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การวิเคราะห์ปัจจัยเสี่ยงของการติดเชื้อกรัมลบในโพรงกระดูก

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Risk Factors Analysis of Gram-Negative Osteomyelitis

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หลักการและเหตุผล: การติดเชื้อในโพรงกระดูกเป็นโรคที่สร้างความเจ็บปวดทรมานกับผู้ป่วยและก่อให้เกิดความยุ่งยากในการรักษากับแพทย์ ปัจจัยที่ส่งผลต่อการรักษาคือการตรวจหาเชื้อก่อโรคได้อย่างรวดเร็วและให้ยาถูกต้อง แต่บางครั้งแพทย์ไม่สามารถตรวจหาเชื้อได้และต้องอาศัยลักษณะทางคลินิกเพื่อให้ยาปฏิชีวนะเบื้องต้นไปก่อน

วัตถุประสงค์: เพื่อรายงานอุบัติการณ์ของเชื้อก่อโรคในภาวะติดเชื้อในโพรงกระดูก ประเมินปัจจัยเสี่ยงและลักษณะทางคลินิกของผู้ป่วยติดเชื้อกรัมลบในโพรงกระดูกจากเชื้อที่พบในเขตภาคอีสานของประเทศไทย

วัสดุและวิธีการ: โดยการรวบรวมรายงานผู้ป่วยระหว่างเดือนมกราคม 2542 ถึง เดือนธันวาคม 2547 จำนวน 135 ราย ที่ได้รับการวินิจฉัยว่าติดเชื้อในระบบกระดูกและกล้ามเนื้อในโรงพยาบาลสกลนคร มีรายงานผู้ป่วย 87 รายถูกคัดออกจากการศึกษา เหลือรายงานผู้ป่วย 48 รายที่ครบถ้วนและให้การวินิจฉัยว่าติดเชื้อในโพรงกระดูก โดยผู้ป่วย 13 รายถูกวินิจฉัยเป็นการติดเชื้อกรัมลบในโพรงกระดูกจากข้อมูลในรายงานผู้ป่วยในหรือผู้ป่วยนอก ส่วนข้อมูลอื่นๆที่เป็นปัจจัยเสี่ยง เช่น อาการ อาการแสดง ตำแหน่งรอยโรค ระยะเวลาของอาการ โรคประจำตัวฯลฯ ได้รับการบันทึกเป็นปัจจัยเสี่ยงเพื่อการวิเคราะห์

สถานที่ทำการศึกษา: โรงพยาบาลสกลนคร จังหวัดสกลนคร ประเทศไทย

รูปแบบการศึกษา: งานวิจัยเชิงพรรณนา

ผลการศึกษา: ในผู้ป่วยติดเชื้อกรัมลบในโพรงกระดูก มีผู้ชาย 7 คน ผู้หญิง 9 คน อายุเฉลี่ย (ส่วนเบี่ยงเบนมาตรฐาน) 53.75±14.18 ปี ส่วนในผู้ป่วยที่ติดเชื้อกรัมลบ มีอายุเฉลี่ย 31.17±26.15 เชื้อก่อโรคกรัมลบ ที่พบบ่อยคือ *Pseudomonas auriginosa* (5/16) ส่วนเชื้อก่อโรคกรัมบวก ที่พบบ่อยคือ *Staphylococcus aureus* พบว่า

Background: Osteomyelitis is painful condition for patients and frustrating their doctors. The key to successful management is early diagnosis, including bone sampling for microbiological and pathological examination to allow targeted and long-lasting antimicrobial therapy. Sometime we can not find the causative organism from the tissue culture and require clinical data to select the empirical antibiotics.

Purpose: To report the incidence of causative organism of osteomyelitis and determine such risk factors as well as clinical features of gram negative osteomyelitis in the Northeast region of Thailand.

Materials and Methods: Between January 1999 and December 2004, 135 patients were diagnosed with musculoskeletal infection at Sakolnakorn Hospital, Sakolnakorn, Thailand. Eighty-seven patients were excluded from the study, leaving forty-eight, who made up the study population. Thirteen patients were diagnosed with gram-negative Osteomyelitis on the basis of gram stain or culture of bone from OPD or IPD records. The signs and symptoms, the bone that were involved, the patient occupation, the duration of symptoms, and any concurrent disease were recorded.

Study design: Descriptive analytic study

Setting: Sakolnakorn Hospital, Sakolnakorn, Thailand

Results: Seven men and nine women had gram-negative osteomyelitis. The mean age (and standard deviation) was 53.75±14.18 years in the group with gram-negative osteomyelitis and 31.17±26.15 years in the

อัตราเสี่ยงของผู้ป่วยที่เป็นเบาหวานมีอัตราเสี่ยงของการติดเชื้อกรัมลบในโพรงกระดูก 6.9 เท่า และการติดเชื้อในโพรงกระดูกที่บริเวณเท้ามีอัตราเสี่ยงจากการติดเชื้อกรัมลบ 5.8 เท่า

วิจารณ์และสรุปผล: โดยสรุปพบว่าเบาหวานและการติดเชื้อในโพรงกระดูกบริเวณเท้าเป็นปัจจัยเสี่ยงต่อการติดเชื้อกรัมลบในโพรงกระดูก ดังนั้นแพทย์ควรเลือกยาปฏิชีวนะที่คลุมเชื้อกรัมลบด้วยเสมอ และควรให้ความสนใจในผู้ป่วยที่อายุมากร่วมกับมีโรคประจำตัวว่าอาจติดเชื้อกรัมลบได้

คำสำคัญ: ปัจจัยเสี่ยง; การติดเชื้อในโพรงกระดูก

group with gram-positive osteomyelitis. The most common gram-negative organism was *Pseudomonas auriginosa* (5/16). The most common gram-positive organism was *Staphylococcus aureus*. The odds of a patients having gram-negative osteomyelitis was 6.9 times greater when he or she had concurrent diabetes mellitus than when he or she did not. Six (37.5%) of the patients with gram-negative osteomyelitis and 3 (9%) of the patients with gram-positive osteomyelitis had involved the bone of foot, so the odds ratio that an infection in the bone of foot was caused by gram-negative organism was 5.3 (95% confidence interval, 1.54 to 35.73; P=0.02).

Discussion and Conclusion: In conclusion, we have shown that diabetes mellitus and involvement of bone of foot were the risk factors of gram-negative osteomyelitis. The physician should select the empirical antibiotic that covered gram-negative organism in this group of patients and pay attention in the patients who are old age with concurrent disease.

Key words: risk factors; osteomyelitis

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Introduction

Osteomyelitis is an inflammation process accompanied by bone destruction and caused by an infecting microorganism. This condition is painful for patients and frustrating their doctors. The high success rates of antimicrobial therapy in most infectious diseases have not yet been achieved in bone infections owing to the physiological and anatomical characteristics of bone. The key to successful management is early diagnosis, including bone sampling for microbiological and pathological examination to allow targeted and long-lasting antimicrobial therapy[1, 2]. Sometime we can not find the causative organism from the tissue culture because of the bad collection technique or wrong culture media. These groups of patient require all clinical data to define the high probability of causative organism.

Staphylococus aureus is the infecting organism in older children and adults with osteomyelitis[3-6]. Although *S aureus* is still the most common cause of osteomyelitis a gradual decrease in such cases has been noted over the past 10 to 15 years[7]. From our clinical point of view, gram-negative organisms are responsible for an increasing number of bone infections in adults. Mixed floral osteomyelitis (gram-positive and gram-negative) has increased in the exogenous type of osteomyelitis4. In our area, the Northeast region of Thailand, the incidence of osteomyelitis caused by *Burkholderia pseudomallei* was increase. The goal of our study was to report the incidence of causative organism of osteomyelitis and determine such risk factors as well as clinical features of gram negative osteomyelitis in the Northeast region of Thailand.

Materials and Methods

Between January 1999 and December 2004, 135 patients were diagnosed with musculoskeletal infection at Sakolnakorn Hospital, Sakolnakorn, Thailand. 62 patients were diagnosed with osteomyelitis and included into our study. 6 patients were excluded because of the incomplete medical records. 56 patients with complete medical records were reviewed in this study. Eight patients were excluded from the study on the basis of a negative gram stain and multiple cultures of all specimens, leaving forty-eight, who made up the study population. All patients were analyses for the clinical risk factors of gram-negative osteomyelitis.

The signs and symptoms leading to the diagnosis were fever with bone pain and swelling. Positive laboratory studies included the rising of white blood cell count, a positive gram stain and culture of bone and/or blood. Thirteen patients were diagnosed with gram-negative osteomyelitis on the basis of gram stain or culture of bone from OPD or IPD records. The same criteria were used for gram-positive osteomyelitis. The signs and symptoms, the bone that were involved, the patient occupation, the duration of symptoms, and any concurrent disease were recorded. All patients were treated with antibiotics and, when necessary, with debridement and/or sequestrectomy.

To compare the group with gram-negative osteomyelitis and that with gram-positive osteomyelitis, a univariate analysis was performed with use of the two-sample Student t test for categorical variables and the Fisher exact test for categorical variables. Multiple logistic regressions was used to identified independent clinical predictors with the same group comparisons used in the univariate analysis. Variables with a p value of < 0.2 in the univariate analysis were chosen as candidates for the multivariate model, and significance was determined with use of the likelihood ratio chi-square test. Statistical analyses were carried out with SPSS software (version 11.0; SPSS, Chicago, Illinois).

Results

Seven men and nine women had gram-negative osteomyelitis, and twenty-two men and ten women had gram-positive osteomyelitis. The mean age (and standard deviation) was 53.75 ± 14.18 years in the group with gram-negative osteomyelitis and 31.17 ± 26.15 years in the group with gram-positive osteomyelitis; the mean duration of symptoms was 14.6 ± 12.8 and 8.9 ± 10.1 days, respectively. Three (18%) of the patients with gram-negative osteomyelitis and five (16%) of those with gram-positive osteomyelitis had involvement of an upper extremity. Eleven (69%) with gram-negative osteomyelitis and 8 (25%) with gram-positive osteomyelitis had a concurrent disease, so the odds ratio that gram-negative osteomyelitis occur with concurrent disease was 6.6 (95% confidence interval, 1.75 to 24.85; P=0.003)

The odds of a patients having gram-negative osteomyelitis was 19.28 times greater when he or she had concurrent diabetes mellitus than when he or she did not. Six (37.5%) of the patients with gram-negative osteomyelitis and 3 (9%) of the patients with gram-positive osteomyelitis had involved the bone of foot, so the odds ratio that an infection in the bone of foot was caused by gram-negative organism was 5.8 (95% confidence interval, 1.22 to 27.63; P=0.027). The other risk factors such as multiple concurrent diseases, duration of symptoms, address, leukocytosis, fever and x-ray finding were not statistically significant (Table 1).

The most common gram-negative organism was *Pseudomonas auriginosa* (5/16). The others were *Escherichia coli* (4/16), *Burkholderlia pseudomallei* (4/16), *Klebsiella pneumoniae* (2/16) and *Salmonella* (1/16). The most common gram-positive organism was *Staphylococcus aureus* (15/32). The others were *β-hemolytic streptococcus* (9/32) and *Staphylococcus epidermidis* (4/32).

Results of the multiple logistic regression analysis confirmed only two independent variables as risk factors for gram-negative osteomyelitis: diabetes mellitus and involvement of the bone of foot. In this analysis, the true odds of a patient having gram-negative osteomyelitis were 6.9 times greater, with 95% confidence interval of 1.33 to 85.54, if the patient had diabetes mellitus than he or she did not. The bones of foot were 5.3 times more likely to be infected with gram-negative organism than were the other bones, with 95% confidence interval of 1.54 to 35.73 (Table 2).

Discussion

Aims of our study were to identify the clinical features and risk factors of gram-negative osteomyelitis. This information should be useful to the physicians for choosing the empirical antibiotics in case of the definite diagnosis can not be made or waiting for the cultures. The risk factors for gram-negative osteomyelitis in our study are the osteomyelitis occurs in the bone of the foot and diabetes mellitus, with an odds ratio 5.3 and 6.9, respectively.

The bones in the foot were commonly affected by gram-negative organism in our study. This finding has been mentioned for some organisms. First, diabetic foot ulcer and osteomyelitis usually caused by mixed organism[4, 8]. Second, osteomyelitis of the calcaneus, commonly caused by *Pseudomonas auriginosa*, can follow apparently innocent puncture wound[3]. In our area, the organism exits in the soil and water of Southeast Asia, *Burkholderlia pseudomallei,* can be the causative organism of osteomyelitis at the bone of foot in the same mechanism.

Table 1 Relationship between clinical and laboratory variables and gram-negative osteomyelitis. Univariate analysis.

Variable	Diagnosis		P-value	Odds ratio	95%CI
	G-negative	G-positive			
Age			0.01✦,*		
Sex			0.095*	0.354	0.10-1.22
Male	7	22			
Female	9	10			
Concurrent disease			0.003✦,*	6.60	1.75-24.85
With	11	8			
Without	5	24			
Multiple concurrent disease				0.302	
No	5	24			
One	6	8			
Multiple	5	0			
Diabetes mellitus			0.001✦,*	19.28	3.38-109.7
With	9	2			
Without	7	30			
History of fracture			0.56	2.07	0.12-35.35
With	1	1			
Without	15	31			
Address			0.44	1.44	0.34-6.09
In-town	4	6			
Out-town	12	26			
Location of osteomyelitis			0.75		
Upper extremity	3	5			
Lower extremity	13	26			
Spine	0	1			
Location of osteomyelitis			0.56	1.2	0.25-5.82
Upper extremity	3	5			
Lower extremity	13	26			
Foot involvement			0.027✦,*	5.80	1.22-27.63
With	6	3			
Without	10	29			
Leukocytosis			1.0	1.0	0.29-3.45
With	10	20			
Without	6	12			
Fever			0.66	1.32	0.37-4.65
With	6	10			
Without	10	22			
Duration of symptoms					0.07*
Acute	10	10			
Subacute	3	15			
Chronic	2	7			
X-ray finding			0.6		
Abnormal	12	20			
Normal	4	11			
Miss	0	1			

✦ = statistically significant, * = Included for multivariate analysis

Table 2 Multivariate model of the patient with gram-negative osteomyelitis

Variable	Odd ratio of patients with gram-negative osteomyelitis	95%CI	P-value
Sex	0.10	0.78-6.23	0.75
Age	1.65	0.73-3.91	0.19
Concurrent disease	0.25	0.02-10.10	0.61
Diabetes mellitus	6.90	1.33-85.54	0.01
Foot involvement	5.26	1.54-35.73	0.02

In our study, most patients with gram-negative osteomyelitis had had a longer duration of symptoms than those with gram-positive osteomyelitis and the same with the duration in the hospital care. The reasons may be the long incubation period of some gram negative organism, Burkholderlia pseudomallei, or the underlying host status[7]. The mean age of the gram-negative osteomyelitis patients was higher than gram-positive osteomyelitis with statistically significant in univariate analysis but not in multivariate analysis.

In conclusion, we have shown that diabetes mellitus and involvement of bone of foot were the risk factors of gram-negative osteomyelitis. The physician should select the empirical antibiotic that covered gram-negative organism in this group of patients and pay attention in the patients who were old age with concurrent disease.

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