METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS — FIRST CASE OF BACTERMIA IN THE UNIVERSITY HOSPITAL, KUALA LUMPUR

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SYNOPSIS

Hospital acquired infections due to *Staphylococcus aureus* pose a major problem in many hospitals. However, even more ominous are infections caused by methicillin-resistant *S. aureus* (MRSA). The first case of a serious infection due to methicillin-resistant *Staphylococcus aureus* occurred in the University Hospital in June 1986. A newborn baby with bacteremia and septic arthritis was treated effectively with a combination of vancomycin and fusidic acid. The methods of spread and control of infection due to these organisms are discussed.

INTRODUCTION

Hospital associated infections due to *Staphylococcus aureus* pose a major problem in many large general hospitals. In the University Hospital, Kuala Lumpur, it accounts for about a quarter (27% in 1983 and 1984, 25% in 1985) of all hospital acquired infections. More ominous and dangerous is the presence of methicillin-resistant *Staphylococcus aureus* (MRSA) in the hospital environment.

Reports from Australia (1,2), the United States (3,4) and the United Kingdom (5,6), suggest an increasing occurrence of nosocomial infection with methicillin-resistant *S. aureus*. In the University Hospital in 1979, 11.5% of all nosocomial infections due to *S. aureus* were found to be methicillin-resistant. In 1981 this figure rose to 13% and then fell to 6.6% in 1983. The percentage of MRSA then rose to 9% in 1984 and then to 18.8% in 1985. All these strains of MRSA were isolated from the flora of hospitalized patients or from surgical wounds, but until now serious conditions like septicaemia or meningitis were not recorded. The first serious infection with MRSA occurred in June 1986 and the following is a report of this case.

CASE REPORT

A premature female infant of 34 weeks gestation, with a birth weight of 1380 g was delivered by emergency caesarean section because of bleeding placenta praevia. Apgar at 1 minute was 1/10 and at 5 minutes 9/10. The baby was resuscitated successfully with external cardiac massage, intermittent positive pressure ventilation and 40% intravenous dextrose and 8.4% sodium bicarbonate. She was subsequently admitted to the special care nursery where she was put on 10% dextrose intravenous drip. She did not require further ventilatory support, but because she was anaemic, haemoglobin level being 9.6 g % at age 3 hours, she was transfused with 25 ml of whole blood. Her condition remained good and by the third day of life, small amount of infant formula was introduced via the nasogastric route. By the sixth day of life, full nasogastric feeds were well tolerated and the intravenous drip was discontinued.

On day 12 she developed a warm, tender swelling over the left knee but there was no effusion nor any radiological change in the joint. The baby was afebrile but there was a leucocytosis of 59,800/ul with 85% neutrophils. Blood for culture was taken and treatment with intravenous crystalline penicillin 100,000 units/kg/day and gentamicin 5 mg/kg/day was commenced. Two days later (14th day of life) fluid was detected in the left knee joint and 2.5 ml of pus was aspirated. A gram stain of this aspirate revealed gram positive cocci. The crystalline penicillin was then replaced with intravenous cloxacillin.

On the 15th day, an arthrotomy was performed due to reaccumulation of pus in the joint. An X-ray taken of the left knee then showed radiolucent areas at the upper end of the tibia. Blood cultures and cultures of knee aspirates grew methicillin-resistant *S. aureus* (MIC to cloxacillin 8 mg/L) which was also resistant to gentamicin. MRSA was also isolated from the umbilical swab. Therapy was changed to intraveous cefoperazone 100 mg/kg/day and amikacin 15 mg/kg/day. Over the next few days the baby's condition did not improve and a repeat X-ray of left knee showed sub-periosteal reaction with new bone formation. A second arthrotomy was performed on the 24th day and pus drained from the knee joint and infrapatellar pouch.

The antibiotic regime was changed in view of the continuing active infection and antibiotic sensitivity results. Intravenous vancomycin 15 mg/kg/day in 12 hourly doses and fusidic acid 20 mg/kg/day in 8 hourly doses were started in place of cefoperazone and amikacin.

Within a week of the new antibiotic regime, the inflammatory changes subsided and there was no further accumulation of pus in the joint. After six weeks of vancomycin and fusidic acid therapy, the general condition of the baby was good and she had gained weight. She was discharged on the 74th day weighing 3,450 gm.

DISCUSSION

It is not known for certain when MRSA first appeared in the University Hospital nor whether it was introduced from an outside source. Awareness of its presence in the hospital environment is essential both for the microbiologists as well as for the clinicians, so that prompt identification and appropriate therapy can be instituted.

Generally "methicillin-resistance" is a generic term which includes resistance to all other penicillinase-resistant semisynthetic penicillins like nafcillin, oxacillin, cloxacillin, dicloxacillin and flucloxacillin. Although in-vitro tests with MRSA may indicate susceptibility to clinically achievable serum concentrations of cephalosporins, tests of bactericidal activity and clinical experience indicate that these strains are also resistant to all cephalosporins (7).

The exact mechanism of resistance to methicillin is not known but current information suggests that the penicillin-binding proteins in the cell wall of MRSA have decreased affinity for methicillins (8,9).

The clinical implication of this unique resistance pattern of MRSA is that treatment of established infections with the cephalosporins will not be successful as shown by the above experience. Vancomycin, rifampicin and fucidin are the only really available antibiotics to which the MRSA is sensitive.

Development of resistance to rifampicin and fucidin has been reported in Australia and would be expected if either were used alone (5). Vancomycin is the only long-established agent to which all MRSA strains are regularly sensitive and it has thus become the mainstay of treatment of these infections, despite its potential toxicity. The newer quinolones, ciprofloxacin and pefloxacin, hold promise (6).

The prevention and control of spread of MRSA is very similar to the difficulties encountered in containing any outbreak due to *Staphylococcus aureus*. There are several important risk factors involved in the acquisition of MRSA infections. These are: duration of hospital stay, severity of underlying disease, intensity and duration of prior antibiotic therapy, prior surgery, and respiratory insufficiency requiring mechanical assistance. Our case certainly had at least two of these risk factors. Generally accepted measures for controlling spread of infection among such patients are: cohorting of infected or colonized patients in the same area, isolation precautions for both infected and colonized patients, and strict handwashing by personnel before and after contact with patients.

Although staphylococci resist dessication and remain viable in dust and other environmental foci for many months, infected humans, both patients and carriers, are the main source of cross-infection. The treatment of carriers with topical antibiotics or skin disinfectants has often been reported to be unsuccessful (1,2) and may be related to the in-vitro resistance of some MRSA to certain disinfectants (10). The new agent mupirocin (pseudomonic acid), derived from *Pseudomonas fluorescens*, seems promising. In an outbreak of MRSA in a urology ward, topical mupirocin eradicated the organisms from carrier sites in all 10 patients treated (11).

Finally the control of antibiotic use has been advocated as an important mechanism for limiting the development of resistance. Unlike resistance to other antimicrobials, the advent of MRSA does not usually seem to be a direct consequence of the use of methicillin or related antibiotics. However, the presence of resistance to so many other antibiotics in MRSA strains does suggest that the survival of such strains may be indirectly favoured by lavish prescribing of these agents (6).

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