***Staphylococcus aureus* with reduced susceptibility to vancomycin**

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(Index words: MIC, VISA strains, teicoplanin, disc diffusion antibiotic sensitivity tests)

Introduction

Staphylococcus aureus is a common cause of hospital and community acquired infections (1). It is also the commonest cause of surgical site infection and causes blood stream infections as well (2).

Anti-Staphylococcal penicillins (methicillin, cloxacillin, flucloxacillin) were successfully used in treating penicillin resistant staphylococcal infections. Since the emergence of methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin has been the mainstay in the treatment for staphylococcal infections. Until recently resistance to vancomycin had not been described. Intermediate level vancomycin resistance, called VISA strains, with minimum inhibitory concentration (MIC) for vancomycin of 8 to 16 mg/l have been reported recently among clinical isolates of MRSA from Japan (3) the USA (4) and France (5). Reduced susceptibility to vancomycin has not been reported previously in Sri Lanka (6). We describe here the first clinical infection due to *Staphylococcus aureus* with reduced susceptibility to vancomycin.

Case report

A 60-year old man was admitted to a surgical ward at the National Hospital in December 2001, with a history of intermittent claudication of 30 months' duration. He was a known diabetic and hypertensive. He underwent aortotomy and endarterectomy of the occluded aorta and replacement with a Gorfex bifurcation graft a week later.

One week after surgery he developed a surgical site infection (SSI), and was treated with oral amoxicillin-clavulanic acid for two weeks. The only isolate was a coliform organism. Subsequent cultures grew MRSA and treatment with intravenous vancomycin 500 mg 8 hourly was given for one week. A patent graft and a good outflow were observed in the CT scan before discharge from hospital.

In April 2002 he was re-admitted with backache and lower limb paresis. There was no response to two weeks of anti-tuberculosis treatment. The CT scan revealed a para-vertebral abscess with destruction of bone at lumbar 4 - 5 level. CT guided aspirate yielded MRSA, and treatment with intravenous vancomycin and fusidic acid was continued for 4 weeks. MRI scan while on treatment revealed pyogenic osteomyelitis of the vertebrae. After intravenous therapy, oral fusidic acid and oral azithromycin were given for another 2 weeks. Antibiotic sensitivity test on this isolate by disc diffusion method (NCCLS) (7) demonstrated resistance to methicillin, gentamicin, cephalosporins, ciprofloxacin, cotrimoxazole and erythromycin, and sensitivity to vancomycin, teicoplanin and fusidic acid (7). Despite treatment, the patient developed a collection of pus at the surgical site in the right groin which yielded MRSA again.

A CT scan revealed erosion of bones at lumbar vertebral level. CT guided aspirate from the bone also yielded MRSA. This isolate was sensitive to vancomycin (zone diameter 15 mm) and teicoplanin (zone diameter 13 mm) by the NCCLS method (7). The isolate was resistant to fusidic acid, ciprofloxacin, cotrimoxazole, ampicillin-salicylic acid, erythromycin, azithromycin and tetracyclines. Treatment with intravenous teicoplanin (400 mg daily for 2 days followed by 200 mg daily) was started in June 2002 as we suspected a reduced susceptibility to vancomycin.

He gradually improved with intravenous teicoplanin. After 6 weeks of treatment a persistent discharge at the incision site was observed which yielded MRSA. This isolate showed a similar sensitivity pattern as the previous isolate. Detection of MIC for vancomycin by the E-test revealed an MIC of 6 mg/l, compatible with reduced susceptibility to vancomycin (8). Further investigation with a sinogram excluded an extension to the hip joint cavity and CT scan showed no evidence of deep seated infection. Intravenous teicoplanin was discontinued after 7 weeks.

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Discussion

The first strain of MRSA (Mu 50) with resistance to vancomycin reported from Japan in 1997, was a strain of MIC > 8 mg/l (3). They also reported a clinical infection refractory to vancomycin therapy caused by MRSA strain (Mu3) with heterogenous vancomycin resistance. Although Mu3 strain was susceptible to vancomycin (MIC 2 mg/l by NCCLS criteria), it produced a subpopulation of cells that resisted a wide range of vancomycin concentrations (2 to 9 mg/l). Isolates with reduced susceptibility to vancomycin can be associated with treatment failures, and these hetero-VISA strains might be precursors of *Staphylococcus aureus* strains that are resistant to vancomycin.

Hetero-VRSA and true VRSA strains have not been reported previously because disc diffusion susceptibility tests usually done in a clinical laboratory cannot detect these strains. The strain that we describe showed resistance at MIC of 6 mg/l by the E-test test method (8), but the NCCLS showed a sensitivity within the normal range. The MRSA strains described in our country previously were susceptible to vancomycin by the E-test method (MIC 0.5 to 4 mg/l) (6).

Staphylococcus aureus with intermediate glycopeptide resistance should be suspected in any patient in whom otherwise appropriate vancomycin therapy for *Staphylococcus aureus* infection appears to be ineffective (1). Our patient had received a short course of vancomycin initially for SSI and later a long course of four weeks when we isolated the MRSA strain with reduced susceptibility to vancomycin. Prompt identification of VISA strains by detecting candidate strains for confirmatory susceptibility testing is critical so that appropriate action can be taken.

With this first report of a VISA strain of *Staphylococcus aureus* we need to be aware of glycopeptide resistance. This may herald the arrival of VRSA strains in the near future.

Acknowledgements

We thank the house officers and the technical staff of the bacteriology section, National Hospital of Sri Lanka.

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