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CASE REPORT

Staphylococcus aureus bacteraemia in children: a formidable foe

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Staphylococcus aureus remains one of the most common causes of bacteraemia in children. In order to evade and overcome the immune responses of its host and any antimicrobial therapies aimed at destroying it, this organism, through various mechanisms, continues to evolve. *Staphylococcus aureus* bacteraemia is a systemic disease; and, multiple organ involvement should be assessed and appropriately managed. This is especially important for the anaesthetist who will be administering general anaesthesia to children presenting for surgical source control.

Keywords: bacteraemia, children, pneumonia, septic arthritis, *staphylococcus aureus*

Case report

A previously healthy seven-year-old boy presented for incision and drainage of his left knee, shoulder and elbow for suspected septic arthritis. Four days prior to presenting at Red Cross War Memorial Children's Hospital (RCWMCH), the child complained first of a painful left knee, then a painful left shoulder. He was taken to a general practitioner and received oral antibiotics. He presented to RCWMCH with systemic fever, coughing, loss of appetite and malaise.

Initial examination in the emergency unit revealed an acutely ill child in compensated septic shock. His left knee and shoulder were found to be warm and swollen, and a small pustule was noted on the medial aspect of his left knee.

While awaiting blood results and chest radiography, fluid resuscitation was commenced and intravenous cloxacillin was administered. The chest radiograph (Figure 1) demonstrated a multi-lobar pneumonia. Radiographs of the left knee (Figure 2(a)) and shoulder (Figure 2(b)) did not convincingly demonstrate joint space effusion. Initial blood results (Table 1 and 2) suggested circulatory, haematological and renal compromise.

The Intensive Care Unit (ICU) was consulted. He was started on a dopamine infusion, received cefotaxime; and, to address his hyponatraemia, he was started on an infusion of 0.9% saline with 5% dextrose. He was reviewed by the orthopaedic team and booked for emergency incision and drainage of his left knee, left shoulder and, prospectively, left elbow. Shortly thereafter, he was transferred to the ICU.

Approximately two hours after admission to the ICU, the child was transferred to theatre by the anaesthetic team. He remained drowsy, tachypnoeic on high flow oxygen and, despite instituting inotropic support, his circulatory status had deteriorated. With inotropic support, he was maintaining a mean arterial pressure of 60 mmHg by non-invasive measurement; but, had no palpable peripheral pulses and a heart rate of 150 beats per minute. Considerations for choosing an appropriate anaesthetic technique were haemodynamic instability, metabolic acidosis, renal dysfunction and a fasting period of approximately 24 h. After application of standard monitoring, general anaesthesia and intubating conditions were achieved with 50 mg ketamine and 6 mg *cis*-atracurium, while administering a bolus of Ringer's lactate. Shortly after induction of anaesthesia, blood pressure became unrecordable and adrenaline was commenced at 0.08 µg/kg/min in place of the dopamine, with reasonable effect. After induction, arterial and central lines were inserted.

From the outset, bag-mask ventilation was difficult as lung compliance seemed poor. Laryngoscopy was performed and non-particulate gastric content noted in the oropharynx. After suctioning, the patient was intubated and the trachea suctioned via the endotracheal tube. A small amount of gastric content was present. A nasogastric tube was inserted, which drained fluid with a ground coffee-like appearance. Ventilation proved difficult with high peak inspiratory pressures and high inspiratory oxygen concentration. Despite an end-tidal carbon dioxide concentration in the normal range, arterial blood gas revealed hypercarbia. The alveolar-arterial oxygen gradient was significantly raised.

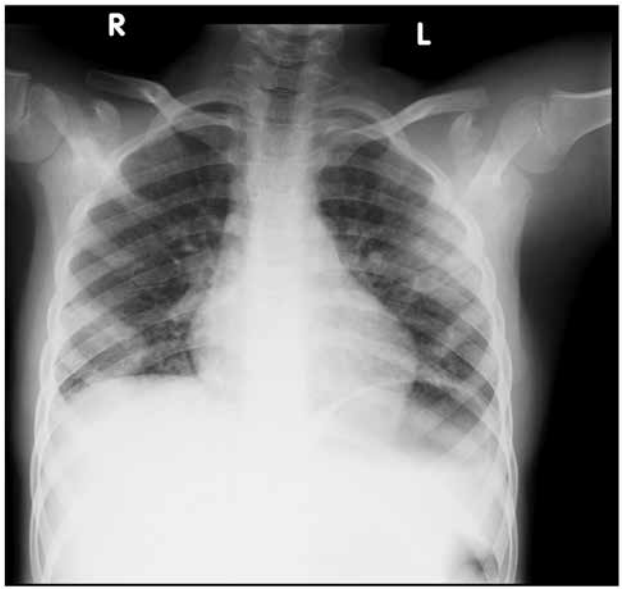

Figure 1: Initial chest radiograph.

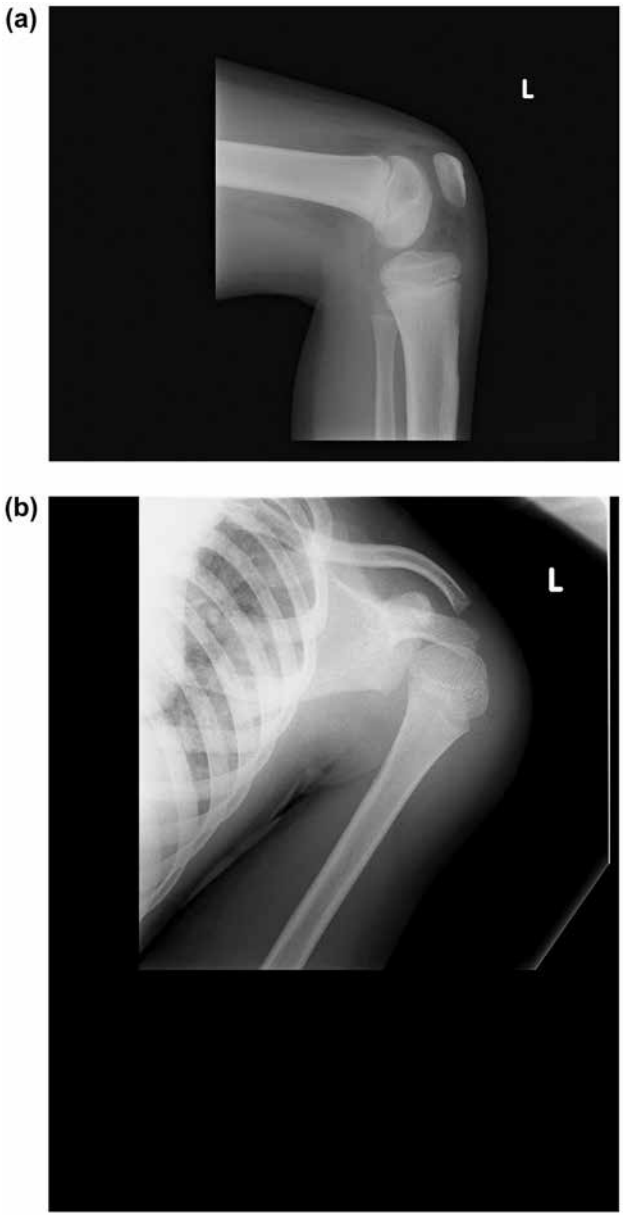

Figure 2: (a) and (b) Radiographs of left knee and shoulder.

Further management in theatre included attempts to optimise the intravascular volume. The orthopaedic surgeon proceeded with arthrotomies of the left knee and shoulder, which were both negative for purulent material. The child was transferred back to ICU ventilated with ongoing inotropic support.

After 8.5 h of incubation, the blood culture taken on admission was positive for a methicillin sensitive *Staphylococcus aureus*. The patient's ICU stay was complicated by a second incident of airway soiling with gastric content due to an accidental extubation during a ventilator exchange. There exists the possibility that aspiration pneumonia contributed to his respiratory morbidity. Over the course of the next 48 h, the child's clinical condition and laboratory markers of organ dysfunction progressively deteriorated (Table 1). A follow-up chest radiograph demonstrated diffuse air-space opacification (Figure 3). High doses of both adrenaline and noradrenaline were required to maintain adequate perfusion pressure at the expense of peripheral circulation (Figure 4). Abdominal ultrasound and echocardiogram did not demonstrate any additional foci of infection. Despite maximal therapeutic measures, the patient demised approximately 60 h after hospital admission.

Table 1: Summary of laboratory values

	Admission (Day 0)	Day 1	Day 2
WBC (x 10^9 cells/L)	4.8	5.68	22.74
Hb (g/dL)	12.8	9.4	8.0
Plt (x 10^9 cells/L)	37	39	80
INR	1.1	1.3	1.4
PTT (sec)	32	38	28.1
Fibrinogen (g/L)	4.6	3.0	3.5
Na (mmol/L)	124	129	133
K (mmol/L)	4.2	4.5	5.2
Cl (mmol/L)	94	99	99
Urea (mmol/L)	10.3	18.1	23.0
Creatinine (µmol/L)	105	150	181
Total bilirubin (µmol/L)	59		238
ALT (U/L)	73		57
AST (U/L)	215		263

Discussion

Staphylococcus aureus is a well-known villain in the medical community, as well as in the educated general population. Since the pre-antibiotic era, mortality due to *Staphylococcus aureus* bacteraemia (SAB) has declined significantly. Over the decades, this decline seems to have stabilised, with mortality rates due to SAB remaining high.[1] Due to prolonged hospital stays and expensive antibiotic therapy for methicillin resistant *S. aureus* (MRSA) infections, SAB imposes a significant burden on hospital resources.

Staphylococcus aureus, a Gram-positive, facultative anaerobe, is one of the normal bacterial flora colonising humans and is well adapted to co-existing with its host. The anterior nares are the most frequently colonised, but the organism may also be found in the axillae, groin and perineum, oropharynx and skin. *S. aureus* transmits easily through physical contact and members of a single household are often colonised by the same strain. About 20% of people in any given population will persistently be colonised with *S. aureus*, with another 30% transiently colonised.[2] An individual's risk of being colonised with *S. aureus* is increased by underlying conditions, such as insulin dependent diabetes mellitus, immunodeficiency, renal failure requiring haemodialysis, intravenous drug abuse and the presence of skin damage.[3]

Few studies have investigated the epidemiology of SAB in South African children, specifically. The most recent study in children was conducted over a 5 year period (2007–2011) and analysed all cases of SAB that presented to RCWMCH. The authors reported 365 episodes of SAB with an annual incidence of 3.28 cases per 100 000 hospital admissions per year. Community acquired infections accounted for 51% of cases, nosocomial for 33% and healthcare-associated infections for 16%. Over five years, the case-fatality rate from 32 deaths due to SAB, was 8.8%. Median time to death was 3.5 days; and, MRSA was the only significant risk factor for mortality.[4]

Table 2: Summary of blood gas values

	Admission (venous)	Post-induction	End of surgery	30 h post admission	50 h post admission	Prior to cardiac arrest
pH	7.27	7.15	7.21	7.26	7.14	7.05
pCO_2 (kPa)	5.7	8.7	7.2	5.4	7.6	9.4
pO_2 (kPa)	5.3	18.8	10.3	8.6	9.3	6.29
SO_2 (%)	63	98	92	90		
BE ecf (mmol/L)	−6.2	−6.3	−6.3	−7.5	−8.7	−10.2
SBC (mmol/L)	18.3	19.7	20.5	18.0	16.6	15.3
Lactate (mmol/L)	4.8	3.1	4.8	1.9		2.7

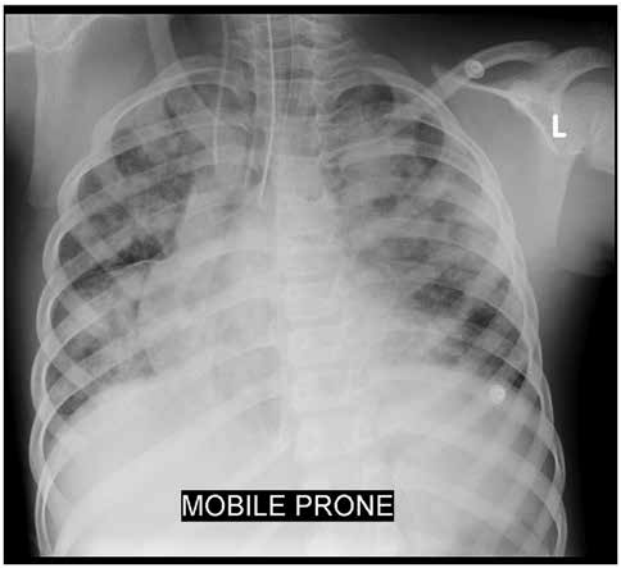

Figure 3: Follow-up chest radiograph.

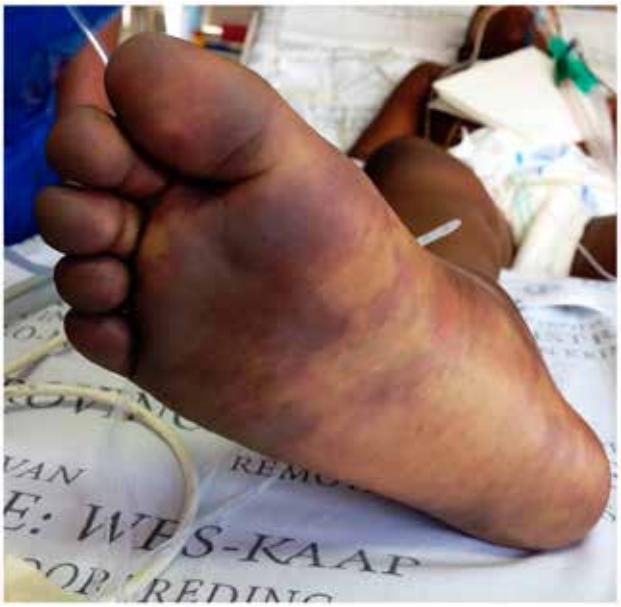

Figure 4: Ischaemia and discolouration of foot.

MRSA first emerged in 1961.[5] In keeping with a worldwide trend, the occurrence of MRSA is on the rise in South Africa. MRSA was responsible for infection in 2%, 31% and up to 59% of cases in studies from 1974, 1995 and 2010, respectively.[6–8] In the recent RCWMCH study, 26% of SAB cases were caused by MRSA. It accounted for 72% of the nosocomial infections and 21% of the healthcare-associated infections. Six cases of MRSA were community acquired. Risk factors for infection with MRSA included being a resident of a long-term care facility, previous MRSA infection, malnutrition, less than one year in age, surgery within the previous year, HIV infection and concurrent tuberculosis.

S. aureus is a pyogenic pathogen and causes abscess formation at both local and metastatic sites of infection.[3] It is capable of producing a multitude of virulence factors, exotoxins and antibiotic resistance determinants, all of which play an important role in its pathogenesis by ensuring success during colonisation, invasion and spread of subsequent infection.[9] Furthermore, *S. aureus* possesses the genes responsible for biofilm formation. Quorum sensing enables *S. aureus* to form biofilms on damaged skin, indwelling devices and heart valves, both healthy and damaged. These slimy biofilms offer protection against host immune responses and antibiotic penetration.[10]

Staphylococcus aureus can be responsible for a wide range of clinical diseases. These can be classified into four groups[2]:

(1) Disease caused by exotoxin release, such as toxic shock syndrome and gastroenteritis. The organism itself need not be present to cause disease when the toxin has been disseminated.

(2) Infections due to direct organ invasion, such as soft tissue infection, septic arthritis and respiratory tract infection

(3) Device related infections, which may occur on any foreign device or prosthesis in the body

(4) Disease due to bacteraemia

Of importance to the anaesthetist is the high propensity of SAB to cause life-threatening complications, which contribute to mortality. These include severe sepsis and septic shock, metastatic foci of infection and cardiac complications. Metastatic seeding can occur to the bladder and kidney, bones and joints, lungs, brain, and the heart and pericardium.[2,10] In the recent RCWMCH study, the most common clinical diagnoses during an episode of SAB were SAB with no identifiable source (33%),

pneumonia with or without empyema (22%), skin and soft tissue infection (17%), and bone or joint infection (12%). A retrospective study over a 12 year period at RCWMCH, identified 38 critically ill children with septicaemia out of 1156 who presented with acute septic arthritis or osteitis. Of the 38 critically ill children, metastatic pneumonia was present in 87% and 53% required a chest drain for empyema. Pericardial effusion requiring drainage was present in 10 children (26%).[11] A 1995 study investigating cardiac complications in 36 children with SAB found endocardial vegetations in four (11 %) of the children, none of which were clinically suspected. Only one child had a pre-existing cardiac abnormality (patent ductus arteriosus). Significant pericarditis was present in two patients (5.5%).[7] Purulent pericarditis may present with severe sepsis, acute constrictive pericarditis or cardiac tamponade. In a 1977 study at RCWMCH, *S. aureus* was responsible for 79% of purulent pericarditis in 28 paediatric cases. A second, additional focus of infection was identified in 90% of *S. aureus* cases, the most common being pneumonia and osteitis.[12]

Anaesthetists are most commonly confronted with children that have a *S. aureus* infection when they present to the operating room for surgical source control of a primary or metastatic infection. It is important that the child is systematically assessed for the presence of complications in order for these to be managed either pre- or postoperatively. Cardiac and respiratory complications, in particular, may contribute to haemodynamic instability. Table 3 summarises pertinent, special investigations that need to be considered based on clinical signs. When MRSA infection is suspected or confirmed, all staff involved in the care of the child should maintain strict contact precautions; the child must be cared for in an isolation unit and the theatre and all equipment used for the case must be disinfected afterwards.

The presence of SAB may be known if a positive blood culture exists but this result may not yet be available at the time of initial surgery. Signs of severe sepsis and septic shock should be sought and treatment promptly instituted. Two thirds of children will have cold peripheries, prolonged capillary refill and diminished pulses characteristic of low cardiac output (CO) and increased systemic vascular resistance (SVR), so-called 'cold' shock. The rest may present with warm peripheries, rapid capillary refill and bounding pulses associated with normal or increased CO and decreased SVR. Hypotension is a late sign.[14]

The American College of Critical Care Medicine provide consensus guidelines for the management of paediatric sepsis. Management includes goal directed fluid therapy, inotropes for fluid refractory shock, early ventilation using lung protective strategies and early empiric antibiotic therapy.[13] If a community acquired *S. aureus* infection is suspected, cloxacillin (50 mg/kg) every 8 hours is appropriate.

Anaesthetic considerations include difficulty with arterial and venous access, the need for ongoing fluid resuscitation, vasopressor and inotrope use, haemodynamic instability on induction, the possible presence of ileus and ventilatory difficulties due to pneumonia and acute lung injury. Anaesthetic drugs should be carefully selected in order to avoid excessive cardiovascular depression. The need for a rapid sequence induction should be balanced against the need to maintain stable haemodynamics. Etomidate increases the severity of illness in septic shock and is not recommended. Ketamine is an acceptable alternative but may also cause direct myocardial depression in patients with depleted endogenous catecholamine stores. High concentrations of volatiles should be avoided. Point-of-care cardiac ultrasound is valuable for excluding pericardial effusion and determining gross systolic function and volume status to guide ongoing fluid therapy, although the optimal type of fluid to use in paediatric sepsis remains unclear.[14,15] The paediatric intensive care team should be involved early to provide ongoing organ support and to further coordinate efforts to definitively manage complications. Antibiotic therapy should be adjusted based on susceptibility testing of the *S. aureus* isolate as soon as the results are known.

Table 3: Special investigations

Clinical signs	Investigation	Pathology
Central nervous system • Focal neurological signs • Raised intracranial pressure (vomiting, decreased level of consciousness, irritability, tight fontanelles, downward gaze)	• Computed tomography or magnetic resonance imaging of brain	Intracerebral abscess Meningitis
Respiratory • Distress • Decreased oxygen saturation • Adventitious sounds on auscultation • Signs of pleural effusion	• Chest radiograph	Bronchopneumonia Lobar pneumonia Empyema
Cardiovascular • May be asymptomatic • Haemodynamic instability • Cardiac murmur	• Point of care echocardiography using the Focus Assessed Transthoracic Echocardiography (FATE) protocol • Formal echocardiogram by cardiologist	Pericardial effusion Constrictive pericarditis Valvular vegetations Haemodynamic consequences of identified pathology
Musculoskeletal • Painful, swollen joints • Soft tissue abscess, cellulitis • Back pain	• Radiographs of affected areas • Abdominal ultrasound • Magnetic resonance imaging of spine	Septic arthritis Osteitis Osteomyelitis Psoas abscess Deep seated metastatic abscesses

Conclusion

Staphylococcus aureus infections are common in the paediatric population and carry significant potential for multi-organ involvement with subsequent morbidity and mortality. Patients often present to the operating theatre for surgical source control of infection and, in order to appropriately adjust anaesthetic management, it is extremely important for the anaesthesiologist to consider, identify and, where appropriate, treat metastatic foci of infection. Septic shock must be recognised and aggressively managed. Point-of-care echocardiography using the focus assessed transthoracic echocardiography (FATE) protocol is a useful tool to assess for the presence of a pericardial effusion, evaluate systolic function and assess volume status. The more experienced provider may note the presence of vegetations.

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