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Community-Associated MRSA—Not So Innocent Sibling per Se: A Case Report

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ABSTRACT

Background: Methicillin-resistant *S. aureus* (MRSA) is a major healthcare burden and is classified as healthcare-associated (HA-MRSA) and community-associated (CA-MRSA). While HA-MRSA is clinically feared, CA-MRSA is often considered less pathogenic. This case report highlights the serious course of illness due to CA-MRSA infection and provides a treatment strategy for the management of such cases.

Case description: A 41-year-old male presented with fever and breathlessness for five days. Upon admission, he was provided empirical treatment for atypical infections and vasopressor support for hypotension. His condition deteriorated, necessitating ventilator support. Although the initial tracheal Bio Fire test indicated MRSA, his clinical manifestations did not match MRSA pneumonia symptoms; however, CA-MRSA was confirmed within 12 h. Skin legions developed within 16 h and progressed gradually from ecchymosis, petechial, and palpable purpura to bullous lesions over 72 h. The antibiotic regimen was modified and optimized with the addition of Clindamycin, Vancomycin, and Meropenem–Colistin. Owing to high IL-6 levels, dual vasopressor support, and acute kidney failure, he was started on early (within 12 h) continuous renal replacement therapy (CRRT) with CytoSorb filter (for 3 days) for cytokine removal. IL-6 levels decreased after two days of CytoSorb use. Subsequently, the patient stabilized with reduced dependence on vasopressor and ventilator assistance.

Discussion: Early diagnosis of CA-MRSA and management with CRRT using CytoSorb may help improve patient outcomes. To our knowledge, this is the first report of clinical management of CA-MRSA with CytoSorb therapy in India that resulted in positive outcomes.

KEYWORDS: community-associated MRSA, CytoSorb therapy, continuous renal replacement therapy, septic shock, extracorporeal hemadsorption, interleukin-6

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I. INTRODUCTION

Staphylococcus aureus, a Gram-positive, non-motile, coagulase-positive coccoid bacterium, is part of the human commensal nasal microbiota in 20–40% of the general population [1]. Although the *Staphylococcus* genus encompasses 52 species and 28 subspecies, *S. aureus* garners the most clinical attention owing to its pathogenic risk. It can become pathogenic upon a breach in the cutaneous and mucosal surfaces, resulting from chronic skin conditions, wounds, or surgical intervention, by infiltrating the underlying tissues or the bloodstream. People on invasive medical device support (peripheral and central venous catheters) or those with compromised immune systems are often susceptible to *S. aureus* infection, which is broadly divided based susceptibility to Methicillin [1]. Despite discontinuation of Methicillin use in humans owing to its

toxicity, the term "Methicillin-resistant *S. aureus*" (MRSA) continues to be used. Compared to MRSA, Methicillin-susceptible *S. aureus* (MSSA), is considered a lesser clinical nuisance owing to its responsiveness to first-generation Cephalosporin. Soon after its detection in 1961, MRSA outbreaks were reported in hospitals worldwide [healthcare-associated MRSA (HA-MRSA)]. Subsequently, a substantial change in MRSA epidemiology was witnessed upon its detection in individuals without previous healthcare contact [community-associated MRSA (CA-MRSA)]. Differences between HA-MRSA and CA-MRSA are summarized in Table I. Interestingly, *S. aureus* strains producing the cytotoxin Panton–Valentine leucocidin (PVL), which causes leukocyte destruction and tissue necrosis, are highly virulent and transmissible [2]. However, whether PVL is pathogenic or an epidemiological marker remains unclear. From an epidemiological perspective, PVL-positivity is associated with CA-MRSA.

CA-MRSA is an MRSA infection in individuals with no history of the following risk factors within the year before a positive MRSA culture report: surgery/hospitalization, permanent indwelling catheters or percutaneous medical devices for dialysis, residence in a long-term care facility, and positive MRSA culture <48 h post-hospitalization. However, little is known about CA-MRSA prevalence in India. This case report highlights the spectrum of virulence, toxic shock syndrome and resistance associated with CA-MRSA in India.

Table I: Differentiating characteristics of HA-MRSA and CA-MRSA

	HA-MRSA	**CA-MRSA**
Discovery	1960s	1980s
At-Risk Population	Residents of Healthcare facilities, diabetics, hospitalised patients, ICU patients, and patients who visit hospitals routinely	Young persons, abandoned and homeless, homosexual males, prisoners and soldiers, intravenous drug abusers
Antimicrobial Drug Resistance	Multidrug resistance may be susceptible to TMP-SMX, Macrolides, and Tetracyclines	Erythromycin and Beta-lactam drugs (Oxacillin, Penicillin),
SCC mec Gene Subtype	I, II, and III present	IV and V present
Medical History	History of colonisation with MRSA, recent surgery, hospitalisation, dialysis, permanent indwelling catheters	No significant healthcare contact or medical history
PVL toxin	Rarely present (less than 5% of cases)	Present in more than 95% of cases
Associated Medical Condition	SSTI, bloodstream-related infections, pneumonia, or catheter-related UTI	SSTI, post influenza necrotizing pneumonia

II. CASE DESCRIPTION

A 41-year-old male who had travelled to Northern India experienced ongoing fever and breathlessness for five days, and was shifted to our hospital for further management. He presented with severe hypotension, requiring vasopressor support, and gradually worsened to respiratory failure along with seizures, needing intubation and ventilator support. He had skin lesions progressing from ecchymosis, petechial, and palpable purpura to bullous lesions, which worsened with rising levels of lactates and acidosis. On a high-risk suspicion, he received an empirical treatment comprising Piperacillin–Tazobactam, Acyclovir, Artesunate, Artesunate ether, and Doxycycline to cover atypical infections upon admission. Subsequently, Vancomycin was added to the regimen on account of his deteriorating state and development of skin and subcutaneous lesions, followed by Meropenem and Colistin. Though the initial tracheal BioFire test (BioFire Diagnostics, UT, USA) indicated MRSA, his clinical manifestations did not match the MRSA pneumonia symptoms. With culture reports awaited and inconclusive neuroimaging report, multifocal encephalopathy was suspected, for which he underwent a lumbar puncture on the second day of admission; however, cerebrospinal fluid (CSF) studies were inconclusive. Subsequent BioFire test within 12 h revealed CA-MRSA infection. Skin lesions developed within 16 h, and Clindamycin was added to counteract the CA-MRSA endotoxin. As the endotracheal cultures revealed CA-MRSA with a resistant pattern of *mec-A/C* & *MREJ* genes, Clindamycin was replaced with Vancomycin, and subsequently with Linezolid. He started developing bilateral lower limb ecchymosis lesions that progressed to blisters, pointing toward the diagnosis of toxic shock syndrome. Considering the florid endotoxin shock, he received intravenous immunoglobulin (IVIG) for five days. By day 10, he showed neurological improvement, and we deescalated the antibiotic regimen to Meropenem and Linezolid.

The patient received early (within 12 h of admission) continuous renal replacement therapy (CRRT) along with hemadsorption using CytoSorb as a cytokine removal therapy

owing to acute kidney injury (decreased urine output, acidosis, high lactate levels) and worsening shock [high levels of septic and inflammatory markers, including high interleukin-6 (IL-6) level >1000 IU] along with sustained vasopressor requirement; notably, CRRT was commenced when Norepinephrine requirement was 0.2 µg/kg/min. Despite fluid resuscitation, the patient required triple vasopressor support to maintain his blood pressure. He remained on ventilator support and haemodialysis with one CytoSorb filter/day for three days; IL-6 levels decreased after two days. Over the next three days, the patient stabilized with lower dependence on vasopressor and ventilator assistance; however, skin lesions worsened to purpura fulminans and limb ischemia. The serial inflammatory markers and elevated urinary myoglobin levels, likely caused by limb ischemia, decreased. The patient was weaned off vasopressor and ventilator support; however, he needed ongoing intermittent dialysis for deranged renal function, which extended his length of stay in the ICU to 19 days.

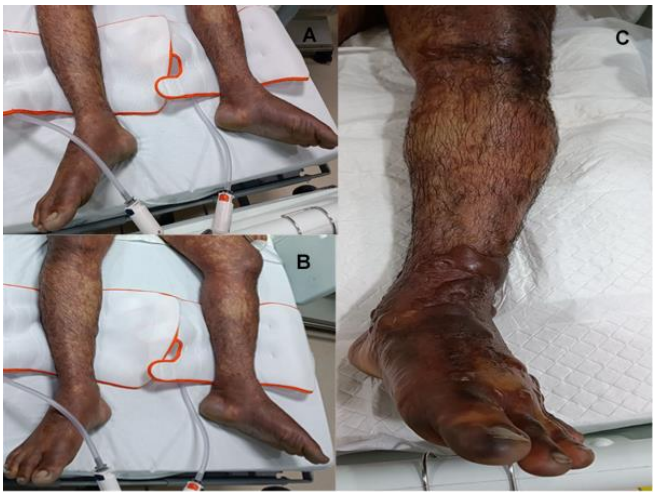

Figure 1: Progressive limb lesion worsening
Images captured at 24 h (A), 36 h (B), and 72 h (C) depict the progression of skin lesions associated with CA-MRSA infection.

III. DISCUSSION

Methicillin resistance is mediated by *mecA* gene, contained in the Staphylococcal chromosome cassette (*SCC-mecA*); it encodes Penicillin Binding Protein 2a (PBP2a). In India, the prevalence of CA-MRSA, characterised by presence of *SCC mec* IV and V genes, is rising [3]. PVL, a pore-forming cytotoxin, is composed of two separate proteins encoded by two adjacent genes (*lukS-PV* and *lukF-PV*). Shohayeb et al. found high prevalence of PVL genes among *mecA*-positive MRSA isolates, irrespective of CA-MRSA or HA-MRSA strains [2]. A single-centre study in India identified 72 *S. aureus* isolates (51 MRSA and 21 MSSA) that showed absolute resistance against beta-lactam antibiotics (Penicillin, Ampicillin, Amoxicillin) but were sensitive towards Macrolide and Lincosamide antibiotics [4]. Gene distribution among these MRSA isolates showed the presence of *femA*, *mecA*, and *lukS* in 100, 94.4, and 69.4% of the isolates, respectively. The antibiotic sensitivity pattern and molecular characterisation showed an increased prevalence of CA-MRSA in the study population [4]. CA-MRSA strains in India frequently demonstrate resistance to multiple antibiotics [3,5], posing significant challenges in clinical management and emphasising the need for tailored treatment strategies in this region. Moreover, resistance to antibiotics is higher in PVL-positive CA-MRSA, necessitating reduction in use of multiple antibiotics and following MRSA-specific treatment [2].

In our patient, the severe, florid CA-MRSA infection necessitated a careful approach to antibiotics. The evolving skin lesions and atypical presentation required an initial empiric antibiotic regimen, with a subsequent transition to Vancomycin, Linezolid, and Meropenem because of high suspicion of a multidrug-resistant CA-MRSA strain that led to suboptimal outcomes. Deteriorating patient condition along with dual vasopressor requirement prompted the use of cytokine removal therapy (CytoSorb) early in the treatment course. This aggressive approach was adopted to counteract the cytokine storm elicited by CA-MRSA infection, contributing to substantial improvement in patient outcomes. Additionally, we revised and optimised the antibiotic therapy to Meropenem and Vancomycin for multidrug resistance. This case emphasises the tribulations of managing infections with rapidly evolving resistance patterns.

CytoSorb has been reported as a potential supportive therapy in patients with septic shock, including those with MRSA infection, and its use has been shown to reduce IL-6 and vasopressor requirements [6]. In a 14-year-old patient with MRSA and Influenza B infection, CytoSorb use decreased the vasopressor requirement [7]. Similarly, CytoSorb use led to a remarkable recovery in an adolescent with *S. aureus* toxic shock syndrome [8]. Scandroglio et al. analysed the impact of CytoSorb on drug clearance in critically ill patients and found it to be safe in the case of Vancomycin administration [9]. Overall, evidence suggests that CytoSorb can be used to treat MRSA infections, particularly in cases of septic shock, although its safety and efficacy need further validation. However, adjunct CytoSorb therapy in CA-MRSA cases has not been previously reported in India.

CA-MRSA strains, prevalent among otherwise healthy individuals, challenge traditional risk profiles associated with MRSA infections. Given their evolving resistance patterns, it is urgent to recognise and effectively manage severe CA-MRSA infections in India. Early initiation of tailored antibiotic regimens and aggressive cytokine removal therapies, especially in the face of high suspicion of multidrug resistance, may significantly facilitate desirable patient outcomes. Rugg et al. reported that the addition of extracorporeal hemadsorption using CytoSorb to standard care in patients with septic shock requiring renal replacement therapy approximately halved the catecholamine requirement

within 24 h [10]. Moreover, they reported significant reduction in in-hospital and 28-day mortality with CytoSorb use. However, high lactate levels may indicate absent benefits in such cases [10]. Patients admitted with such fulminant toxic shock syndrome with CA-MRSA can be managed with early extracorporeal hemadsorption therapy using CytoSorb with CRRT.

CONCLUSIONS

Although CA-MRSA is perceived as less virulent than HA-MRSA, the present case study calls attention to the detrimental side of CA-MRSA. Its early diagnosis and management with CRRT using CytoSorb as an adjunct may help improve patient outcomes. This case report outlines central concerns in diagnosing and managing multidrug-resistant CA-MRSA. To our knowledge, this is the first report from India wherein clinical management of CA-MRSA with adjuvant CytoSorb therapy was implemented and positive outcomes have been recorded.

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