MRSA Infection in Patients Hospitalized at Sanglah Hospital: A Case Series

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ABSTRAK

Laporan ini merupakan laporan pertama mengenai infeksi MRSA di RS Sanglah. Kami menelusuri 8 kasus MRSA dari catatan laboratorium antara Januari hingga Mei 2011, kemudian dilanjutkan dengan mengumpulkan data dari catatan medis pasien-pasien tersebut. Lima kasus dengan sepsis, 1 kasus osteomyelitis, dan dua lainnya masing-masing dengan mediastinitis dan pneumonia. Pasien-pasien ini segera dipindahkan ke ruang isolasi yang dilengkapi dengan teknik perlindungan khusus yang ketat. Selanjutnya dilakukan kultur bahan dari hapusan rongga hidung, tenggorok dan aksila pasien serta para petugas kesehatan yang kontak langsung dengan pasien, namun tidak didapatkan kolonisasi MRSA. Lima pasien menunjukkan respons yang baik dengan pemberian Vankomisin atau Linesolid. Tiga di antaranya meninggal akibat syok septik sebelum hasil kultur dan tes kepekaan antibiotika selesai. Semua strain kuman ini didapatkan dalam waktu setelah 48 jam perawatan dan juga menunjukkan beberapa faktor risiko infeksi MRSA yang didapat di rumah sakit. Tes kepekaan antibiotika menunjukkan kekebalan terhadap ß-laktam, namun semua strain masih peka terhadap beberapa antibiotika non ß-laktam yang lain sebagaimana dilaporkan pada infeksi MRSA yang didapat di komunitas. Pada masa mendatang diperlukan penelitian lebih lajut menggunakan pemeriksaan biomolekuler untuk mengetahui pengaruh dan perubahannya secara lengkap mengenai infeksi MRSA.

Kata kunci: *MRSA, kepekaan antibiotika, pengobatan.*

ABSTRACT

This is the first report of MRSA infection in Sanglah Hospital. We reviewed eight patients with MRSA infection from microbiologi laboratory records between January and May 2011, than followed by tracing medical records to obtained data of the patients. Five of cases with sepsis, 1 case with osteomyelitis, and the two others with mediastinitis and pneumonia. The patients were kept in private isolated room and barrier-nursing technique was strictly followed. Further action was culturing specimen taken from the patients nose, throat, axilla, and samples taken from the health care workers, with no MRSA colonization were found. Five patients demonstrated good respond to intravenous administration of either vancomycin or linezolide. Three were died due to septic shock before the laboratory culture and antimicrobial susceptibility availabled. All of the strains isolated more than 48 hours after admission and also demonstrated clinical risk factors for hospitalized acquired MRSA (HA-MRSA). These strains had resistance to ß-lactams but remain susceptible to many non ß-lactam antibiotics, as reported in some community acquired MRSA (CA-MRSA) isolates. Future study using molecular typing required to fully understand the magnitude and ongoing evolution of MRSA infections.

Key words: *MRSA, Antimicrobial susceptibility, treatment.*

INTRODUCTION

Infections caused by methicilin–resistant Staphylococcus aureus (MRSA) have become a global health concern during the past 2-3 decades. Since then the epidemiology of MRSA infections has changed dramatically. The prevalence of MRSA has steady increased since the first clinical isolate was described in 1961. This was soon after the introduction of Methicillin for clinical used. Certain strains of MRSA were found to have the propensity to spread very quickly in hospitals. In 2005 the US estimated there were 94.360 invasif MRSA infection with approximately 18.650 associated hospital death.[1,2] In some countries in Asia, MRSA accounts for more than 70% of nosokomial S. aureus isolates. MRSA infection are associated with greater length of stay, higher mortality and increased cost.[3,4] Studies of the global epidemiology frequently have not included MRSA obtained from persons living in developing nations. There is only limited prevalence data on MRSA epidemiology in Indonesia. MRSA infection is related to its potential for nosocomial transmission and limited number of antibiotics available for its treatment. This is the first report of MRSA infection in Sanglah hospital, Bali Indonesia.

CASE ILLUSTRATION

Eigth patients with severe infection were found to be MRSA positive from January to May 2011. *Staphylococcus aureus* were identified by colony morphology, coagulation of citrated rabbit plasma with EDTA. Multidrug susceptibility was determined by Cefoxitin disk. The medical record of patient were reviewed and the risk factors for MRSA infection were recorded. Health care workers and all of the patients were screened for MRSA carriage by the nasal swabs technique and found no MRSA.

The demografic and clinical data of patients are shown in **Table 1 and 2**.

Table 1. Demographical and clinical data of patients with MRSA infection

Variables	Patients (isolate)							
	1	2	3	4	5	6	7	8
Date of MRSA isolation	January 2011	March 2011	March 2011	April 2011	April 2011	April 2011	April 2011	May 2011
Specimen	pus	blood	blood	pus	sputum	blood	blood	blood
Sex/Age (years)	F/65	M/45	M/73	M/2	M/73	F/6	M/43	M/29
Race	Balinese	Balinese	Balinese	Balinese	Balinese	Balinese	Balinese	Bima
Rehospitalization/ Transfered	Yes	No	No	Yes	No	Yes	Yes	Yes
Appropriate antibiotic usage	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Comorbid condition	Fr. Os femur	Hemorrhagic stroke	Fr.os patella, DM	VSD	Hemorrhagic stroke	Combustio	Spleen rupture	Adeno Ca Prostat
Surgery	Ortho-paedic	Neuro-surgery	Ortho-paedic	Sternos-tomy	Nil	Debride ment	Laparo-tomy	Pancysto stomy
Infection type	Osteo-myelitis	Sepsis	Sepsis	Medias-tinitis	Pneumonia	Sepsis	Sepsis	Sepsis
Therapy (iv)	Linezolide	Vanco-mycin	Vanco-mycin	Vanco-mycin	Vancomycin	Vanco-mycin	Vanco-mycin	Linesolide
Outcome	Cured	Cured	Died	Died	Cured	Cured	Cured	Died
Length of stay	30 days	38 days	41 days	20 days	13 days	21 days	98 days	43 days

Table 2. Antimicrobial susceptibility pattern of MRSA isolates

Patients	*Antibiotics								
	Cefox	Ery	CC	Sxt	Cip	Cef	Gen	Van	Lin
1	R	S	S	-	R	R	R	S	S
2	R	I	S	I	R	R	R	S	S
3	R	S	S	R	R	R	R	S	S
4	R	S	S	I	R	R	R	S	S
5	R	R	R	R	R	R	S	S	S
6	R	I	S	S	R	R	R	S	S
7	R	S	S	S	R	R	R	S	S
8	R	S	S	I	R	R	R	S	S

*Cefox=Cefoxitin, Ery= Erythromycin, CC= Clindamycin, Sxt= Trimethoprim-sulfamethoxazole, Cip=Ciprofloxacin, Cef= Cefotaxime, Gen= Gentamycin, Van= Vancomycin, Lin= Linesolide

Case 1

A 65-year old male patient had been rehospitalized with osteomyelitis in one week after having an-operation of right collum femur fracture. MRSA infection was not identified at the time of treatment. The surgery site developed into a phleghmon with painfull swelling. He initially treated with ceftriaxon and then continued with quinolone, but no improvement. MRSA infection was proven by a positive MRSA pus culture in 1 month admission.

Case 2

A 45-year old male patient was transfered from a private clinic due to loss of contiousness. He had suffered for several years from cronic hypertension and then had haemorragic stroke. Post trepanation intensive care was required, endotracheal tube and indwelling urine catheter were instituted. One month later, tracheal granuloma was diagnosed, which developed into sepsis syndrome. Despite treatment with antibiotics including cefotaxime and meropenem, the symptoms worsened to gastrointestinal haemorrhage. Bacterological blood test revealed an MRSA infection one month after operation.

Case 3

A 73-year old male patient who had a 15-year history of diabetes mellitus, hypertension and cronic kidney disease has been admitted to the hospital due to left patellar bone fracture that required surgery. During periode of post operation care, he suffered from pneumonia which then developed into sepsis syndrome. A bacteriological blood culture showed the presence of MRSA in three week observation periode.

Case 4

A 2-year old male patient had been readmitted to the hospital due to mediastinitis. Three weeks after returning home from hospital after a-closure operation on congenital ventricular septal defect (VSD), he suffered from high fever and sign of surgical site infection. Treatment in hospital included debridement and combined antibiotics therapy, to which the condition did not respond satisfactorily. One week later, MRSA was identified from surgical wound specimen.

Case 5

A 73-year old male patient suffered haemorrhagic stroke. He had medical treatment with intravenous line and indwelling urine catheter. One week after the treatment, he showed symptom of pneumonia accompanied by productive cough and an irritable, persistent shorthness of breath. MRSA was found in sputum bacteriologic test.

Case 6

A 6-year old female patient who was transferred from Singaraja (North Bali) general hospital with second degree wide combustion. The patient had 3 times surgical procedure during treatment in burn unit. Problem that apper in this phase was skin damage due to burn-induced

inflammation or infection process and problem of wound closure. MRSA was found in the specimen taken from the combustio wound.

Case 7

A 43-year old male patient who had severe abdominal injury with spleen rupture due to traffic accident that required laparotomy. One week later he experienced swelling and pain throughout the abdominal area. Due to a suspected surgical site infection, debridement was performed. During the periode of observation, the infection was treated with repeated dose of antibiotics . Two months later, sepsis syndrome developed. MRSA was identified in blood bacteriological test.

Case 8

A 67-year old male patient was transferred from Mataram general hospital, with urine bladder mass. In 2008 he had a-prostatectomy operation due to prostate adenocarcinoma. Treatment in hospital included pancystostomy and supportive therapy but 1 month later during a medical examination he showed symptom of pneumonia. Following several day of antibiotic treatment, sepsis syndrome was developed. A bacteriological blood culture showed the presence of MRSA.

DISCUSSION

MRSA is a term applied to a special strain of Staphylococcus called Methicillin Resistant *Staphylococcus aureus* which is resistant to ß-lactam antibiotics. MRSA infection can be classified into community–acquired MRSA (CA-MRSA) and hospital–acquired MRSA (HA-MRSA). CA-MRSA is acquired by persons who have not been recently (within the past year) hospitalized or had a medical procedure (such as dialysis, surgery, catheters). These infection manifest usually as skin infections and occur in otherwise heathly people. When looking at MRSA types, CA-MRSA was less likely to cause bacteremia than was HA-MRSA (65% vs 77%), but it was more likely to be associated with cellulitis (23% vs 8%) and endocarditis (13% vs 5%) than was HA-MRSA. Almost 18% of the patients died while hospitalized for MRSA. CA-MRSA contribute to invasive illness in hospitalized patients, but most the invasive MRSA disease is still associated with healthcare-related strains.[5,6] Although prevention, control, and management of HA-MRSA infections remain problematic, community-associated MRSA infections have emerged as increasingly prevalent and serious problem. CA-MRSA isolates have a tendency to be susceptible to other antibiotic classes and often are resistant only to ß-lactams antibiotics, while HA–MRSA is tipycally a multidrug resistant organism. The lack of resistance to multiple antibiotics suggest a community origin, because antibiotic selective pressure is much lower within the community than in hospitals, and the survival advantage of multiple drug resistance is lower. In this report, five of these cases developed sepsis syndrome, and the three others with mediastinitis, osteomyelitis and pneumonia. All cases were more likely to be resistant to ß-lactams but remain sensitive to many non ß-lactam antibiotics (including erythromycin, clindamycin and trimethroprim-sulfamethoxazole), as reported in some CA-MRSA isolates.

Initially, MRSA was almost exclusively a nosocomial pathogen, and even today healthcare-associated MRSA (HA-MRSA) infections remain a significant challenge. HA-MRSA infection is acquired by person admitted to hospital for more than 48 hours or those have medical history of MRSA infections or colonization during previous admission. The proportion of nosocomial S aureus infections demonstrating methicllin resistance nearly doubled, increasing from 36% to 64% between 1992 and 2003.[4,5] MRSA has become a commonly encounterd pathogen in clinical setting. The elderly, the clinical ill patients and those who have endured a prolonged hospital stay are the most concern patients group. Other important predisposing factors for the infection are: some kind of the lesion on the skin/ mucosal barrier (e.g. surgical wound, decubitus, and invasive dwelling divices: intravenous catheter, urinary catheter, mechanical ventilation, etc.), recent exposure to broad spectrum antibiotic therapy, and staying in intensive care unit. Common sites of HA-MRSA are surgical wound infection, urinary tract infection and pneumonia. The mortality rates for

nosokomial MRSA infection are approximately 50% for bacteraemia and 33% for pneumonia.[7] We note that all of the patient with co-morbid condition, seven of cases related to surgery care exposure. In another one case was recognize as pneumonia with medical treatment due to acute haemorrhagic stroke. All of strains have been isolated after 48 hours of hospitalization.

Intravenous antimicrobial agents are appropriate for patients with severe staphylococcal infection, particularly patient requiring hospitalization. Vancomycin remains a first-line therapy for severe infections caused by MRSA. Other intravenous agents such as linezolide, tigecyclin, daptomycin, clindamycin and quinopristin-dalfopristin may appropriate to be considered in some circumstances. As with methisillin-resistance, prevalence of resistance to non betalactam agents varies geographically and is likely to change over time. Local susceptibility patterns of community *S. aureus* isolates should be monitored and the information used to guide empiric management decision.[5,6] Five of the eigth cases demonstrated good respond to intravenous administration of either vancomycin or linezolide (based on result of cultures and antimicrobial susceptibility testing) for 7-14 days. Unfortunately 3 patients died due to septic shock.

Transmission of MRSA occurs mainly by contact transmission and droplet infection. Patients who already have an MRSA infection or who carry the bacteria on their bodies but do not have symptoms (are colonized) are the most common sources of transmission. The carrier state is clinically significant because any surgical intervention or exudative skin colonization predisposes the MRSA carrier to MRSA infection. Carriage of MRSA also plays an important role in the dissemination of this microorganism with in health care facilities, as well as into the community. The most common way of transmission is through human hands, especially health care workers' hands. Hands may become contaminated with MRSA by contact with infected or colonized patients. Surgical wound infection and contamination occurs mainly trough contact with hands of health care worker or environmental surfaces contaminated with body fluid containing MRSA. Droplet infection is another type of transmission which causes pneumonia and in such a case, the patient is infectious trough droplet infection to the surrounding patients and health care workers. Several studies have demonstrated that carrier of MRSA are at greater risk for developing serious infection. And while 25% to 30% of population is colonized with Staphylococcus aureus, approximately 1% is colonized with MRSA.[8,9] So health care workers (including physicians, nurse and paramedicals) who carry MRSA colonies in their nostrils and skin are responsible for increase risk of getting surgical wound infections to patients when they deal with. Nasal colonization with MRSA does not appear to have played a role in these MRSA cases. We identified throat, axilla and nasal swabs among the patients and health care workers but found no MRSA.

We prepared a protocol which describes the tasks to be performed when an MRSA positive case occurs in the hospital. The protocol is based on the current International consensus guidelines includes performing hand hygiene, placing the patients in private isolated room with cleaning and decontamination facilities, and intravenous injection of either Vancomycin or Linezolide.[1,9,10] The hospital patients safety team organized education on hand hygiene (handwashing or using alcohol hand gel) and isolation rules (through placing infected patients in private rooms or cohorting patients with similar infecton status) at our hospital. However clinical studies are required to clarify further therapeutic usses on timing, dosing & choise of optimum treatment and useful.

CONCLUSION

This case series demonstrates the potential severity and rapid clinical progression of MRSA infections that can occur in the indoor hospital patients. Making a diagnosis of MRSA infections is challenging; although microbial confirmation of the diagnosis is clearly required, a combination of epidemiologic, hystorical, physical examination, laboratory and radiographic findings may suggest this diagnosis, particularly in critical ill patient with rapidly progressive disease. In addition to appropriate supportive care, prompt initiation of

antibiotic therapy with activity against MRSA is warrated.

This report aims at creating an awarness among physician about the posibility of MRSA infection in high risk patients, especially those on surgical wound infections, pneumonia, osteomyelitis, burn patient, bacteremia and sepsis syndrome. Our hope is that this report will provide a starting point for future research into Methicilline-resistant Staphylococcus aureus infection to validate these findings and provide impetus for initiatives to improves antimicrobial drug use.

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