MRSA (Methicillin-Resistant Staphylococcus Aureus) Osteomyelitis : Factors and Results Compared to Non MRSA Osteomyelitis

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ABSTRACT

MRSA (Methicillin-resistant staphylococcus aureus) osteotomyelitis is a disabling disease. We retrospectively reviewed factors and results of 12 cases of MRSA osteomyelitis compared to 34 non MRSA osteomyelitis. Factors such as age, underlying disease, previous internal fixation, site and type (Cierny-Mader classification) were not significantly different between the two groups, but there was a predominance of males over females in the MRSA group. Laboratory investigations showed no differences in hematocrit, white blood cell count and erythrocyte sedimentation rate. Polyorganism was more common in MRSA osteomyelitis. Results were less satisfactory in the MRSA group because of significantly higher rates of hospitalization, length of stay, number of surgeries and healing time. Amputation, sepsis and mortality rates were not significantly different because of the small number of patients between the groups. In conclusion, we have shown that factors associated with developing MRSA osteomyelitis are trauma cause, previous internal fixation and femoral location. The results of treatment of MRSA osteomyelitis were less satisfactory than those of non MRSA group.

INTRODUCTION

Chronic osteomyelitis is common orthopaedic infections. The most common causative organism of chronic osteomyelitis is staphylococcus aureus[1,2,3]. However both gram-positive and gram-negative resistant strains are now being increasingly reported[4,5]. MRSA (Methicillin-resistant staphylococcus aureus) was reported soon after introduction of methicillin in Europe. This nosocomial infection can cause septic arthritis and osteomyelitis[6,7] MRSA osteomyelitis has been sporadically reported during the last 10 years[6,7,8,9,10,11]. The antibiotics of choice for MRSA are vancomycin, teicoplanin, fosfomycin, rifampicin and fusidin[3,7,12,13,14]. Treatment involves both medical and surgical approaches. Medical treatment includes prolonged systemic and oral antibiotic. Surgery is indicated when there is pus formation, sequestrum, soft tissue defect and the need for stabilization[1]. Treatment is expensive and time consuming for both the patient and medical staff[2]. Complications of chronic osteomyelitis are serious such as pathologic fractures, septicemia, limb loss or even death.[1,2,6]. There have been no previous reports comparing factors or results between MRSA and non MRSA osteomyelitis.

The objective of this study was to compare factors such as age, sex, underlying disease, cause, site, type, hematocrit, white blood count (WBC), erythrocyte sedimentation rate (ESR), culture, number of local antibiotics used and results (length of stay, healing time, amputation rate, rate of sepsis and mortality rate) between MRSA and non MRSA osteomyelitis.

MATERIALS AND METHODS

We retrospectively reviewed 12 MRSA osteomyelitis and 34 non MRSA osteomyelitis patients who were admitted to Songklanagarind Hospital between January 1994 and January 1999. All patients were followed up for at least 1 year. Medical records and radiographs were reviewed regarding factors such as age, sex, cause, underlying disease, site, type, previous internal fixation, laboratory investigations (culture, hematocrit, ESR, WBC) and results: number of surgeries, number of local antibiotics used, number of hospitalizations, length of stay, healing time, amputation rate, rate of sepsis, and mortality rate.

Underlying diseases are host factors that have adverse effects on wound healing include both local and systemic factors. Local factors are chronic lymphedema, venous stasis and extensive scarring. Systemic factors are malnutrition, immunodeficiency, diabetes, old age, and renal or liver failure.

Causation of chronic osteomyelitis was divided into trauma, such as open fracture or previous internal fixation in closed fracture and nontrauma causes such as hematogenous or contiguous spreading. The types of chronic osteomyelitis were categorized by using Cierny-Mader anatomic classification[15], which divided the disease into 4 groups. Type I : medullary osteomyelitis, depicts inflammation of the medullary surface. Type II : superficial osteomyelitis, involve primarily the superficial cortex of the bone. Type III : localized osteomyelitis, involves both superficial and medullary areas, and type IV : diffuse osteomyelitis, in which the entire segment of bone is destroyed.

The causative organisms reported in both groups were based on tissue culture at the time of surgery, not from the drainage or sinus tract.

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Patients who were diagnosed MRSA osteomyelitis must have had at least two repeated positive tissue cultures of MRSA organism. Patients in non MRSA osteomyelitis that had negative culture (no growth on tissue culture) had histopathologic and radiographic evidence of chronic osteomyelitis.

Healing time was determined by the arrest of clinical signs and the radiographic signs.

Statistical analysis.

All nonparametric factors were compared by Chi-square test except sepsis rate and mortality rate using the Fisher exact test because of the small number of cases. Two-sample t-test was used for parametric factors such as age, WBC, ESR, and hematocrit, while Mann-Whitney test was used among factors (number of surgeries and hospitalizations, length of stay, healing time) because of their nonnormal distribution data.

RESULTS

There were 12 MRSA osteomyelitis and 34 non MRSA osteomyelitis patients in this study. Males were significantly more than females in the MRSA osteomyelitis group. The underlying disease of the patients in this study were comparable in both groups. The most common underlying disease was diabetes. The MRSA group had a higher rate of previous internal fixation than the other group (41.7% and 17.6%). Internal fixation used in both groups were plating or nailing. Ten of 11 cases in the MRSA group were caused by trauma, especially involving open fractures, while only 29.4% of the patients in the non MRSA group had the same cause. Femoral involvements were more common than tibias in MRSA osteomyelitis, while tibias were the most common site of involvement in the non MRSA group. The number of local antibiotics used in the MRSA group was significantly higher than in the non MRSA osteomyelitis group. Furthermore, 80% of MRSA patients had received more than 2 courses of a local antibiotic (Septopal) (Table 1).

The most common type (Cierny-Mader anatomic classification) of chronic osteomyelitis was diffused osteomyelitis in both groups. Localized osteomyelitis was more common than medullary type. There was no superficial osteomyelitis in this study (Figure 1).

The laboratory investigation showed comparable results of both hematocrit, white blood cell count and ESR in both groups. However, the number of patients with MRSA osteomyelitis had polymicrobial organisms more commonly than the other group. 30% of non MRSA osteomyelitis patients had negative tissue cultures (Table 2).

The most common causative organism in non MRSA osteomyelitis was S. aureus (52.8%), while P. aeruginosa was the most common gram-negative bacillus found in both groups. The combined organisms in the MRSA group were mostly gram-negative bacilli (72.1%) (Table3).

The outcome parameters revealed that treatment in the MRSA group encountered more resistance and were more time consuming. The length of stay, the number of hospitalizations and the number of surgeries were significantly higher in MRSA osteomyelitis patient than in the non MRSA group. The healing time was markly delayed (8 months) in the MRSA group. The amputation rate was 23.1% and 17.3% in the MRSA and non MRSA groups, respectively. The most common indication for amputation was failure to reconstruct the limb. There were no cases of sepsis or death in the MRSA group, while 11.8% of patients in the non MRSA group had sepsis due to both gram-positive cocci and gram-negative bacilli and one patient in this group died from K. pneumoniae sepsis (Table 4).

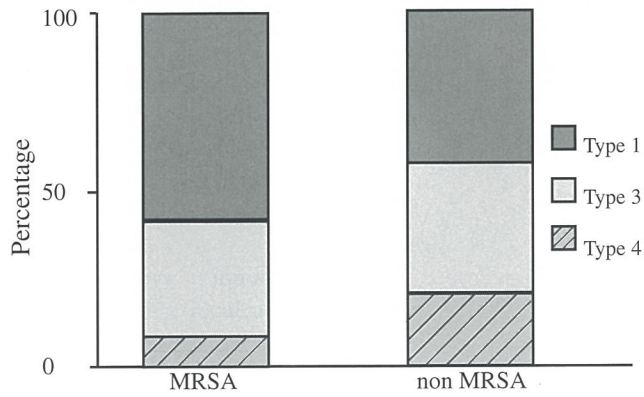

Fig. 1 Showed types of chronic osteomyelitis (Cierney-Mader classification) in both groups.
Type 1 : medullary osteomyelitis, Type 3 : localized osteomyelitis and Type 4 : diffused osteomyelitis.
There was no type 2 (superficial osteomyelitis) in this study.

DISCUSSION

Methicillin-resistant staphylococcus aureus (MRSA) isolated from cases of chronic osteomyelitis has been rising recently[16,17]. The infection can spread from open wounds,contamination during internal fixation or by hematogenous dissemination. Patients with MRSA osteomyelitis in this study had previous internal fixation 41.7%. Internal fixation such as plate or nail alter host defence mechanisms and promote microorganism resistance[18]. Host factors also may play a role in developing MRSA osteomyelitis. We found that patients with MRSA osteomyelitis had more underlying disease than

Table 1. Demographic data and factors between MRSA and non MRSA osteomyelitis

	MRSA	Non MRSA	P-value$_1$	P value$_2$
- Age (mean,SD)	36.0 (14.7)	28.1 (19.1)	.101	
- Sex (M:F)	11:1	25:9		.047
- Underlying disease	33.0%	17.6%		.257
- Cause (trauma)	91. 7%	29.4%		.000*
- Previous fixation	41. 7%	17.6%		.094
- Site (femur)	58.3%	20.6%		.035*
- Local antibiotic used (more than 1 course)	41. 7%	0.0%		.001*

1 = P value from t-test

2 = P value from Chi-square test

Table 2. Compared laboratory investigations between two groups mean (SD)

	MRSA	Non MRSA	P-value$_1$	P value$_2$
- Hematocrit (%)	37.9 (5.0)	37.1 (1.2)	.365	
- WBC(cell/ml)	8645.4 (3103.0)	10262.5 (4702.2)	.290	
- ESR (mm/hr)	36.0 (11)	38.5 (12)	.957	
- Culture positive (> 2 organisms)	25.0%	3.0%		.013*

1 = P value from t-test
2 = P value from Chi-square test

Table 3. Showed causative or combined organisms of both groups

Organism	MRSA (%)	Non MRSA (%)
- S. aureus	9.09%	52.77%
- S. epidemidis	9.09%	-
- Strep gr. A	9.09%	11.11%
- P. aeruginosa	27.27%	19.44%
- E. coli	18.18%	3.12%
- Enterobacter cloacae	9.09%	3.12%
- Others	36.37%	10.44%

Table 4 . Compared results of both groups (median [range])

	MRSA	Non MRSA	P value$_1$	P value$_2$	P value$_3$
- Number of hospitalization	4.0 (1-7)	1.0 (1-16)	.001*		
- Number of surgeries	4.0(1-6)	2.0(1-4)	001*		
- Length of stay	94 .0(30-143)	17.5 (8-133)	.0001*		
- Healing time (month)	8.0 (2-48)	4.0 (2-20)	.001*		
- Amputation rate	23.1%	14.3%		.419	
- Pathologic fracture rate	8.0%	11.76%		.214	
- Sepsis rate	0.0%	11.76%			.419
- Mortality rate	0.0%	2.9%			.548

1 = P value from Mann-Whitney test
2 = P value from Chi-square test
3 = P value from Fisher' exact test

those with non MRSA osteomyelitis, but the difference was not statistically significant. Femur was the most common site of involvement in MRSA osteomyelitis in this study, same as reported by Sheftel and associates[7]. Local antibiotic used (Septopal) in the MRSA group was rather unsuccessful compared to the non MRSA group (80% of the patients received treatment of more than 2 courses) which might explain the resistance of this organism to gentamicin[19].

Laboratory investigation showed that most cases of osteomyelitis have elevated erythrocyte sedimentation rates (ESR), while both hematocrit and white blood count were normal. The most common organism was S. aureus in the non MRSA group as previously reported[1,2,3,4]. The combined causative organisms of MRSA osteomyelitis were usually gram negative, especially P. aeruginosa, which represented nosocomial infection. The incidence of negative culture from non MRSA osteomyelitis was high (30.3%) compared to the other studies[1,2] may be due to presurgical antibiotic administration in most subjects in this study.

The higher number of hospitalizations, length of stay, and number of surgeries represented how difficult it is to eradicate this infection compared to the non MRSA osteomyelitis and it also showed the cost of treatment. The most common cause of frequent hospitalization was recurrent infection. The prolonged length of stay was partially due to the need for intravenous antibiotic. The antibiotic against MRSA used in our hospital was either vancomycin or fosfomycin, which did not result in serious adverse side effects. The healing time, which represents the course of the disease, was longer in the MRSA group. The prolonged time to heal showed both impaired host defences and a very resistant organism. Complications such as amputation rate were more pronounced in the MRSA group. However, there was no sepsis or death in MRSA osteomyelitis patients even though the patients in this group had a higher rate of underlying disease.

In conclusion, we have shown that factors such as trauma, previous internal fixation and femoral location are the factors associated with developing MRSA osteomyelitis and the results of treatment of MRSA osteomyelitis were less satisfactory than those of non MRSA osteomyelitis.

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