

## Pediatric Pneumonia Death Caused by Community- acquired Methicillin- Resistant *Staphylococcus aureus*, Japan

**To the Editor:** Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), which carries genes for Panton-Valentine leukocidin (PVL), has become a major concern worldwide (1–3). CA-MRSA is mainly associated with skin and soft tissue infections in young, otherwise healthy, persons in the community (3) and also with life-threatening sepsis and community-acquired pneumonia (preceded by influenza) (1,3,4). The role of PVL in the pathogenesis of staphylococcal infections is controversial. Whereas Labandeira-Rey et al. (5) provided data that PVL, in combination with staphylococcal protein A, destroys respiratory tissue and bacteria-engulfing immune cells, Voyich et al. (6) and Bubeck Wardenburg et al. (7) showed that PVL was not essential for the pathogenesis of skin disease, sepsis, or pneumonia in a mouse model.

Several types of CA-MRSA clones exist, e.g., CA-MRSA belonging to multilocus sequence type (ST) 1 (called the USA400 clone) and ST8 (called the USA300 clone), which have been major clones in North America (recently, USA300 is becoming more prominent); CA-MRSA belonging to ST80, which has been a major clone in Europe; and CA-MRSA belonging to ST30, which is distributed worldwide, including Japan (2,8). MRSA carrying the PVL gene (a marker of CA-MRSA [ST30]) comprises 0.1% of MRSA isolated in hospitals in Japan (9). We describe a fatal case of pediatric pneu-

monia and septic shock from CA-MRSA in Japan.

A 16-month-old, previously healthy boy was admitted to the hospital for fever and shortness of breath on August 30, 2006. He had had cold-like symptoms for 14 days and fever for the 2 previous days. On examination, hordeolum of the right eyelid and cyanosis were observed; the patient's blood pressure was 106/ (undetectable) mm Hg, tachycardia 185 beats/min, tachypnea 72 breaths/min, and temperature 39.8°C. He had bilateral coarse breath sounds, and bronchovesicular breath sounds over the right lung. Chest radiography indicated lobar consolidation and pleural effusion on the right side. Laboratory analysis showed leukocytopenia, thrombocytopenia, elevated C-reactive protein level, and hypoxemia.

Intravenous administration of sulbactam/ampicillin and cefotaxime, and oxygen inhalation was started. Oxygen saturation did not improve, and laboratory values of disseminated intravascular coagulation (DIC) were observed: platelet count 121 K/mm<sup>3</sup>, fibrinogen level 528 mg/dL, fibrin degradation products 37.7 µg/mL, prothrombin time 1.86 international normalized ratio, and D-dimer 37.7 µg/mL. The condition was considered septic shock, and consequently the boy was transferred to the pediatric intensive care unit, where he required intubation and mechanical ventilation.

Sulbactam/ampicillin was switched to meropenem, and cefotaxime was continued. On day 2 after admission, chest radiography showed bilateral consolidation. On day 3, blood culture yielded MRSA, and cefotaxime was changed to vancomycin. Meropenem therapy was continued to cover possible mixed bacterial infection. Immunoglobulin therapy and DIC syndrome treatment (nafamostat mesilate, ulinastatin, freeze-dried concentrated human antithrombin III) were also started. On day 4, computed tomographic examination detected pneumothorax and

atelectasis. Because laboratory data confirmed the presence of only MRSA, meropenem was changed to flomoxef (which belongs to the oxacephem family of β-lactam antimicrobial agents) on the expectation that a possible synergistic effect of flomoxef and vancomycin might occur. No major changes occurred on days 5 and 6. On day 7, in addition to bilateral infiltrates on chest radiography, the oxygen index was 65 (partial pressure of arterial oxygen/fraction of inspired oxygen), and the patient was considered to have acute respiratory distress syndrome. A percutaneous cardiopulmonary support system (a portable heart-lung machine that provides temporary circulatory support) was used, but in spite of treatment, there was no improvement, and the child died on day 10 after admission (September 8). An autopsy was not performed.

Molecular characterization of MRSA isolated from the blood was performed as described previously (8,9). Isolated MRSA (strain NN32) was positive for PVL, belonging to ST30:*spa*19:staphylococcal cassette chromosome *mec* (SCC*mec*)IVa, and was resistant to only β-lactam antimicrobial agents (Table).

To date, all cases of PVL-positive CA-MRSA infections officially reported in Japan were caused by strains belonging to ST30 (9). All these strains can be classified into 2 types on the basis of *spa* type (Table), for example, ST30:*spa*19:SCC*mec*IVc. This type includes strain NN1, isolated from an 11-month-old patient with bullous impetigo (8); strain NN12, isolated from a 17-year-old patient with cutaneous abscess/osteomyelitis (8); strain NN31, isolated from an 18-year-old patient with pelvic abscesses (9); and strain EB00449, isolated from a 27-year-old patient with cutaneous abscesses (9). Another type is ST765 (single locus variant of ST30):*spa*43:SCC*mec*IVx. This type includes strain DB00319, isolated from a 61-year-old hospital inpatient (9).

Table. Characteristics of PVL-positive MRSA strains reported in Japan since 2000\*

Type, gene, or resistance		PVL-positive MRSA				
		Present strain	Previous strains			
		NN32	NN1	NN12, NN31	EB 00449	DB 00319
Types	CC	30	30	30	30	30
	ST	30	30	30	30	765
	<i>spa</i>	19	19	19	19	43
	<i>agr</i>	3	3	3	3	3
	SCC <i>mec</i>	IVa	IVc	IVc	IVc	IVx*
	Coagulase	IV	IV	IV	IV	IV
Toxins						
Leukocidins	<i>lukS-PV, lukF-PV</i> †	+	+	+	+	+
	<i>lukE-lukD, lukM</i>	-	-	-	-	-
Hemolysins	<i>hla, hlg, hld</i>	+	+	+	+	+
	<i>hlb</i>	-	-	-	-	+
	<i>hlg-v</i>	-	-	-	-	-
Staphylococcal enterotoxins	<i>sea</i>	-	-	-	-	+
	<i>tst, seb, sec, sed, see, seh, sej, sek, sep</i>	-	-	-	-	-
	<i>egc</i> ‡	+	+	+	+	+
	<i>seu</i>	+	+	+	+	+
Exfoliative toxins	<i>eta, etb, etd</i>	-	-	-	-	-
Others	<i>set</i>	+	+	+	+	+
	<i>edin</i>	-	-	-	-	-
Adhesins						
	<i>icaA, sdrD, sdrE</i>	-	-	-	-	-
	<i>icaD, cna</i> ,§	+	+	+	+	+
	<i>eno, fnbA, fnbB, ebpS, clfA, clfB, fib, sdrC, bbp</i> ¶					
Drug resistance and penicillinase plasmid	Aminoglycosides			GEN# KAN#*		GEN** KAN** STR** ERY** CLI**
	Macrolides					
	Lincosamides					
	Tetracycline			TET#		
	Penicillinase plasmid (kb)	+	+	+	+	+
		(33)	(33)	(33)	(33)	(40)**

\*PVL, Panton-Valentine leukocidin; MRSA, methicillin-resistant *Staphylococcus aureus*; SCC*mec* IVx, staphylococcal cassette chromosome *mec* type IV with unknown subtypes; +, positive; -, negative; GEN, gentamicin; KAN, kanamycin; STR, streptomycin; ERY, erythromycin; CLI, clindamycin; TET, tetracycline.

†GenBank accession nos. for the PVL gene sequences from strains NN32 and NN1 are AB286959 and AB186917, respectively.

‡*egc*, enterotoxin gene cluster, including *seg, sei, sem, sen, seo* genes.

§*cna*, gene encoding for collagen binding protein (adhesin).

¶*bbp*, gene encoding for bone sialoprotein binding protein (adhesin).

#Drug resistance encoded by a conjugative drug resistance plasmid (pGKT1) (8).

\*\*Multidrug-resistant penicillinase plasmid encoding for resistance to GEN, KAN, STR, ERY, and CLI, in addition to penicillin resistance (9).

The molecular characteristics of strain NN32 were similar to those of strain NN1, except for SCC*mec*IV subtypes (Table). Moreover, pulsed-field gel electrophoresis patterns (data not shown) and the PVL gene sequences of the 2 strains (NN32 and NN1) were identical (Table).

This case of CA-MRSA ST30 infection in a child represents a progression from common cold-like symp-

toms (occurring outside the influenza season) to fatal pneumonia, despite intensive therapy, including the administration of sensitive antimicrobial agents. CA-MRSA ST30 contains several genes that mediate adhesion (e.g., *cna* and *bbp*) and toxin genes (PVL and *egc*, which encode for at least 5 superantigens, including staphylococcal enterotoxin G, I, M, N, and O). The gene cluster *egc* is associated

with septic shock (10). Further studies are needed to clarify the pathogenesis of community-acquired pneumonia caused by CA-MRSA.

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## Rarity of Influenza A Virus in Spring Shorebirds, Southern Alaska

**To the Editor:** Knowledge of avian influenza (AI) virus and its host epidemiology and ecology is essential for effective monitoring and mitigation (1). Applicability of global and continental-scale models will be key for expanding this knowledge base. Research in the Delaware Bay area, eastern United States, suggests an ecologic and epidemiologic viewpoint of AI virus in wild birds in which shorebirds (family Scolopacidae) are predominant hosts in spring; however, research in Alberta, Canada, suggests that waterfowl are such in autumn (2,3). AI virus surveillance in Europe (4) suggests that the spring aspect of this scenario does not apply there. To increase knowledge of AI transport among shorebirds in spring in the North Pacific, we conducted AI virus surveillance during the springs of 2006 and 2007 at the Copper River Delta area of Alaska. Millions of birds congregate at this location in the spring, resulting in the highest spring shorebird concentrations in the New World (5). We also sampled gulls (Laridae), which are common and heretofore unsurveyed for AI in this ecosystem.

In 2006 and 2007, 1,050 shorebirds (Western Sandpiper, *Calidris mauri*, and Least Sandpiper, *C. minutilla*) and 770 Glaucous-winged Gulls (*Larus glaucescens*) were sampled during peak spring migration at Hartney Bay, Cordova, Alaska (60°28'N 146°8'W; Table). Fresh fecal samples were obtained from tidal flats within <1 to 90 min after identified flocks were dispersed, and samples were placed in sterile medium (brain heart infusion buffer with 10,000 U/mL penicillin G, 1 mg/mL gentamicin, and 20 µg/mL amphotericin B) and either kept cool (<1 week) before transport to Fairbanks (2006) or placed into liquid nitrogen within 2 h of collection