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Abstract (publication only)

Daptomycin non-susceptibility in patients with severe methicillin-resistant Staphylococcus aureus (MRSA) infections previously treated with glycopeptides

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Objective: To describe the clinical and microbiological features of three cases of severe methicillin resistant Staphylococcus aureus (MRSA) infections in which daptomycin non-susceptibility (DNS) was detected. Methods: DNS was detected in 3 MRSA strains isolated from the blood cultures (BCs) of patients admitted to two medical wards in a large general hospital in Rome (Italy) over a 4-month period. The patients' charts were retrospectively reviewed and clinical data were recorded. The MRSA strains were sent to a reference laboratory for identification and susceptibility confirmation and for further molecular studies. Results: The study cases include two left-site infective endocarditis (IE) on prosthetic valve, and one surgical site infection (SSI) after a femur osteosynthesis. All the 3 MRSA strains were susceptible to daptomycin at the beginning of antimicrobial treatment and all were confirmed to be DNS after glycopeptide therapies. In particular, in the case n. 1 the strain was confirmed as VISA and in case n. 3 as hVISA. The two IE cases were initially treated with teicoplanin and vancomycin, and later their BCs yielded DNS MRSA strains. The SSI case was a co-infection with MRSA and Pseudomonas aeruginosa and was initially treated with teicoplanin and meropenem. After two weeks of antibiotic therapy the patient developed a septic shock with isolation from BCs of a DNS MRSA strain. The patient received linezolid for 4 further weeks; clearance of bacteraemia and clinical improvement were observed after three days of linezolid treatment. Two weeks after the end of linezolid treatment, the patient became febrile again and BCs yielded a daptomycin susceptible MRSA strain. Clinical and microbiological details are reported in the table. Conclusions: Clinicians should be aware of reduced susceptibility to glycopeptides and DNS occurrence in patients with severe MRSA infections, mainly in presence of prosthetic material and after exposure to glycopeptides.

Table. Clinical and microbiological data of the three MRSA infections

Case	Sex, age and underlying conditions	Type of infection	Date and site of first MRSA isolation	Susceptibility (MIC µg/ml)	Date and site of second isolation	Susceptibility (MIC µg/ml)	Antibiotic therapy (type, dosage and date)	Outcome
1	Female, 69 year old, underwent biological aortic valve replacement and mitral valve anuloplasty one month before	IE on mitral and biological aortic valves	02/04/12 BCs	Daptomycin (0.75) Vancomycin (1) Teicoplanin (≤0.5) Gentamycin (0.5) Linezolid (1) Trimethoprim/ sulphamethoxazole (≤10)	13/04/12 BCs	Daptomycin (2) Vancomycin (8) Teicoplanin (32) Gentamycin (≤1) Linezolid (2) Trimethoprim/ sulphamethoxazole (≤1/19) Quinupristin/ Dalfopristin (≤0.25)	-Teicoplanin (800 mg/day first 24hours, 400 mg/day second day, 200 mg/day from the third day)plus Gentamycin (80mg Bid) for 7 days - Daptomycin (350mg day) plus Rifampicin (600mg day) for 15 days - Linezolid (600 mg bid) plus Gentamycin (160 mg day) for 9 days - Quinupristin/Dalfopristin for 14 days	BCs negative under treatment with Linezolid and later with Quinupristin/Dalfopristin Non MRSA-IE related death
2	Female, 90 years old, COPD, CHF, biological aortic valve replacement 14 months before	IE on biological aortic valve	21/04/12 BCs	Daptomycin (0. 5) Vancomycin (≤ 0.5) Teicoplanin (≤0.5) Gentamycin (≤1) Linezolid (1) Trimethoprim/ sulphamethoxazole (≤1/19)	29/04/12 BCs	Daptomycin (2) Vancomycin 1) Teicoplanin (2) Gentamycin (≤0.5) Linezolid (2) Trimethoprim/ sulphamethoxazole (<10)	-Teicoplanin (400 mg/day first 24 hours, 200 mg/day from the second day) for 5 days -Vancomycin (1000 mg/day) until death	MRSA-IE related death after 13 of treatment
3	Female, 84 years old, CRF CHF, undewent femur osteosynthesis three weeks before	SSI complicated with septic shock	19/01/12 Surgical wound tissue	Daptomycin (0.25) Vancomycin (≤0.5) Teicoplanin (≤0.5) Gentamycin (0.5) Linezolid 2 Trimethoprim/ sulphamethoxazole (≤1/19)	04/02/2012 BCs	Daptomycin (2) Vancomycin (2) Teicoplanin (4) Gentamycin (2) Linezolid (2) Trimethoprim/ sulphamethoxazole (≤1/19)	- Meropenem (1000 mg bid) plus Teicoplanin (400 mg day first 48 h, then 200mg/day) for 15 days - Linezolid 600 mg bid for four weeks	DS MRSA strain was isolated from BCs two weeks after the end of linezolid. Daptomycin treatment was started for a diagnosis of spondylodiscitis. Patient died after 6 weeks with active infection.

BCs blood cultures; CHF chronic heart failure; COPD chronic obstructive pulmonary disease; CRF chronic renal failure; DS daptomycin susceptible; IE infective endocarditis; MRSA methicillin resistant *Staphylocccus aureus;* SSI surgical site infection.