SCC] *mec*-, and *agr*-typing, in addition to pulsed-field gel electrophoresis [PFGE]), likewise, the antimicrobial drug–resistance phenotypes and genotypes, and virulence genes were determined (*1*,*2*). All 3 MRSA isolates were typed as sequence type (ST) 398, *spa*-type t011, SCC*mec*V, and *agr*I. The 3 isolates had the same resistance phenotype, including to β-lactams, tetracycline, clindamycin (but not erythromycin), ciprofloxacin, and levofloxacin. We confirmed the presence of *mec*A, *tet*M, *tet*K, and *vga*(A) genes by PCR and sequencing; however, PCRs for *lnu*(A), *lnu*(B), *lnu*(C), *lnu*(D), *cfr*, *vga*(C), *lsa*(B), and *tetL* genes were negative. Primers used for detection of *vga*(A) gene were F-5′-GAAACTCTTATTC GAACYATTCTAGC-3′ and R-5′-GGTTCAATACTCAATCGACT-GAG-3′. Specific amino acid changes in the quinolone-determining region of GyrA and ParC proteins (S84L and S80F, respectively) were detected by PCR and sequencing (*1*). All 3 MRSA isolates were negative by PCR for the Panton-Valentine leukocidin, toxic shock syndrome toxin 1, and exfoliative toxins A and B.

The patient lived with his wife and 2 sons near a pig farm. Both sons worked on the farm; the patient, but not his wife, helped sporadically on the farm. Nasal samples from the 3 family members indicated MRSA carriage in 1 son but not in the other son or the patient's wife. The characteristics of the nasal MRSA strain recovered from the son were identical to those previously detected in MRSA strains from the patient (Table). In addition, nasal swabs from 18 pigs on the farm were randomly taken, and MRSA isolates were detected in 9 (50%) pigs; 1 MRSA isolate per animal was further characterized. Eight isolates were typed as ST398/t011/SCC*mec*V/*agr*I, and the remaining one as ST398/t1451/SCC*mec*V/*agr*I. All animal isolates had the same resistance phenotype and genotype as the MRSA isolates from the patient and son. None harbored the studied virulence factors (Table). All isolates had an unusual clindamycin-resistance/erythromycin-susceptibility phenotype and harbored the *vga*(A) gene.

We analyzed all MRSA isolates of human and animal origins by *Apa*I-PFGE (*2*) and compared patterns as previously recommended (*3*). Only 1 pulsotype (A) and 3 closely related subtypes were identified (A1, A2, and A3). One MRSA isolate obtained from pleural fluid of the patient, 2 isolates from nasal swabs (patient and son), and most isolates from animals showed the same PFGE pulsotype and subtype (A1). Alternatively, 1 MRSA isolate from bronchial aspirate of the patient and 2 isolates from animals showed closely related patterns (subtypes A2 and A3).

Other studies have suggested clonal spread and transmission of MRSA ST398 between pigs and persons who work with them (*4*,*5*). This microorganism has been generally associated with skin and soft tissue infections in humans (*6*). Nevertheless, severe infections by ST398 also have been sporadically described, and the report of 7 pneumonia cases associated with mechanical ventilation in central Europe is relevant (*7*). In general, ST398 isolates have fewer virulence factors than do other clones of MRSA (*2*); nonetheless, human infections from Panton-Valentine leukocidin–positive ST398 isolates have been reported (*8*). The immunocompromised status of patients in intensive care units could favor dissemination of ST398 in this environment.

MRSA ST398 implicated in the described empyema was resistant to the first-line antimicrobial agent used for treatment (levofloxacin, MIC 4 mg/L) that was associated with amino acid changes in GyrA and ParC proteins, which could have accelerated the deteriorating evolution of the patient's respiratory infection. The atypical clindamycin-resistance/erythromycin-susceptibility phenotype detected in our human and animal MRSA strains is infrequently detected in clinical MRSA isolates from humans. Nevertheless, this phenotype might be emerging among livestock MRSA isolates, as we and others (*9*,*10*) have observed. The *vga*(A) gene detected in these isolates could be responsible for this resistant phenotype, as has been recently reported by others (*10*).

In conclusion, we report potential pig-to-human transmission of MRSA ST398. MRSA ST398 can be associated with severe respiratory pathology in immunocompromised patients, and these microorganisms could also be resistant to other first-line antimicrobial agents, such as fluoroquino-

Table. Characteristics of methicillin-resistant *Staphylococcus aureus* strains recovered from humans and animals, Spain, 2009*

Strain	Origin	SCC*mec* type	MLST/*spa* type	*agr*	PFGE	Antimicrobial resistance phenotype	Resistance genes detected	Amino acid change	
								GrlA	GyrA
C2355	Patient, pleural fluid	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2354	Patient, bronchial aspirate	V	ST398/t011	I	A2	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2634	Patient, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2664	Son, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2669	Pig 1, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2670	Pig 2, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2694	Pig 3, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2695	Pig 4, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2697	Pig 5, nasal swab	V	ST398/t011	I	A3	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2698	Pig 6, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2700	Pig 7, nasal swab	V	ST398/t011	I	A3	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2704	Pig 8, nasal swab	V	ST398/t011	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L
C2706	Pig 9, nasal swab	V	ST398/t1451	I	A1	OXA-CLI-TET-CIP-LEV	*mecA*, *tetK*, *tetM*, *vga*(A)	S80F	S84L

*All strains were susceptible to fusidic acid, fosfomycin, gentamicin, tobramycin, mupirocin, trimethoprim-sulfamethoxazole, vancomycin, teicoplanin, quinupristin/dalfopristin, and tigecycline. SCC, staphylococcal cassette chromosome; MLST, multilocus sequence typing; PFGE, pulsed-field gel electrophoresis; ST, sequence type; OXA, oxacillin; CLI, clindamycin; TET, tetracycline; CIP, ciprofloxacin; LEV, levofloxacin.

lones, used to treat these infections. Moreover, the unusual clindamycin-resistance/erythromycin-susceptibility phenotype might be a key marker (in addition to tetracycline resistance) for the possible presence of livestock-associated MRSA.

C.L. has a fellowship from the Ministerio de Ciencia e Innovación of Spain. E.G.-S. has a fellowship from the Gobierno de la Rioja of Spain. This work was partially supported by Project SAF2009-08570 from the Ministerio de Ciencia e Innovación of Spain and Fondo Europeo de Desarrollo Regional.

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DOI: 10.3201/eid1701.100307

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Intensive Care Unit Admission for Pandemic (H1N1) 2009, Reunion Island, 2009

To the Editor: We report results of the prospective surveillance system established in the largest intensive care unit (ICU) of Reunion Island (25 beds). This system covers 500,000 residents (62% of the total population) and monitors the daily status of patients >17 years of age who had a positive reverse transcription–PCR (RT-PCR) for pandemic (H1N1) 2009 virus. Reunion Island is a French overseas territory in the Southern Hemisphere, with health care facilities similar to those of mainland France. Patients were followed up until discharge from the ICU or death. Data were collected during July 15–September 30, 2009.

Of 148 patients with confirmed pandemic (H1N1) 2009 infection admitted to the hospital, 13 (9%) patients (8 female) were admitted to the ICU. These corresponded to 7% of all 187 patients admitted to the ICU during the same period. Median age was 39.4 (±19) years (range 17–69 years). Ten patients were admitted for respiratory failure related to viral pneumonitis, 1 for pulmonary edema with severe chronic coronary insufficiency, 1 for congenital adrenal insufficiency with reversible multiple organ failure, and 1 for status epilepticus. Eleven (85%) patients had underlying concurrent medical conditions: 3 were overweight (body mass indexes 38, 32, and 29.3 kg/m^2); 1 was pregnant and had asthma.

Four (31%) patients died. One was a 28-year-old woman with cerebral motor infirmity and severe chronic restrictive respiratory failure. An 18-year-old woman with aplasia after receipt of an allograft for Hodgkin lymphoma died of cerebral hemorrhage while receiving extracorporeal membrane oxygenation. A 52-year-old man admitted for pulmonary edema with severe coronary insufficiency died of multiple organ failure. A 33-year-old man with no known concurrent medical conditions died of acute respiratory distress syndrome. Time from ICU admission to death ranged from 15 to 85 days (mean 36.5 ± 32 days). Mean age of patients who died was 32.5 ± 14.3 years.

Chest radiographic findings were abnormal for all patients except 1, who was admitted for fever and convulsions (Huntington chorea). Bilateral pulmonary embolism was confirmed in an obese patient who survived.

Mean time between onset of clinical signs and ICU admission was 6.9 ± 3.2 days. Mean time between admission to ICU with diagnosis confirmed by RT-PCR and initiation of antiviral treatment was 1.8 ± 1.7 days and between illness onset and initiation of antiviral treatment, 8.8 ± 3 days (range 4–16 days). Mean length of ICU stay was 26.3 ± 29.3 days. Patients remained in the ICU for a total of 201 bed-days (402 per million residents). The maximum daily occupancy of the ICU was 10 beds per million residents.

Five patients received steroids for severe hypotension or asthma-like clinical illness. Severe hypotension developed in 5 patients, and they received vasopressors. No patient received intravenous immunoglobulins. Ten (77%) patients required mechanical ventilation for a median of 11.5 ± 12.2 days. One patient required high-frequency ventilation, 3 required extracorporeal membrane oxygenation, and 1 required hemodialysis. Multiple organ failure developed in 3. All patients were empirically given antibacterial drugs. Secondary infections were either documented or strongly suspected for 5 patients.

All patients received oral oseltamivir beginning 4–16 days after illness onset and continuing for 2–17 days (mean 7.2 ± 4.3). Zanamivir was administered 1 time by inhalation through the ventilator. Viral loads in respiratory specimens ranged from 4×10^3 to 6.9×10^7 copies/mL (mean 1.4×10^5). Two patients excreted virus in their bronchoalveolar lavage specimens for a prolonged time (14 days).

The most prominent biological findings were elevated serum levels of procalcitonin, C-reactive protein, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, and creatine kinase. Eight patients had lymphopenia (<1,200 cells/mm^3).

Our findings are consistent with findings of other studies of severe or fatal viral pneumonia in younger patients than are usually affected in a normal influenza season (*1–4*), particularly in patients with concurrent medical conditions. In our study, the 3 overweight patients survived. Obesity is associated with increased severity of illness, but not always with death, in critically ill patients (*5*). We confirm that previously healthy young persons can die of pandemic (H1N1) 2009, although at a much lower rate than those infected in the initial outbreaks