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COMMUNITY ASSOCIATED METHICILLIN RESISTANT *S.aureus* (CA-MRSA) INFECTIONS

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ABSTRACT

Staphylococcus aureus is a bacterium commonly found on the skin, axillae, perineum, and in the nares of healthy individuals. At least 30% of the population may permanently or intermittently carry *S. aureus. Staphylococcus aureus* is one of the most common and important pathogen, responsible for the majority of nosocomial infections. *S.aureus* is an opportunistic bacterium, normally, part of the human micro-flora but, attacks immediately when the immune system of the host becomes susceptible. MRSA associated with healthcare has posed a major problem throughout the world. The recent rapid rise of community-associated MRSA (CA-MRSA) has further added to the burden of MRSA infections. Thus, attention has been increasingly focused on the severity and frequency of infections caused by MRSA, and its greater clinical and economic impact compared to methicillin-susceptible *S. aureus* (MSSA). Infections caused by community-acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA) have become epidemic over the last decade. Treatment of infections caused by this organism is problematic due to its resistance to many drugs. Recent reports of community-associated MRSA (CA-MRSA) infections in patients with no known risk factors have serious public health implications. Therapeutic options for these infections are untested; therefore, the potential exists for high morbidity and mortality.

KEY WORDS: CA-MRSA, Soft tissue infections, Nasal carriage, Morbidity.

INTRODUCTION

Staphylococcus aureus is one of the most common and important pathogen, responsible for the majority of nosocomial infections. *S.aureus* is an opportunistic bacterium, normally, part

of the human micro-flora but, attacks immediately when the immune system of the host becomes susceptible. Even though *S.aureus* can be found in different parts of the body but anterior nares are the principal ecological sites in humans [1]. A study had reported nasal carriage as a major risk factor for *S.aureus* infection that differs from person to person [2]. It had been reported that 20% of the healthy individuals carry *S.aureus* persistently, 60% intermittently and 20% never carry *S.aureus*. In the beginning MRSA nosocomial infections were largely detected in large tertiary hospitals and in intensive care units where colonized and infected patients as well as colonized health care personnel were the major cause of cross infection. Presently, MRSA is one of the most widespread pathogens in hospitals of all sizes globally. Worldwide reports had indicated the increasing prevalence of MRSA in hospitals. The National Nosocomial Infections Surveillance (NNIS) System report a 51.3% methicillin rate amongst *S.aureus* strains from 18,397 intensive care unit patients between 1998-2002 in USA [3] that indicate an increase of 25% comparative to the rates reported during 1995-1999 [4].

Acquisition of this organism is typically associated with particular settings (health care institutions, such as hospitals and long-term care facilities) and patient groups (patients with prolonged hospitalization, past antimicrobial use, indwelling catheters, decubitus ulcers, postoperative surgical wounds, and use of intravenous drugs or treatment with enteral feedings or dialysis [5–7]. In recent years, there have been several reports of community-associated MRSA (CA-MRSA) infections throughout the world, including several outbreaks in the United States [8-11]. Most of these outbreaks have been associated with a single-clone strain. Transmission has occurred by close physical contact in situations involving children in day-care centers, children and adults on Indian reservations, athletes, military personnel, correctional facilities, and men having sex with men [12-14]. Of concern, these patients are otherwise healthy individuals with no known risk factors for MRSA acquisition [15]. The prevalence of MRSA infections is increasing in the community [16]. MRSA acquired in the community is referred as community acquired MRSA (CA-MRSA). while as MRSA acquired in the hospital is termed as health care-associated MRSA (HA-MRSA). This division is imperative, because CA-MRSA and HA-MRSA may behave differently. CA-MRSA strains are especially aggressive, causing skin and soft tissue infections, fasciitis [17], necrotizing pneumonia [18], and blood stream infections [19]. Recent investigations have exposed a number of characteristics that differentiate CA-MRSA from health care associated MRSA (HA-MRSA) strains (Table 1).

Table 1. Comparison of CA-MRSA and HA-MRSA.

	HA-MRSA	CA-MRSA
Health care contact	Yes	No
Mean age at infection	Older	Younger
Skin and soft tissue infections	35%	75%
Antibiotic resistance	Many agents	Some agents
Resistance gene	SCC*mec* Types I, II,III, V	SCC*mec* Type IV
Strain type	USA 100 and 200	USA 300 and 400
PVL toxin gene	Rare (5%)	Frequent (almost 100%)

VIRULENCE FACTORS

The appearance of CA-MRSA has created interest in identifying the virulence factors responsible for its pathogenesis. Though the pathogenesis is partly silent, several virulence factors have been concerned. A virulence factor epidemiologically linked to CA-MRSA is Panton-Valentine leukocidin PVL. Van de Velde in 1894 discovered Panton Valentine Leukocidin (PVL) due to its ability to lyse leukocytes. It was named after Sir Philip Noel Panton and Francis Valentine when they associated it with soft tissue infections in 1932 [20, 21]. It is a cytotoxin, one of the β-pore forming toxins. It had been reported that presence of Panton Valentine Leukocidin is mainly associated with increased virulence of certain strains of *Staphylococcus aureus*. Various studies had analyzed its presence in majority of CA-MRSA isolates associated with necrotic lesions of skin and mucosa including necrotic hemorrhagic pneumonia [22, 23 and 24]. Other virulence factors including arginine catabolic mobile element and phenol-soluble modulin have also been linked to CA-MRSA pathogenicity.

RISK FACTORS

The following risk factors should increase suspicion for CA MRSA in patients with compatible signs and symptoms. History of MRSA infection or colonization in patient or close contact, high prevalence of CA MRSA in local community or patient population, recurrent skin disease, crowded living conditions (e.g. homeless shelters, military barracks), history of incarceration, participation in contact sports, skin or soft tissue infection with poor response to B-lactam antibiotics, recent and/or frequent antibiotic use, injection drug use, member of Native American, Pacific Island, Alaskan Native populations, child under age 2 years, male with history of having sex with men and shaving of body hair [25].

EPIDEMIOLOGY

S.aureus is largely disseminated throughout the world with its primary natural reservoir in human beings. It had been associated with serious skin and soft tissue infections in the community settings [26, 27]. A mortality rate of 20-25% still occurs with these pathogenic bacteria despite the availability of the high quality antibiotics [28]. Various particular sites like nares, axillae, vagina and damaged skin surfaces are colonized with *S.aureus*. About 30-50% healthy people are colonized with this particular bacterium with 10-20% persistently colonized [29]. In USA maximum number of community acquired MRSA infections had been reported from the persons without having any traditional risk factor [30, 31, 32], which has made the epidemiology of MRSA too difficult to understand [33].

There were many intermittent reports of CA-MRSA infections during 1980 but 1999 marked the launch of an endemic in USA [34]. CA-MRSA clones USA-300 and USA-400 account for 60-75% of all *S.aureus* infections in the USA community [34]. Similar rising rates of CA-MRSA infections were recorded in UK [35], Australia [36], and Taiwan [37]. In India, CA-MRSA had been studied in pyoderma and other infections [38, 39, 40 and 41].

Carriage of *S.aureus* had been recognized as an important risk factor for infection especially deep seated infections and septicemia [2]. Extensive outbreaks of CA-MRSA infections were described in athletics and pediatric populations [42, 43]. Two different studies revealed the introduction of highly virulent clones of CA-MRSA in to hospital settings [44, 31]. CA-MRSA is liable for around 30% of *S.aureus* infections in hospitals of USA that has put extra burden on health care facilities [31].

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CLINICAL FEATURES

Staphylococci are liable for an embarrassment of infections, including cellulitis, boils, skin abscesses, surgical site infections, endocarditis, osteomyelitis and bacteraemia. Skin and soft tissue infections owed to CA-MRSA naturally present as purulent infections, nothing like simple cellulitis. In a study of 422 cases of skin and soft tissue infections, 59% were owed to CA-MRSA [45]. These are occasionally localized in the areas. *S. aureus* tends to colonize axilla or groin. Non-purulent skin and soft tissue infections due to CA-MRSA sometimes present as an erythematous lesion with a necrotic center. Patients frequently feature the lesion to a spider bite [Fig. 1] but have no exposure. CA-MRSA may act differently than its methicillin sensitive and health care-associated strains. There might be increased transmission between hosts as CA-MRSA is more likely to be secluded from individuals with

household contacts with recent skin and soft tissue infections than community-acquired MSSA [46]. Compared with HA-MRSA, CA-MRSA is more likely to cause skin and soft tissue infections and form abscesses [47]. These may be more severe, and require increased surgical attention [48].

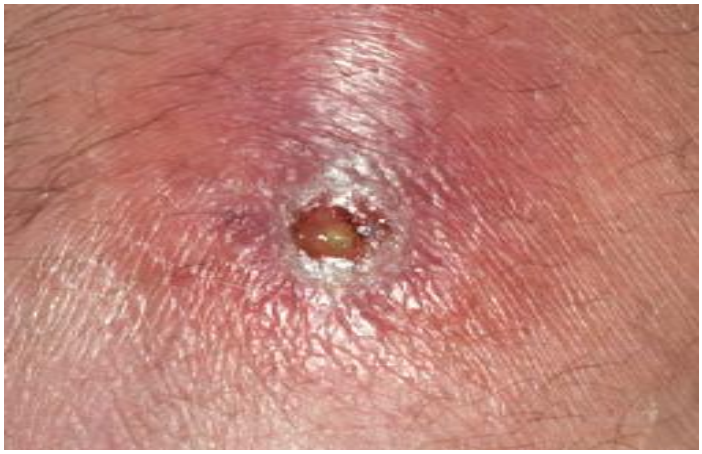

Fig. 1 spider bite infection of an MRSA strain

TREATMENT

CA-MRSA has progressively become a significant cause of SSTIs. Thus, it is important for clinicians to consider CA-MRSA when treating patients with possible staphylococcal infections. Infections caused by CA-MRSA plunge into a wide spectrum, ranging from simple skin and soft tissue infections, which can be treated in outpatient settings, to ruthless sepsis and toxic shock syndrome, which require hospitalization and antagonistic treatment. Since CA-MRSA strains are likely susceptible to a broad range of non-β-lactam antibiotics**.** Researchers have articulated new interest in the exploit of clindamycin, tetracyclines, and trimethoprim-sulfamethoxazole (TMP-SMX) in treating MRSA infections, as these drugs normally have action against CA-MRSA [49, 50]. For severe infections requiring hospitalization together with intravenous antibiotics, vancomycin and newer agents, such as linezolid, quinupristin-dalfopristin, and daptomycin, can be feasible options. Clindamycin relics a viable treatment option for CA-MRSA, as it demonstrates in vitro susceptibility to most MRSA isolates. Trimethoprim-sulfamethoxazole is one more antibiotic with achievable activity for treatment of CA-MRSA.

But, limited clinical studies and patient cases have set up TMP-SMX to be useful in treating MRSA infections. Minocycline is a tetracycline antibiotic that has been used in the ancient times for the treatment of MRSA [51]. Doxycycline, one more tetracycline compound, has a

comparable vulnerability profile. Vancomycin has been proved as a secure and effectual treatment option for MRSA. Linezolid has high-quality diffusion into skin and soft tissue infections and is accessible in an oral formulation. Although it is measured a bacteriostatic agent, linezolid has demonstrated efficacy in skin and soft tissue infections, bacteremia, and pneumonia caused by gram-positive bacteria. Linezolid shows action against MRSA. Daptomycin is an original lipopeptide antibiotic accepted by the FDA in 2003 for treatment of convoluted skin and soft tissue infections, together with those caused by MRSA. This drug has established a lot o interest, because of its action against multidrug-resistant gram-positive bacteria, particularly MRSA [52]. For non-complicated *S. aureus* skin and soft tissue abscesses, incision and drainage therapy, devoid of antibiotics is generally adequate.

DECOLONIZATION

Persons colonized with MRSA are possible sources of patient to patient transmission through health care workers, in healthcare settings. Measures to decolonize patients and staff with topical intranasal mupirocin have been used to control outbreaks and ongoing transmission in health care settings. One prospective and randomized study examined use of nasal mupirocin, chlorhexidine washes and oral rifampin with doxycycline for suppression of MRSA carriage [53]. It may be useful then, to introduce an institution ample decolonization routine, likely to involve mupirocin ointment and chlorhexidine washes along with heightened awareness of high-quality hygiene.

Control of CA-MRSA in community

1. Good communications between hospitals discharging patient's home with MRSA with curers or family members, community nurses and General Practitioners and between hospital and community hospitals or long-stay residential units, are essential in minimizing spread. There is little risk of transmitting MRSA to healthy people who are at low risk of becoming infected.
2. Patients should be informed that the risk to healthy relatives or others outside the hospital setting is extremely small unless, they are hospital workers with patient contact when they may pose a risk to other patients. Because there is little risk of transmitting MRSA to healthy members of the community and there is minimal risk of them becoming infected eradication of MRSA carriage in the community is generally not required.

3. Good hand washing practice is the single most important infection control measure. Caretakers should wash their hands with soap and water after physical contact with the infected or colonized person and before leaving the home.

4. Disposable gloves should be worn if contact with body fluids or dressings and hands should be washed after removing the gloves. Cuts or breaks in the skin of curers should be covered with impermeable dressings.

5. Linens should be changed and washed if they are soiled and on a routine basis. The patient's environment should be cleaned using standard detergents routinely and when soiled with body fluids (IPC, 2005).

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