

## A Fatal Case of Community Acquired Methicillin Resistant *Staphylococcus aureus* Brain Abscess in a Previously Healthy Adolescent

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### ABSTRACT

*A 16-year-old adolescent presented with fever, lethargy and vomiting associated with mild dehydration. This was followed less than 24-hours later by loss of consciousness, seizures and clinical brain death. She had no prior medical illness, no hospital or frequent antibiotic exposure. There was no evidence of soft tissue or skin infection. Management included intravenous fluids, ampicillin and cefotaxime parenterally, dexamethasone, endotracheal intubation and mechanical ventilation. Her neurologic examination remained unchanged with areflexia, flaccid paralysis and fixed pupils. Post-mortem examination revealed an eight-centimetre right fronto-parietal lobe brain abscess. Cultures were positive for methicillin resistant Staphylococcus aureus. Although formerly a nosocomial pathogen affecting debilitated patients in the hospital setting, S aureus that is methicillin resistant is emerging as a community acquired pathogen affecting previously well patients.*

## Un Caso Fatal de Estafilococo Dorado Resistente a la Meticilina, Adquirido en la Comunidad, por una Adolescente Previamente Sana

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### RESUMEN

*Una adolescente de 16 años de edad se presentó con fiebre, letargia y vómitos, asociados con deshidratación ligera. Estos síntomas fueron seguidos en menos de 24 horas por pérdida de conciencia, ataques y muerte clínica del cerebro. Con anterioridad, la paciente no había tenido enfermedad médica, ni hospitalización, ni tratamiento frecuente con antibióticos. No había evidencia de tejidos blandos o infección de la piel. El tratamiento incluyó líquidos intravenosos, ampicilina y cefotaxima de forma parenteral, dexametasona, entubación endotraqueal, y ventilación mecánica. El examen neurológico permaneció invariable con areflexia, parálisis flácida, y pupilas fijas. El examen post-mortem reveló un absceso cerebral de ocho centímetros en el lóbulo fronto-parietal derecho. Los cultivos resultaron positivos al Staphylococcus aureus resistente a la meticilina. Aunque visto anteriormente como un patógeno nosocomial que afecta a los pacientes debilitados en el entorno hospitalario, el S aureus resistente a la meticilina está surgiendo como un patógeno extrahospitalario (ie adquirido en la comunidad) y afecta a pacientes previamente sanos. <sup>1</sup>Equivalente acuñado aquí para el término inglés case-ness, a saber, criterios que definen el estatus de caso sobre la base de la presencia de sintomatología clínicamente significativa.*

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### INTRODUCTION

Methicillin resistant *Staphylococcus aureus* emerged as a pathogen around 1970. Hospitals in the United States of America (USA) reported that 5% of cultures of *S aureus* were resistant to methicillin by 1990 (1). The patients most likely to be infected included hospitalized, debilitated patients,

either the very old or very young, patients in burn units, intensive care units or neonatal care nurseries. These areas are subjected to continuous antibiotic pressure (1). Around 1995, cases of community acquired methicillin resistant *S aureus* began to appear in previously healthy individuals (2). Initially, risk factors for community acquisition were identified, including chronic illness, long term care, recent or frequent hospital admissions, frequent antibiotic exposure, an ill family member, a medical caregiver in the family or prior surgery (3–9). More recently, patients with no risk factors are presenting with community acquired methicillin resistant *S aureus* infections (2, 10–14).

This report concerns a healthy 16-year-old girl who had no identified risk factors, and who presented with non-specific symptoms progressing rapidly and unexpectedly to a fatal outcome. Post-mortem examination revealed a large brain abscess in the right fronto-parietal lobe due to methicillin resistant *Staphylococcus aureus*. The presentation and management are described, with a discussion of the current status of methicillin resistant *Staphylococcus aureus* as an emerging disease in the Caribbean as well as in the rest of the world.

#### CASE REPORT

The patient was a 16-year-old adolescent female transferred from Princess Alexandra Hospital in Anguilla to Holberton Hospital in Antigua and Barbuda. She had a two-day history of fever, vomiting and lethargy. Her initial examination revealed mild dehydration and no meningeal signs. She was treated with oral rehydration fluids and antacid. She had a history of a heart murmur, but had no prior symptoms related to her heart, was not taking prophylactic antibiotics or other medication. She had no chronic disease, frequent hospital visits or antibiotics, recent surgery or family members working in the healthcare field. On the day of transfer, she developed sudden loss of consciousness with tonic left sided movements suggestive of seizure activity. She then became unresponsive, with dilated, fixed pupils and no spontaneous movement or respiration. She was given ampicillin and ceftriaxone parenterally in Anguilla. No central intravenous line was placed at any time. She had endotracheal intubation and mechanical ventilation and was transferred to Antigua and Barbuda for further assessment.

Examination at the Holberton Hospital in Antigua and Barbuda revealed pulse rate of 97 beats per minute, temperature of 36.4°C, and blood pressure was 86/40 mmHg. There was no evidence of head or scalp trauma. Pupils were 7 mm in diameter and non-reactive and there was an endotracheal tube in place with intermittent mandatory ventilation at 14 breaths per minute *via* the ventilator. No abnormalities were noted in the facial area. The lungs were clear to auscultation. There were normal heart sounds with a systolic heart murmur, grade 2 – 3/6 along the left sternal border. The abdomen was soft without mass or organomegaly. The extremities were normal. No cutaneous rash, sore or abscess was noted.

The neurologic examination revealed an unresponsive patient with no spontaneous movements, no response to painful stimuli, flaccid paralysis and no reflexes. No respirations were noted except with the ventilator.

Laboratory results showed haemoglobin of 10.5 g/L, haematocrit 29%, white blood cell count 12 300 x 10<sup>9</sup>/L, platelet count 103 000 x 10<sup>9</sup>/L, serum glucose 9.62 mmol/L\*, sodium 132 mmol/L, potassium 3.1 mmol/L, chloride 96 mmol/L, urea 4.9 mmol/L, creatinine 88µmol/L, amylase 142 IU/L\*, alanine aminotransferase 115 IU/L\*, aspartate aminotransferase 142 IU/L\*, creatine kinase 759 IU/L\*, MB fraction 29 IU/L\*, alkaline phosphatase 81 IU/L, gamma-glutamyl transpeptidase 62 IU/L\*, lactate dehydrogenase 1601 IU/L\*, total bilirubin 39 micromol/L\* (\* = elevated value).

Management included ampicillin and cefotaxime 2 grams each intravenously every four hours. Dexamethasone 10 mg was given intravenously, then 4 mg every six hours. Fluid restriction and mannitol were not given due to hypotension. Intravenous fluids, 5% dextrose in normal saline, were given at 2.4 litres per 24-hours to maintain blood pressure and correct electrolyte deficiencies. The patient developed hypotension, which was treated with a 20 ml/kg bolus of lactated Ringers solution. There was little response, so a dopamine infusion of 10 mcg/kg/min was begun.

Hypernatraemia (sodium 158 mmol/l) developed on the third day, suggesting possible central diabetes insipidus. The patient remained afebrile during her hospitalization. The differential diagnoses included intracerebral haemorrhage, viral encephalitis, bacterial meningitis, cerebral abscess or emboli. Imaging studies including computed tomography of the brain and echocardiography were scheduled but the patient's clinical instability prevented transport. The blood pressure did rise to normal, antibiotics and steroids were continued for five days. The observation period was felt to be adequate to eliminate the possibility of a post-ictal state or unknown ingestion. The clinical examination did not change over five days. Following discussions with the family regarding brain death and last rites, the ventilator support was discontinued.

The post-mortem examination revealed an eight centimetre diameter abscess in the right fronto-parietal lobe of the brain (Fig 1a). Culture of the abscess revealed gram positive cocci in clusters (Fig 1b). The organism was identified as *S aureus*. On antibiotic sensitivity testing using the Kirby-Bauer disc diffusion test, the bacteria was resistant to methicillin, erythromycin and clindamycin; it was sensitive to cotrimoxazole, gentamycin, ciprofloxacin and vancomycin (Fig 1c). No other sensitivity testing was done. No other significant findings were seen on the post-mortem examination, including the heart and heart valves.

#### DISCUSSION

Methicillin resistant *S aureus* has become a major problem worldwide (1, 15, 16). This organism emerged as a nosocomial pathogen in the 1980s, and affected mostly hospitalized,

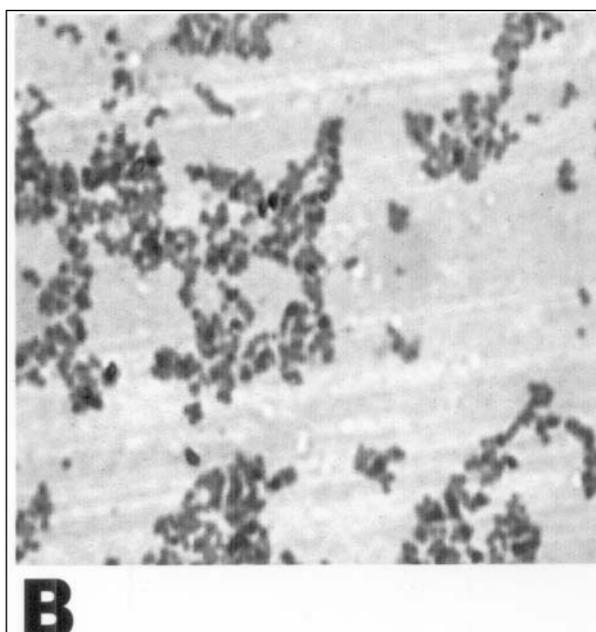
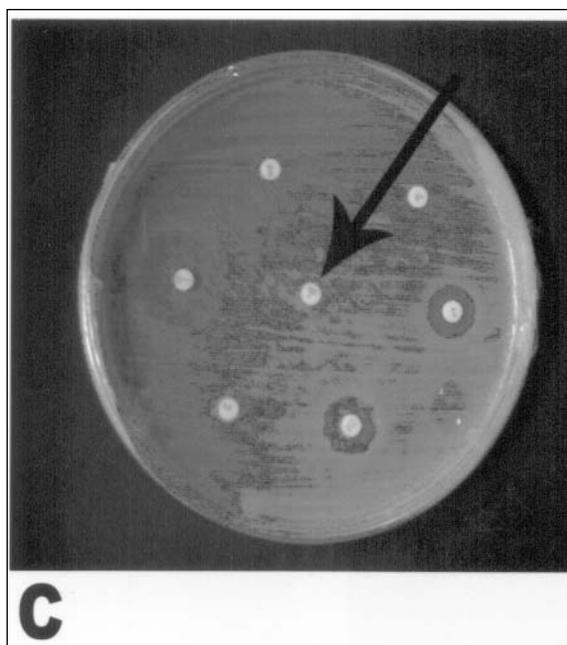
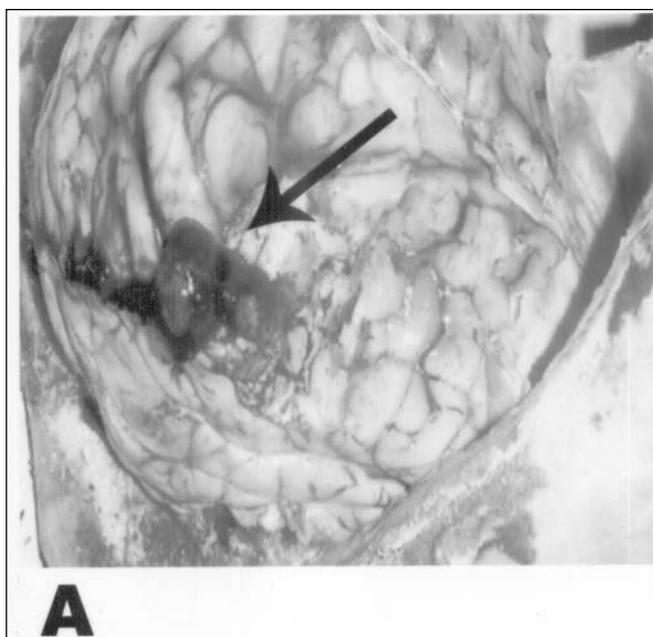


Figure: Confirmation of methicillin resistant *Staphylococcus aureus*. A. Arrow indicates the right fronto-parietal lobe brain abscess from which the culture was taken. B. Gram stain revealing clusters of gram positive cocci, identified as *Staphylococcus aureus*. C. Kirby-Bauer disc-diffusion plate with arrow identifying resistance to methicillin.

debilitated patients, the very old and very young, and was most commonly isolated from burn units, intensive care units and neonatal nurseries (1, 15, 16). Although initially seen in developed countries, it began to appear as a nosocomial pathogen in the Caribbean region in the late nineties (17–21).

In the mid 1990s, methicillin resistant *S. aureus* began to emerge in patients not having hospital exposure as noted for nosocomial infections (2–6). In Chicago, USA, the increase in infection in children without hospital exposure was 10 per 10 000 from 1988 to 1990 to 259 per 10 000 from 1993 to 1995 (2). These community-acquired cases of methicillin resistant *S. aureus* were initially seen in patients having newly defined risk factors. These included recent or

frequent hospital stays, transfer from an extended care facility, an underlying illness such as diabetes mellitus, chronic lung disease, renal insufficiency, frequent antibiotic exposure, attendance at childcare centres, a family member with these factors or a family member in the healthcare field (3–9). More recent cases have not been associated with these factors (10–14).

Initially, community acquired methicillin resistant *S. aureus* infections appeared to be related to strains isolated in the hospital (5, 6, 9, 22–24). More recent studies suggest that resistant strains are emerging *de novo* in the community rather than being spread from the hospital (25–29). Recent hospital reports show the percentage of infections with methicillin resistant *S. aureus* that are community acquired range from 30% to 74% with an average of 48% (4–7, 10–11, 14, 26, 30–31). Community acquired methicillin resistant *S. aureus* represent 8 to 20% of all methicillin resistant *S. aureus* isolates according to a population based survey from the USA (32).

Community acquired methicillin resistant Staphylococcal infections tend to be less invasive than hospital acquired infections (6), with most cases involving skin and soft tissue infections (3, 4, 6, 12, 13, 15, 29, 33, 34) with these sites accounting for 75 to 93% of isolates (3, 4, 15, 29, 33, 34). Pneumonia, osteomyelitis, bacteraemia and death have been reported infrequently (6, 9, 13, 15, 33) in healthy adolescents without risk factors (35). This case represents an unusual presentation of a healthy teenager with no risk fac-

tors having a brain abscess due to community acquired methicillin resistant *S aureus*.

Studies on nasal cultures from patients in communities reveal 1 to 8% nasal carriage of methicillin resistant *S aureus* (8, 36, 37). The community acquired strains of methicillin resistant *S aureus* are somewhat more sensitive to other antibiotics than hospital acquired strains (11, 12, 14, 15, 24, 30, 33, 34, 38) although not always (7). Nearly all strains are sensitive to vancomycin, but clindamycin, ciprofloxacin, gentamicin and cotrimoxazole may be effective. Erythromycin and other beta-lactam antibiotics are not effective (4, 11, 12, 14, 15, 24, 30, 34, 38). The methicillin resistant *S aureus* in this case was sensitive to ciprofloxacin, gentamicin and cotrimoxazole in addition to vancomycin. Community acquired strains are now beginning to move into hospitals, further complicating the problem (39).

Children presenting with skin and soft tissue infections may have methicillin resistant *S aureus* as the causative agent. In this case, the rapid nature of the disease progression prevented consideration of these therapeutic alternatives. This case will probably not be an isolated occurrence in the Caribbean region with a recent report showing that 12.5% of hospital acquired and 4.1% of community acquired *Staphylococcus aureus* in Trinidad and Tobago were methicillin resistant (38).

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