CASE REPORT

The Challenge of Diagnosing and Treating Staphylococcus aureus Invasive Infections in a Resource-limited Sub-Saharan Africa Setting: A Case Report

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ABSTRACT

Background: Community-acquired methicillin-sensitive Staphylococcus aureus (CA-MSSA) is responsible for the majority of skin and soft-tissue infections. CA-MSSA can also cause life-threatening infections, possibly in relation to particular virulence factors, including Panton–Valentine leukocidin (PVL).

Methods: We describe a severe CA-MSSA necrotizing pneumonia complicated with multifocal osteomyelitis, pericardial effusion and endocarditis in a 6-year-old boy admitted to a Mozambican hospital. Staphylococcus aureus isolation and antibiotic susceptibility testing were performed by conventional microbiology. Additionally, microarray assay was used for molecular characterization.

Results: Blood culture confirmed the presence of S. aureus susceptible to most antimicrobial agents, including methicillin. Molecular characterization confirmed the presence of PVL, together with alpha and beta haemolysin genes.

Conclusions: To our knowledge, this is the first reported case of disseminated CA-MSSA disease with confirmed PVL exotoxin in sub-Saharan Africa. PVL-positive CA-MSSA should be considered in the differential diagnosis of community-acquired pneumonia, making laboratory testing a higher priority.
KEYWORDS: *Staphylococcus aureus*, community-acquired infections, Panton–Valentine leukocidin, necrotizing pneumonia, virulence factors, Sub-Saharan Africa.

INTRODUCTION

*Staphylococcus aureus* (SA) is a leading cause of skin and soft-tissue infections (SSTIs), but also of more invasive diseases like endocarditis, pneumonia and septic arthritis/osteomyelitis.

Contrarily to what occurs in the developed world, SA disease ranks low on the public-health agenda in low-income countries, particularly when compared with other infectious diseases such as malaria, tuberculosis or HIV/AIDS. Although the majority of SA infections are SSTIs, SA-related invasive disease is a major cause of childhood morbidity and mortality that far exceeds the burden found in developed countries [1–3].

Over the past few decades, management of SA has become a therapeutic challenge following the emergence of methicillin-resistant SA (MRSA) strains, an increasingly important public health problem, owing to their circulation not only as nosocomial pathogens, but also predominantly at the community level worldwide [4–6].

In Western countries, the epidemiology of SA is well documented, but in resource-limited countries, the epidemiology of SA and particularly the presence of virulence factors that may condition its prognosis are still poorly characterized.

It has been estimated that 30–50% of children born in a rural setting in Africa will probably die before the age of 5 years without any medical intervention [7]. This in part is because of difficult access to the health system, leading to delayed presentation to the hospital, scarce and often dysfunctional health care systems and infrastructures and poorly motivated health staff [5]. In the context of scarce functioning microbiology surveillance systems in sub-Saharan Africa, the majority of these deaths are not further investigated so the contribution of bacterial disease, and in particular SA, to child mortality is probably underestimated [7].

We present a case of confirmed SA-disseminated infection, including a detailed etiological investigation, antimicrobial sensitivity tests and the investigation for the presence of a range of virulence factors [e.g. Panton–Valentine leukocidin (PVL) and haemolysins among others]. We were also able to diagnose and characterize its complications, which included endocarditis with pericardial effusion, pyomyositis and bilateral necrotizing pneumonia with empyema. The case was admitted at the Manhiça district hospital (MDH), a 110-bed referral hospital for the Manhiça district located 80 km north of Maputo province. In this district, the Manhiça Health Research Centre (Centro de Investigação em Saúde da Manhiça) jointly with the MDH has been running since 1998 a morbidity surveillance at MDH linked to an ongoing wider demographic surveillance system (DSS) conducted in the District of Manhiça (population 160 000 Inhabitants). The data collected in Manhiça DSS comprises household and individual characteristics, socio-economic assets, vital data, migration, individual health history and cause of death, among others [8]. Through these two surveillance platforms, we were able to track the patient at home after hospital discharge and determine his final outcome.

CASE REPORT

A previously healthy 6-year-old boy presented to the emergency department of MDH, in Southern Mozambique, with a 3 day history of high fever, weakness and productive cough, as well as a 1 day history of shivering and dyspnea. One week before admission, the child had suffered a traumatism to his right knee and experienced progressive pain and swelling since then. On admission, the temperature was 39.8°C, and on examination, he presented chest in drawing (intercostal), tachycardia (130/min), tachypnea (50/min) and hypotension (80/50 mmHg). Pulmonary auscultation revealed crackles over the lower and middle, right and left lung fields, while chest X-ray (CXR) showed patchy alveolar opacities and bilateral infiltrates (Fig. 1), with a possible bulla in the right lung. Initial laboratory tests showed a white blood cells count of 21 000/l with neutrophilia (75.1%). Blood samples were collected for culture. Tests for malaria
slide for microscopy) and HIV (rapid diagnostic test) were also performed and negative.

With the provisional diagnosis of acute community-acquired pneumonia, the patient was empirically treated with penicillin and gentamycin as per local guidelines in severe infection, and was switched to ceftriaxone according to patient’s increasing dyspnea requiring oxygen support and signs of septic shock. A new CXR revealed bilateral infiltrates with multiple cavitating lesions (Fig. 2). Necrotizing pneumonia was suspected, and the only available intravenous (IV) antibiotic that would cover a possible MRSA was cotrimoxazole, which was added to the treatment. The next day blood culture confirmed the growth of MSSA, resistant to amoxicillin-clavulanate but sensitive to other antibiotics tested.

Respiratory distress improved but persistent low-grade fever, intermittent pain in both knees and ankles and swelling and tenderness of the right arm was suggestive of embolic complications. Incisional drainage at the level of the left soleus and right biceps muscles provided 250 and 300 ml of pus, respectively. At this point, and as a result of the limitations for treatment available at MDH, transfer of the child to MCH (the tertiary referral hospital in Mozambique’s capital) was organized. When the family overheard this possibility, they decided to abscond from the hospital with the child, with the drainages in place. Fortunately, this patient was living in the area under DSS and was easily located and brought back to hospital.

Throughout his admission in MDH, fever spikes occurred on a daily basis, and a repeat CXR revealed cardiomegaly. A basic echocardiography was performed using a portable echocardiography machine, which evidenced a large vegetation on the tricuspid valve and an important pericardial effusion with fibrin septa. Suspecting a right heart endocarditis as
cause of the septic embolism to the lungs, we decided to transfer (prior agreement with the child’s mother in her local language) the child to MCH where humeral and tibia osteomyelitis and tricuspid endocarditis with pericardial effusion were confirmed. Vancomycin plus gentamycin were administered intravenously for 10 days, as no other IV anti-staphylococcal agents were available. After significant improvement, the child was switched to oral flucloxacillin.

Molecular characterization of the isolates was performed using microarray assay (Iconoclust, Alere Technologies) capable to screen for >320 virulence factors, and the results showed the presence of PVL, alpha and beta haemolysins. When the child was finally clinically improving, a skin vesicular rash appeared. Staphylococcal scalded skin syndrome was ruled out after the first 24 h, when the more typical rash appearance of varicella was evident. The patient also responded well to treatment with acyclovir. Our patient experienced a prolonged hospitalization and was finally discharged after 50 days of admission.

Informed consent was obtained from the patient’s family for description of the case, which included permission for displaying pictures of the case.

**DISCUSSION**

Invasive bacterial diseases continue to have a devastating impact on childhood morbidity affecting mainly previously healthy children and young adults [6]. Since the 1990s, MRSA clones have emerged as a global public health concern both at the hospital and community settings. The virulence of SA is generally considered to be multifactorial and due to the combined action of several virulence determinants. The main virulence factors of SA that have potential to cause tissue injury and inflammation in the lung are SpA, α haemolysin, β haemolysin and PVL [1, 2]. In turn, necrotizing pneumonia is associated with an action of SpA, α haemolysin and β haemolysin that cause cell damage and play a role in inflammation and necrosis of the respiratory epithelium. PVL, a SA exotoxin that induces lysis of monocytes and neutrophil granulocytes have been temptatively associated to an adverse prognosis; however, the role of such virulence factor in causing necrotizing and disseminated disease is still controversial [9, 10]. Typically, invasive PVL producing SA results in necrotizing pneumonia, characterized by hemoptyis, leukopenia, high fever and cavitary lung lesion on CXR, often requiring mechanical ventilation [11, 12]. In paediatrics, an association

**FIG. 2.** Chest radiograph on day 10 of hospitalization, showing bilateral infiltrates with multiple cavitating lesions (arrow).
of osteomyelitis and septic pulmonary embolisms due to PVL positivity in community-acquired methicillin-sensitive Staphylococcus aureus (CA-MSSA) has also been described [13].

We describe the case of a child, without prior history of hospitalization, who presented with a complex case of respiratory distress and bone pain, complicated by necrotizing pneumonia, pericarditis, multifocal osteomyelitis and CA-MSSA bacteraemia.

Interestingly, population analysis of global MSSA isolates associated with PVL have recently indicated that PVL-positive MSSA and MRSA are phylogenetically related [10]. In this region, few reports exist on SA infections, and our case is the first report of severe invasive and disseminated disease with CA-MSSA with proven PVL exotoxin. Few reports have indicated a different clonal structure and profile of virulence factors in SA isolates from sub-Saharan Africa. Indeed, it is striking that reports from African countries have recently described a high prevalence of PVL-positive MSSA isolates in Nigeria and Mali and have supported the hypothesis that at least one common European MRSA clone associated with PVL could originate from African MSSA clones [14, 15].

The optimal treatment of SA-invasive infections has not been established. An effective treatment should target SA but additionally also the toxin production with antibiotics like clindamycin, linezolid or rifampicin if suspected [1]. Drainage of the supplicative collection, if possible, is suggested to confirm the underlying aetiology but also to remove PVL-containing tissues. By the time, the diagnosis of necrotizing pneumonia is made, the pathology secondary to CA-MSSA and PVL is probably well advanced and it may be difficult to neutralize the organism and the consequences of its virulence factor. Early diagnosis and intervention may be critical in improving outcomes of necrotizing pneumonia; so we recommend considering CA-MSSA among pathogens that cause community-acquired pneumonia, in patients presenting to casualty with respiratory and joint and bone symptoms being PVL noted as a virulence factor of deep skin with large abscesses, such as furuncles and cellulites and increasingly been noted in association with osteomyelitis [16, 17].

In conclusion, CA-MSSA is an increasingly recognized disease in Africa, and can lead to invasive life-threatening infections. The case we present is an example of a successfully treated patient without any sequelae owing to early recognition of the problem and the prompt initiation of adequate antimicrobial therapy. Providing health care in Africa is a complex problem. More resources to assist in the prevention and understand the trends in antibiotic-resistance and virulence factors of infectious diseases that affect this population are needed, quick diagnosis being an essential concept.

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REFERENCES