Genotypic Characterization of Methicillin-resistant Staphylococcus aureus from a Teaching Hospital

J. Junnie1,∗, Y. Hanifah2, K.L. Thong1

1 Institute of Biological Science, Faculty of Science, Universiti Malaya, Kuala Lumpur, Malaysia
2 Department of Medical Microbiology, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia

Background: Methicillin-Resistant Staphylococcus aureus (MRSA) is a serious cause of nosocomial infection in Malaysia. Sixty-six MRSA isolates recovered from patients from Universiti Malaya Medical Centre, KL over a 4-year period (2003–2007) were studied to determine the clonal relationship of sporadic (year 2004 and 2007) and outbreak (year 2003) isolates.

Methods: Polymerase chain reaction was carried out on the isolates to detect the mecA gene which is primarily responsible for the methicillin resistance in Staphylococcus aureus. Pulsed-field gel electrophoresis (PFGE) of Small-digested chromosomal DNA and antimicrobial susceptibility tests were carried out.

Results: Antimicrobial susceptibility tests generated 34 antibiograms with 100% of isolates being susceptible to vancomycin. Majority of the isolates showed susceptibility towards fusidic acid (91%), clindamycin (82%), vancomycin (100%) and rifampin (89%), indicating that these antibiotics will be effective in treating MRSA infections. A dendrogram based on the clustering of the antibiograms showed two major clusters (AM1 and AM2), with AM2 being primarily sporadic isolates. The majority of outbreak isolates were represented by 3 distinct antibiograms that clustered in AM1. Isolates susceptible to gentamicin, sulfamethoxazole-trimethoprim (SXT) and tetracycline gave distinctly different PFGE profiles, and were clustered together. Chi-square or Fishers exact test showed that there was a significant difference (p < 0.05) in antimicrobial resistant between sporadic and outbreak isolates for amikacin, SXT, tetracycline and gentamicin.

Fifty-nine isolates (89%) were mecA positive and showed the presence of the 533bp amplicon, while 7 isolates (11%) were mecA negative. These 7 isolates however showed phenotypic resistance to methicillin. Genotyping by PFGE showed 55 profiles, consisting of 13–17 bands. Among the 25 outbreak isolates, 22 PFGE profiles were obtained, suggesting that the outbreak did not originate from a single point source. Majority (93%) of isolates from year 2007 were clustered together. The diverse PFGE profiles obtained from the sporadic isolates indicated that MRSA were genetically diverse, and the diversity may be explained by the patients coming from different hospital wards.

Conclusion: The morbidity on pneumococcal pneumonia is still remaining underestimated problem in our area and requires careful epidemiology surveillance. There is tendency to forming of epidemic clone which could play role in appearance of nosocomial pneumococcal infections in patients with hematology diseases.

doi:10.1016/j.ijid.2008.05.692

44,003

Genotypic Characterization of Methicillin-resistant Staphylococcus aureus from a Teaching Hospital

J. Junnie1,∗, Y. Hanifah2, K.L. Thong1

1 Institute of Biological Science, Faculty of Science, Universiti Malaya, Kuala Lumpur, Malaysia
2 Department of Medical Microbiology, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia

Background: Methicillin-Resistant Staphylococcus aureus (MRSA) is a serious cause of nosocomial infection in Malaysia. Sixty-six MRSA isolates recovered from patients from Universiti Malaya Medical Centre, KL over a 4-year period (2003–2007) were studied to determine the clonal relationship of sporadic (year 2004 and 2007) and outbreak (year 2003) isolates.

Methods: Polymerase chain reaction was carried out on the isolates to detect the mecA gene which is primarily responsible for the methicillin resistance in Staphylococcus aureus. Pulsed-field gel electrophoresis (PFGE) of Small-digested chromosomal DNA and antimicrobial susceptibility tests were carried out.

Results: Antimicrobial susceptibility tests generated 34 antibiograms with 100% of isolates being susceptible to vancomycin. Majority of the isolates showed susceptibility towards fusidic acid (91%), clindamycin (82%), vancomycin (100%) and rifampin (89%), indicating that these antibiotics will be effective in treating MRSA infections. A dendrogram based on the clustering of the antibiograms showed two major clusters (AM1 and AM2), with AM2 being primarily sporadic isolates. The majority of outbreak isolates were represented by 3 distinct antibiograms that clustered in AM1. Isolates susceptible to gentamicin, sulfamethoxazole-trimethoprim(SXT) and tetracycline gave distinctly different PFGE profiles, and were clustered together. Chi-square or Fishers exact test showed that there was a significant difference (p < 0.05) in antimicrobial resistant between sporadic and outbreak isolates for amikacin, SXT, tetracycline and gentamicin.

Fifty-nine isolates (89%) were mecA positive and showed the presence of the 533bp amplicon, while 7 isolates (11%) were mecA negative. These 7 isolates however showed phenotypic resistance to methicillin. Genotyping by PFGE showed 55 profiles, consisting of 13–17 bands. Among the 25 outbreak isolates, 22 PFGE profiles were obtained, suggesting that the outbreak did not originate from a single point source. Majority (93%) of isolates from year 2007 were clustered together. The diverse PFGE profiles obtained from the sporadic isolates indicated that MRSA were genetically diverse, and the diversity may be explained by the patients coming from different hospital wards.

Conclusion: The morbidity on pneumococcal pneumonia is still remaining underestimated problem in our area and requires careful epidemiology surveillance. There is tendency to forming of epidemic clone which could play role in appearance of nosocomial pneumococcal infections in patients with hematology diseases.

doi:10.1016/j.ijid.2008.05.692

44,003

‘Click Chemistry’ Synthesis of Macrolide Derivatives with Anti-MRSA and Anti-VRE Activity

T. Sunazuka1,∗, A. Sugawara1, K. Nagai1, T. Hirose2, Y. Yamaguchi2, H. Hanaki2, K.B. Sharpless3, S. Omura2

1 Kitasato University, Tokyo, Japan
2 The Kitasato Institute, Tokyo, Japan
3 Scripps Institute, San Diego, CA, USA

Although macrolides, including erythromycin A (EMA), have been widely prescribed for more than 50 years, the emergence of widespread bacterial resistance is a serious and expanding problem. There is a great medical need for new macrolide antibiotics to specifically cope with the problems of antibiotic resistance, especially to combat methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE) strains of bacteria. We have now re-examined various derivatives of EMA, previously synthesized at The Kitasato Institute, evaluating them against 12 types of Gram-positive bacteria, including macrolide-resistant strains, and one Gram-negative organism. We found that 11,12-di-O-butryl-8,9-anhydroerythromycin A 6,9-hemiketal (EM413) showed moderate minimum inhibitory concentration (MIC) against four types of MRSA strains and two types of VRE strains. We subsequently investigated several 11,12-di-O-acyl-8,9-anhydroerythromycin A 6,9-hemiketal derivatives to elucidate their structure-activity relationships against anti-MRSA and VRE bacteria. After screening various diacyl compounds, 11,12-di-O-isobutyryl-8,9-anhydroerythromycin A 6,9-hemiketal (EM1015) was found to be active against MRSA and VRE strains. Furthermore, to obtain higher potency compounds, we synthesized new 8,9-anhydroerythromycin A 6,9-hemiketal derivatives using a copper catalyzed azide-alkyne cyclization reaction (‘click chemistry’). Using click chemistry, we replaced the cladinosine moiety on the C3 hydroxy with a -CH2-CCH group, to enable a fast SAR. This was done because the cladinosine of EMA is not essential for its antibacterial activity, plus this moiety induces macrolide-drug-resistance. We then discovered that the propargyl and some triazole groups can be substituted, instead of cladino-