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ASPECTS OF TREATMENT*

Streptococcus milleri and surgical sepsis

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Abstract

For many years Viridans streptococci have been considered as commensal organisms in a wide variety of sites in the human body and only regarded as significant pathogens in subacute bacterial endocarditis. However, in recent years some reports have suggested that a particular species, *Streptococcus milleri,* can be a virulent pathogen, producing life-threatening sepsis particularly in surgical patients. We review here our experience of this organism in 23 general surgical patients over a 3 year period, and postulate that prophylactic use of antibiotic combinations such as gentamicin and metronidazole in patients undergoing colo-rectal surgery may be a factor promoting its emergence as a significant pathogen. Patients with established sepsis due to *Streptococcus milleri* should be considered for long-term antibiotic therapy as part of the treatment of their abscesses.

Introduction

Streptococcus milleri was first described by Guthof in 1956 *(1)*, following its isolation from dental root abscesses. This strain was non-haemolytic on sheep's blood agar, and possessed no Lancefield antigens. In 1962, Ottens and Winkler *(2)* identified a biochemically similar group of non-haemolytic streptococci (which they termed 'indifferent' streptococci) from dental root canals. However, over half their isolates carried Lancefield antigens of group F, G, or C. In 1972, Colman and Williams *(3)* demonstrated that these organisms were the same species as Guthof's *Streptococcus milleri*, and expanded the species further to include other streptococci (some of them β-haemolytic) with common biochemical and structural properties, despite antigenic differences. They included *Streptococcus milleri* in the viridans group of streptococci, although only about 20% of isolates actually show α haemolysis *(4)*. Support for this classification has been provided by Ball and Parker (*4*) and Poole and Wilson *(5)*. In these series, 30% to 70% of isolates carried Lancefield antigens, over half of which were group F.

Many strains of *Streptococcus milleri* show enhanced growth under anaerobic conditions, and are therefore sometimes described as 'microaerophilic' or 'anaerobic' streptococci *(4)*. Indeed, some even require the addition of carbon dioxide for optimum growth in the laboratory (*4,6)*. The organism has now been isolated as a commensal from teeth, nasopharynx, and gastro-intestinal tract *(7)*.

However, it is only in recent years that it has been recognised as a significant pathogen. Despite a number of reports, detailed in our discussion, *Streptococcus milleri* is not well known to surgeons generally and we feel clinicians should be aware of the potential pathogenicity of this organism. We have paid special attention to its isolation in our own patients, and have tried to identify reasons for its emergence as a pathogen.

Patients and methods

The present report covers the three-year period November 1977 to October 1980 inclusive. For the first eighteen months of this period, we studied all patients from the general surgical wards, including both serious and minor infections. For the second eighteen months, we studied only those patients with serious life-threatening infections in one surgical unit (The University Unit). The overall effect of this approach is to understate the number of infections due to *Streptococcus milleri* in the full 3 years. During the study period, any streptococci grown on aerobic and anaerobic culture from patients with significant infections were identified to species level by the methods of Parker and Ball *(8)*. For present purposes, 'significant infection' is defined as the presence of pus, or a positive blood culture. Full details of our isolation techniques can be obtained from the authors on request.

Results

The patients' ages ranged from 17 to 69 years, and there was no bias to either sex. There were 10 patients with life-threatening serious infections with *Streptoooccus milleri* (mostly intra-abdominal abscesses) in the 3 year period. In 7 of these the organism was isolated in pure culture on one or more occasions. Many of the patients had multiple drainage procedures for abscesses, and resolution was only achieved after the addition of antibiotics active against *Streptococcus milleri*, usually high-dose penicillin.

Two patients died, one from recurrent carcinoma 10 months after initial surgery, the other of pulmonary embolism at 3 months. At the time of her death, she still had an active pelvic abscess containing *Streptococcus milleri* and this abscess may have contributed to the formation of a pelvic vein thrombosis.

There were 13 patients with minor abscesses in the first 18 month period. These were mainly wound abscesses, but some persisted for up to 2 months, despite drainage.

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Possibly the most interesting finding of the study is the antibiotic therapy given to the patients with major abscess, *prior* to the formation of those abscesses. Six of the ten patients with serious abscesses containing *Streptococcus milleri* had previously received gentamicin and metronidazole in combination, usually given at the time of operation as prophylaxis against wound infection.

One patient had received gentamicin and lincomycin, one gentamicin and ampicillin and one flucloxacillin only. Only one patient had not previously received any antibiotics.

Discussion

For many years the Viridans streptococci were regarded as having low pathogenicity, and the only serious infection ascribed to them was subacute bacterial endocarditis. As most isolates are sensitive to penicillin few clinical microbiologists considered it necessary to identify them to species level *(9)*, and, therefore, reported *Streptococcus milleri* as 'a non-haemolytic streptococcus' or alternatively as 'a microaerophilic streptococcus'. However, in 1975 Bateman, Eykyn, and Phillips *(10)* reported three cases of liver abscess in which *Streptococcus milleri* was the sole organism isolated. Subsequent reports from two microbiological reference laboratories *(8,9)* have shown it to be the most common of the viridans group to be associated with serious pyogenic infection.

Streptococcus milleri has been associated with endocarditis, brain abscess, meningitis and pleural empyema, but its most common association is with abdominal infection or operations *(8,11)*. It is a significant pathogen in appendicitis, particularly where there is pus formation *(12,13)*. Moore-Gillan, Eykyn, and Phillips *(14)* reported sixteen cases of liver abscess, of which thirteen contained *Streptococcus milleri*. These authors, too, emphasised the preponderance of strains with Lancefield group F antigen. In most cases, this organism is grown as part of a mixed faecal flora, but in the more severe infections it is often isolated in pure culture *(5,11)*. A pure culture was obtained in 7 of our 10 patients with major *Streptococcus milleri* infection. This implies suppression of the other organisms usually found in abdominal abscesses, such as Bacteroides species and coliforms.

Reviewing our own serious cases we can identify a group of patients who had previously received treatment with the antibiotic combination gentamicin and metronidazole. This was usually given as prophylaxis against wound infection, but sometimes as treatment of established sepsis with mixed faecal flora. This combination will suppress Bacteroides species and coliforms, but is not active against *Streptococcus milleri* which is a commensal in the faeces in 20–50% of subjects *(7,11)*. *Streptococcus milleri* could then become a pathogen by overgrowth, in much the same way as Candida species overgrowth can occur in patients receiving broad-spectrum antibiotics.

The addition of a third antibiotic, such as penicillin, would produce a combination active against streptococci. However, we feel that a three drug regimen is unnecessarily cumbersome. Additionally, some microbiologists, concerned about the emergence of gentamicin resistant organisms, have advocated that for prophylaxis gentamicin should be replaced by co-trimoxazole or a cephalosporin *(15)*, reserving gentamicin for the treatment of life-threatening sepsis. Such new two-drug combinations have been shown to be effective *(16)* and would have the additional advantage of being active against *Streptococcus milleri*.

In view of the popularity of gentamicin plus metronidazole, we are likely to continue seeing patients with established abscesses involving *Streptococcus milleri*, and we advocate a scheme of management for these. In the majority of patients, the abscess will resolve following simple drainage, either surgical or spontaneous. There will remain, however, a small number of patients in whom sepsis persists, despite surgical drainage. In this group of patients, radical débridement of the abscess cavities is impossible without serious risk of injury to adjacent bowel or vital structures. Drainage can be achieved, but there remains some infected necrotic material which continues to 'seed' fresh abscesses, often at intervals of some months. We believe this small group of patients should be considered for long-term treatment with an antibiotic active against *Streptococcus milleri*, in addition to surgical drainage.

Streptococcus milleri is always sensitive 'in vitro' to penicillin and ampicillin *(17)*, and in most patients one of these will be the drug of choice. Where it is not possible to use a penicillin (for example, because of drug sensitivity) erythromycin, a cephalosporin, or co-trimoxazole are usually effective. We recommend the antibiotic be given for some weeks beyond clinical resolution of the infection, and that the patient's blood should be tested at intervals for bactericidal levels of the antibiotic against the strain of *Streptococcus milleri* isolated from that patient.

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