Glycopeptide intermediate resistant *Staphylococcus aureus*

Last week, the Public Health Laboratory Service in England reported an isolation of a glycopeptide resistant methicillin resistant *Staphylococcus aureus* (MRSA) (1). The organism was isolated from a patient with endocarditis who had failed to respond to treatment with this antibiotic used in combination with gentamicin and rifampicin. The strain was resistant to vancomycin (minimum inhibitory concentration (MIC) 8-16 mg/L, depending on the testing conditions). Such strains have been termed glycopeptide intermediately resistant *Staphylococcus aureus* or GISAs, and were first described by Hiramatsu and colleagues in Japan in 1997 (2,3). Since then, they have been identified in France, Scotland, and the United States (US).

The emergence of these strains in various parts of the world is significant, as glycopeptides (vancomycin or teicoplanin) are the preferred agents for the empirical treatment of suspected MRSA infections. In the case described above the patient had been receiving vancomycin for several days, a risk factor for selection of GISA. The infection was successfully treated by changing the antibiotics given to a combination of linezolid, gentamicin, and rifampicin.

GISAs are difficult to detect with conventional antimicrobial disc susceptibility tests. More sophisticated glycopeptide susceptibility testing methods (for example, E-tests, breakpoint dilutions or MIC testing (1,3)) should be used for isolates from patients who are failing to respond to glycopeptide antibiotics.

*S. aureus* strains have also been encountered in which a subpopulation of the strains are resistant to glycopeptides; so called ‘heteroresistant’ GISAs (1,3). It is unclear whether this ‘heteroresistance’ results in a failure to respond to glycopeptide therapy. Such strains have been confirmed in Japan, the US, and the United Kingdom (UK).

Thus far no highly glycopeptide resistant MRSA have been described, although high-level glycopeptide resistance (*van*) genes have been shown to transfer to *S. aureus* in various laboratory and animal models from glycopeptide resistant enterococci (4). Fortunately, the selection for glycopeptide resistance in this recent English strain was in an epidemic strain of MRSA (EMRSA-16) – a strain susceptible to several other antimicrobials. Follow up screening of staff and patients did not identify any further cases, although the EMRSA-16 strain has been shown both in the UK and abroad to spread very readily.
There are several important messages here. A global campaign is currently underway to manage and monitor the prescription of antimicrobials (antimicrobial stewardship). When caring for seriously ill patients, however, there is often a need for glycopeptide treatment and GISAs should be considered as one of the reasons for such treatments failing. A new EMRSA (EMRSA-17) that is resistant to many antibiotics has been described recently in the UK; some of these strains acquired elevated MICs of teicoplanin, although not of vancomycin (5). If GISAs were to emerge in EMRSA-17 or in other similarly resistant strains, there would be very few therapeutic options (for example, linezolid, quinupristin-dalfopristin), and resistance to these can emerge, albeit very infrequently. Vigilance is required. This publication ensures that these incidents are communicated rapidly. Other initiatives such as the HARMONY EU MRSA database (http://www.phls.co.uk/International/Harmony/Harmony.htm), showing the spread of MRSA throughout the EU, and the EARSS project (http://www.earss.rivm.nl/) are important sources of information on control measures and the current debate on the control of antimicrobial resistance in the EU.

References:


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