

Value of the minimum bactericidal concentration of antibiotics in the management of a case of recurrent *Streptococcus bovis* septicaemia

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SUMMARY After prostatectomy a 60-year-old man developed *Streptococcus bovis* septicaemia. The patient did not respond to treatment with a combination of ampicillin and erythromycin and in vitro antagonism between these antibiotics was demonstrated by minimum bactericidal concentration (MBC). The value of determining the MBC of antibiotics used in the treatment of septicaemia is emphasised.

Streptococci group D usually gain entry to the blood circulation via the genitourinary tract, and men with prostatic disease are prone to bacteraemia with these organisms, especially after surgery or instrumentation of the genitourinary tract. *Streptococcus bovis* is a group D streptococcus and usually very sensitive to penicillin, unlike the enterococci, also in this group, which are usually resistant.

We report a case of recurrent septicaemia due to a resistant *S bovis*, the management of which illustrates the essential value of the minimum bactericidal concentration (MBC) of antibiotics in determining the appropriate bactericidal treatment.

Case report

In a 60-year-old caucasian male a urinary tract infection developed after transvesical prostatectomy which settled on treatment with ampicillin. Three weeks later the patient was readmitted with pyrexia, confusion, right-sided headache and a left hemiplegia. Computerised tomographic scan showed a right parietal infarct. The patient's haemoglobin was 14.3 g/l and erythrocyte sedimentation rate (ESR) (Westergren) was 12 mm in the first hour. He was given gentamicin and metronidazole, but his fever remained unaltered. A set of blood cultures grew *S bovis*. No heart murmurs were heard. After a five-day course of intravenous cefuroxime 750 mg

eight-hourly, his fever subsided. Within two months the patient returned with a deep vein thrombosis in his leg and pyrexia. Four separate blood cultures again grew *S bovis*. He was given ampicillin and streptomycin and his temperature resolved.

Night sweats and generalised aches and pains developed soon after his return home, resulting in admission four months later. At that time his haemoglobin was 10.7 g/dl and ESR (Westergren) was 40 mm in the first hour. The patient was examined, but no heart murmur could be heard, and no further embolic episode ensued. Radiography of chest and joints were normal, as were the intravenous pyelogram and barium enema. Three further sets of blood cultures grew *S bovis*.

The combination of persisting bacteraemia together with embolism was tentatively diagnosed as infective endocarditis although no heart murmur was heard.¹ The patient's initial treatment was intravenous benzyl penicillin (3 megaunits given four-hourly) and gentamicin 80 mg eight-hourly. The fever began to remit after 48 h. However, as there was no synergy between penicillin and gentamicin and as the minimum inhibitory concentration (MIC) of ampicillin was much lower than for penicillin, and in combination with erythromycin gave a low MIC (see laboratory investigations below), treatment was changed to ampicillin 1 g four-hourly and erythromycin 500 mg eight-hourly. The patient still failed to respond, the fever returned, and the MBC of the combination showed the organism to be viable at high antibiotic concentrations despite preliminary encouraging MIC values. The patient continued treatment with just intravenous ampicillin, 1 g four-hourly for six weeks, and

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then oral amoxycillin 500 mg six-hourly for three months. The patient has since remained afebrile and well.

LABORATORY INVESTIGATIONS

A standard procedure was adopted for determining the MIC and MBC of antibiotics.² The MIC and MBC of penicillin to the *S bovis* was 2 µg/ml and of gentamicin 20 µg/ml. Using gentamicin at 1 µg/ml and then 5 µg/ml throughout the test, the MIC and MBC of the combination was 2 µg/ml.

For ampicillin the MIC and MBC were 0.5 µg/ml. There was no fall in the MIC and MBC when this drug was combined with gentamicin. The MIC of erythromycin was 0.25 µg/ml but the MBC was > 16 µg/ml. Erythromycin combined with ampicillin gave an MIC < 0.03 µg/ml but an MBC > 16 µg/ml.

No synergy was shown with ampicillin or gentamicin in combination with rifampicin and vancomycin.

Discussion

In 1942, Rammelkamp demonstrated resistance of bacteria to antibiotics using a broth dilution method upon which present day MIC, MBC techniques are based³ and Robbins and Tompsett showed that combined antibiotic therapy was effective in treating enterococcal endocarditis,⁴ a finding confirmed in the laboratory by Watanakunakorn, who went on to show that penicillin combined with gentamicin exhibited a synergistic bactericidal effect against enterococci.⁵

Streptococcus bovis tends to be highly susceptible to penicillin.^{6,7} This micro-organism, however, like the enterococci was resistant to penicillin and gentamicin. In this case no synergy could be demonstrated with this combination or with a combination of ampicillin and gentamicin. So the potentially toxic gentamicin was omitted from the regime in favour of erythromycin, which combined with ampicillin

showed good synergy for MIC. This was misleading, for the MBC of the combination showed the antibiotics to be antagonistic, which was reflected by deterioration in the patient's condition; and which led to the use of ampicillin alone.

This patient emphasised the importance of basing treatment on the MBC of antibiotics, the MIC cannot be relied upon for any guidance as to treatment in such cases of recurrent septicaemia because of the tolerance of some organisms to high concentrations of antibiotics.

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