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Original article

Incidence of Community-associated Methicillin-resistant *Staphylococcus aureus* Infections in a Regional Hospital

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Abstract

Background and Objective: Since the early 2000s, the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections among the community of people lacking known healthcare risk factors has increased. This MRSA infection is referred to as community-associated MRSA (CA-MRSA) infection and is distinct from hospital-associated MRSA (HA-MRSA) infection, which occurs among people with known healthcare risk factors. Understanding the epidemiology of CA-MRSA infections is critical; however, this has not been investigated in detail in Japan. Our objective was to investigate the incidence of CA-MRSA infections in a regional hospital.

Patients and Methods: We investigated CA-MRSA isolates and infections in a rural regional hospital by reviewing medical records of one year. Infections were classified as CA-MRSA if no established risk factors were identified.

Results: During 2008, 31 *Staphylococcus aureus* (*S. aureus*) isolates were detected in 29 unique patients, with 1 methicillin-sensitive *S. aureus* (MSSA) isolates obtained from 19 patients (66%) and MRSA obtained from 10 patients (34%). In the 10 patients with MRSA, the number of HA-MRSA and CA-MRSA cases were nine (32% of patients with *S. aureus* isolates) and one (3%), respectively. The patient with CA-MRSA was diagnosed with cellulitis due to CA-MRSA. All nine patients with HA-MRSA exhibited colonization.

Conclusion: We observed a CA-MRSA case in a regional hospital in Japan, suggesting that incidence trends of CA-MRSA should be considered in future research and treatment.

Key words: community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA), hospital-associated MRSA (HA-MRSA), skin and soft tissue infection (SSTI), incidence, colonization

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Introduction

Over the past decade, a new clinical presentation has emerged that is characterized by patients in the community without risk factors and hospital contact not presenting methicillin-resistant *Staphylococcus aureus* (MRSA) infections. This new entity is referred to as community-associated MRSA (CA-MRSA) infection and is distinct from hospital-associated MRSA (HA-MRSA) infection, which occurs in people with risk factors[1, 2]. CA-MRSA infection was first reported in the early 1980s, and its incidence has continued to increase since the early 2000s, thereby making it a major health concern[3, 4]. In the United States, the estimated annual incidence reported by a multisite surveillance study was 18–26 cases per 100,000 people in 2002[1]. Another study in a public hospital in Chicago found that the incidence of CA-MRSA skin and soft tissue infections increased from 24 cases per 100,000 people in 2000 to 164 cases per 100,000 people in 2005[4].

The epidemiology of CA-MRSA is not well discussed in Japan. In a colonization study, Hisata surveyed the nasal cavities of 818 healthy children and detected MRSA in 35 children (4.3%)[5]. Based on genetic characteristics, two-thirds of these 35 children were categorized as having CA-MRSA. Knowledge of the epidemiology of bacterial infections is important for appropriate decision-making in the empiric treatment of infections. Our objective was to investigate the incidence of CA-MRSA infections in a regional hospital.

Patients and Methods

This study relied on a retrospective review of medical records. It was conducted at a regional hospital located on a remote island in northern Japan with a population of approximately 5,600 inhabitants. This regional hospital is the only hospital on the island. All outpatient medical records from January 1, 2008 through December 31, 2008 were in-

Table 1 Characteristics of *Staphylococcus aureus* isolates in the outpatients

	No. (%) of patients	Mean age (range)	Sex male/female	No. of specimen samples	No. of specimen materials			
					Sputum	Skin wound	Throat swab	Miscellaneous†
*S aureus**	29	54 (3–95)	17/12	31	18	5	5	3
MSSA	19 (66%)	43 (3–95)	9/10	20	9	3	5	3
MRSA	10 (34%)	79 (38–94)	8/2	11	9	2		
HA-MRSA	9 (31%)	84 (76–94)	7/2	10	9	1		
CA-MRSA	1 (3%)	38	1/0	1		1		

* MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; CA, community aquired; HA, hospital acquired. † Joint fluid, 2; Aural discharge, 1.

vestigated in terms of the patient medical history and the *S. aureus* isolates from clinical cultures. The total number of outpatients was 30,848, out of which 634 patients were admitted. *S. aureus* isolates exhibited growth in culture tests irrespective of the presence of symptoms in patients. *S. aureus* isolates were divided into two categories, *S. aureus* colonization and infection. Colonization meant that *S. aureus* produced no symptoms in the patient, whereas infection meant that *S. aureus* produced symptoms as a causative bacterium.

HA-MRSA cases were defined as patients with (1) an MRSA infection identified after 48 hours of admission to the hospital; (2) a history of hospitalization, surgery, dialysis or residence in a long-term care facility within 1 year of the date of MRSA culture; (3) a permanent indwelling catheter or percutaneous medical device (e.g., gastrostomy tube or Foley catheter) present at the time of culture; or (4) a known positive culture for MRSA prior to the study period[6]. Cases that had none of the above features were classified as CA-MRSA. This study was approved by the institutional review board of Rishiri Central Hospital.

S. aureus was identified using routine laboratory methods (catalase-positive, tube coagulase-positive Gram-positive cocci). Methicillin resistance was demonstrated by oxacillin resistance using automated broth microdilution (BML, Inc., Tokyo, Japan) in accordance with the guidelines of the Clinical and Laboratory Standards Institute[7]. We performed susceptibility testing on the isolates using broth microdilution according to the breakpoints established by the guidelines.

Results

During 2008, *S. aureus* isolates were observed in 31 samples from of 29 unique patients (Table 1). In each group (MSSA and MRSA), two isolates were obtained from one patient at a two-month interval. In both cases, these two isolates exhibited the same antibiotic susceptibility. Among the 29 patients, 19 (66%) exhibited methicillin-sensitive *S. aureus* (MSSA), and 10 (34%) exhibited MRSA. In the 10 patients with MRSA isolates, there were nine cases of HA-MRSA (comprising 32% of the 29 patients with *S. aureus* isolates) and one case of CA-MRSA (3%). The nine patients with HA-MRSA isolates exhibited colonization of MRSA. The patient with CA-MRSA was diagnosed with cellulitis due to CA-MRSA after a culture of pus revealed MRSA, even though he had not been exposed to healthcare environments. All 10 MRSA isolates were resistant to the following antibiotics: benzylpenicillin, ampicillin, sulbactam/ampicillin, amoxicillin, piperacillin, cefazolin, cefotiam, sulbactam/cefoperazone, ceftazidime, ceftriaxone, cefepime, cefmetazole, cefdinir, cefcapene pivoxil, flomoxef, imipenem/cilastatin, meropenem, gentamicin, erythromycin, clarithromycin and azithromycin. The CA-MRSA isolates exhibited susceptibility to chloramphenicol and vancomycin and resistance to clindamycin and aminoglycosides such as gentamicin and amikacin (Table 2). The nine HA-MRSA isolates exhibited susceptibility to chloramphenicol and vancomycin. Susceptibility to amikacin, clindamycin, minocycline and fosfomycin varied among the HA-MRSA isolates.

Discussion

The CA-MRSA case in the current study presented with suppurative cellulitis of the right index finger, which is a skin and soft tissue infection (SSTI). This was successfully treated with incision and drainage followed by antibiotic therapy[8]. Based on the site of infection, CA-MRSA infections are divided into two types: non-SSTIs and SSTI. Non-SSTI manifest as severe and life-threatening infections including necrotizing pneumonia, necrotizing fasciitis and severe sepsis and represent rare cases[6, 9, 10]. SSTIs manifest as furuncles, carbuncles, abscesses, cellulitis or, rarely, necrotizing fasciitis[1, 6]. Previously, SSTIs were considered to be caused by either MSSA or *Streptococcus pyogenes*; however, clinicians must now consider CA-MRSA a causative agent as well. A few cases of SSTI due to genetically proven

Table 2 Antibiotic susceptibility patterns of MRSA isolates*

Case No.	Age	Sex	MRSA type	Amikacin	Clindamycin	Minocycline	Chloramphenicol	Vancomycin	Fosfomycin
1	38	m	CA	R	R	I	S	S	I
2	76	f	HA	R	R	R	S	S	R
3	78	m	HA	R	R	R	S	S	R
4	82	m	HA	S	S	S	S	S	S
5	83	m	HA	I	R	S	S	S	R
6	84	f	HA	S	R	I	S	S	I
7	85	m	HA	R	R	R	S	S	R
8	85	m	HA	R	R	R	S	S	R
9	89	m	HA	R	R	R	S	S	I
10	94	m	HA	S	S	S	S	S	S

* MRSA, methicillin-resistant *Staphylococcus aureus*; CA, community acquired; HA, hospital acquired; S, susceptible; I, intermedate; R, resistant.

CA-MRSA have been reported in Japan[11, 12]. By extrapolation of our data revealing one case of CA-MRSA infection among 5,600 inhabitants and 634 admissions, the annual incidence of CA-MRSA infections was estimated as 18 per 100,000 people and 157 per 100,000 admissions in 2008.

In our study, MSSA and MRSA accounted for 66% and 34% of the *S. aureus* isolates, respectively, and all isolates of *S. aureus* excluding one were colonizations. This ratio of MSSA to MRSA is consistent with previously reported studies on *S. aureus* colonization, which demonstrated that the ratio of MSSA to MRSA in the anterior nares was 67%–33%[9, 13]. In the present study, the group with MSSA isolation was younger than the group with MRSA; the mean ages were 43 and 79 years, respectively. This is because the average age of the five patients with MSSA detected from throat swabs was seven years (Table 1). This result is in accord with previous findings showing that MRSA is more commonly observed in the elderly than in children[6].

CA-MRSA is distinguishable from HA-MRSA at the molecular level, as well as in the clinical course[3, 5, 6]. It often carries the gene Panton–Valentine leukocidin (PVL), which encodes cytotoxins that destroy leukocytes and may cause tissue necrosis[3]. PVL is responsible for the increased pus formation and tissue necrosis observed in patients infected with CA-MRSA. In contrast, only 5% of MSSA and HA-MRSA isolates express the PVL gene. MRSA has a mutated penicillin-binding protein 2a encoded by a gene called mecA that confers resistance to methicillin and all β-lactam antibiotics. All MRSA isolates possess the mobile chromosomal staphylococcal cassette cartridge (SCCmec), which houses the mecA gene. There are five types of SCCmec. HA-MRSA strains express SCCmec types I, II and III. CA-MRSA strains express type IV or V, two smaller versions of SCCmec[3]. The smaller size of SCCmec type IV is responsible for the susceptibility of CA-MRSA to a wider range of antibiotics, as it does not carry the genes for drug resistance. HA-MRSA tends to be multidrug-resistant, and CA-MRSA is susceptible to narrow-spectrum non-β-lactam drugs such as fluoroquinolones, clindamycin, trimethoprim-sulfamethoxazole and tetracyclines[1, 3]. From this evidence, we inferred that our CA-MRSA case has clones that are genetically HA-MRSA. Currently, the CA-MRSA and HA-MRSA classifications are no longer distinct in the United States, since patients can develop MRSA colonization in one realm and develop manifestations of infection in another[14]. In a study of 102 patients with CA-MRSA infections, 29% had molecular typing consistent with HA-MRSA[15].

The present study has several limitations. First, the retrospective design leads to selection bias and recall bias. Second, CA-MRSA was distinguishable from HA-MRSA at the molecular level as well as in the clinical course in previous studies[3, 5, 6]. We examined the present data in light of previously reported clinical data. However, in primary care, molecular testing is time-consuming and resource-intensive, and the requisite laboratory training and personnel are often not available. Accordingly, it is reasonable to classify MRSA cases in primary care based on clinical data including health care risk factors, infection type (SSTI and non-SSTI) and susceptibility patterns[16]. Given that the prevalence of CA-MRSA isolates and infections has recently increased, population-based surveys of CA-MRSA are required in Japanese communities.

Conclusion

We observed a CA-MRSA case in a regional hospital in Japan, suggesting that incidence trends of CA-MRSA should be considered in future research and treatment.

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