Journal of Infection and Public Health (2015) 8, 364—368

http://www.elsevier.com/locate/jiph

Prevalence of Panton-Valentine leukocidin-positive methicillin-susceptible *Staphylococcus aureus* infections in a Saudi Arabian hospital

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Received 2 November 2014; received in revised form 10 January 2015; accepted 23 January 2015

KEYWORDS
Panton-Valentine leukocidin;
Methicillin-susceptible *Staphylococcus aureus*;
MSSA

Summary Panton-Valentine leukocidin (PVL) is a two-component toxin associated with the toxicity and virulence of *Staphylococcus aureus*. The presence of PVL is well documented in community-acquired methicillin-resistant *S. aureus* (CA-MRSA) and is observed in methicillin-susceptible *S. aureus* (MSSA) with variable prevalence. We assessed the prevalence of PVL in a sample of 93 MSSA patients in a healthcare facility in Eastern Saudi Arabia using real-time PCR for lukSF-PV genes. The presence or absence of PVL was correlated with age, gender, hospitalization status, infection site and antibiotic resistance. PVL was detected in 28 (30%) patient samples. PVL was associated with a greater likelihood of resistance to trimethoprim—sulfamethoxazole (a resistance of 39.2% of PVL-positive isolates compared to 6.1% of PVL-negative isolates) ($p < 0.0007$). These results suggest a significant prevalence of PVL expression in MSSA strains in the study population and call for monitoring of and surveillance programs for PVL status and the selection of appropriate antibiotic treatments.

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http://dx.doi.org/10.1016/j.jiph.2015.01.010

Introduction

Staphylococcus aureus are nasal, commensal Gram-positive cocci, which colonize in 20—30% of the human population [1], as well as livestock and domestic animals [2,3]. As a human pathogen, *S. aureus* causes infections ranging from mild skin and soft tissue infections to life-threatening sepsis, pneumonia, and toxic shock syndrome. *S. aureus* pathophysiology depends on the presence of virulence factors, including those present on the cell surface and secreted factors. One virulence factor associated with *S. aureus* toxicity is the Panton-Valentine leukocidin (PVL), a two-component toxin that acts by forming pores in the mitochondria [4]. The dual leukocidin PVL toxin components, LukS and LukF, are encoded by the adjacent prophage *lukS* and *lukF* genes [5,6]. PVL reduces immune resistance in a number of ways; for example, it causes neutrophil lysis or apoptosis [4,7] and targets complement receptors [8]. In humans, PVL is associated with skin and soft tissue infections (SSTI), bone and joint infections and necrotizing pneumonia [9]. PVL has been linked to exacerbation of bone loss in osteomyelitis [10] and is proposed as an important virulence factor in keratitis associated with *S. aureus* infection [11].

The prevalence of PVL in methicillin-resistant *S. aureus* (MRSA) is well documented. It is highly expressed in community-acquired (CA)-MRSA strains. However, PVL is expressed in healthcare-associated (HA)-MRSA. PVL is a relatively stable marker of CA-MRSA and is associated in particular with the staphylococcal cassette chromosomes (SCCmec) types IV and V [5,6,12]. The role of PVL in CA-MRSA virulence is debated. In humans, it is associated with increased virulence [6], but animal studies have yielded conflicting results, with a possible immunomodulatory role suggested beyond the cytotoxic effects [13—15].

PVL has also been observed in methicillin-susceptible *S. aureus* (MSSA) strains. Although the epidemiology has not been as extensively established as in MRSA, recently, interest has increased in this field of research. PVL prevalence in MSSA infections varies between countries, from low levels (0.7—2.9%) in Northern Spain, Ireland and Portugal [16—18] to 37% in New Zealand and even higher in African countries, such as Nigeria [19], Cameroon, Madagascar, Morocco, Niger, and Senegal [20]. PVL-positive MSSA has been associated with SSTI [21,22] and cases of necrotizing pneumonia [23,24]. Risk factors for PVL-positive MSSA include Pacific ethnicity, young age, SSTI diagnosis, community-acquired onset of infection, need for surgical intervention, prior hospitalization and smoking [21,25,26].

Because of the wide variation in incidence of PVL-positive MSSA between countries, it is important to characterize MSSA PVL prevalence and risk factors in Saudi Arabia. No such comprehensive analysis has been performed previously, although an isolated case of PVL-positive MSSA was reported in a child with acute osteomyelitis [27] and among 37.6% of 101 MRSA isolates in Jeddah [28]. This study presents data on PVL prevalence in 93 patients with MSSA from a healthcare facility in the Eastern Province of Saudi Arabia.

Materials and methods

Bacterial isolates

A total of 93 MSSA clinical isolates were randomly collected from the Dhahran Health Center, Microbiology Section, from January until December 2013. These specimens were obtained at the request of the attending physician for clinical reasons. The identification of the strains and antibiotics profiles were performed using the VITEK II system. The isolates were sent to the molecular diagnostic laboratory for PVL gene testing. Each isolate was isolated from a different patient.

DNA extraction

Genomic DNA was extracted using the Roche MagNa pure compact nucleic acid isolation kit I, DNA bacteria protocol, according to the manufacturer instructions. Briefly, each strain was resuspended in 0.2 ml of 0.85% saline.

Detection of lukS PV gene

The extracted DNA was screened with the TIB-MOLBIOL LightMix® CA-MRSA PCR kit, Cat# 40-0325-16.

Clinical data

Electronic clinical records were reviewed to ascertain the following demographic data: patient age, gender, and hospitalization.

Results

MSSA isolates were obtained from a total of 93 patients with an age range of 11 months to 99 years. Most infections (72%) were obtained from sputum, blood, semen or urine samples, catheter-related infections, wounds or abscesses. The patients were