Neonatal Infection with *Streptococcus milleri*

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*Streptococcus milleri* is a known commensal of the female genitourinary tract, but its pathogenicity in neonates has been reported in only a few cases. During a period of one year in an obstetrical unit, *Streptococcus milleri* was isolated from nine neonates and from one foetus after a spontaneous abortion. In seven of the nine newborns, neonatal infection was assessed and *Streptococcus milleri* was the lone pathogen involved, associated with positive blood or vaginal cultures in four mothers. Because *Streptococcus milleri* requires special conditions for identification, it is probably underestimated as a cause of neonatal infection and septic abortion.

*Streptococcus milleri* was first described in 1906, but it has undergone several name changes since then (1). In 1989 Whiley and Beighton (2), on the basis of the DNA-DNA hybridization and different phenotypic properties, specified *Streptococcus anginosus* among the 'Streptococcus milleri' group. These strains are usually isolated from genitourinary and gastrointestinal sources and are frequently associated with other pathogens (3). *Streptococcus milleri* has been implicated in infections of the female genital tract, such as uterine abscesses (4), sometimes in association with intrauterine devices, vaginal discharge, abortions (5) or severe neonatal infections (6).

We report here the isolation of *Streptococcus milleri* strains from 9 neonates and 1 foetus spontaneously aborted at 19 weeks’ gestation, all within a period of 12 months in an obstetrical unit.

**Materials and Methods.** From September 1993 to September 1994, clinical samples (gastric aspirates, placenta, blood, skin, nose, anus and ear swabs) for bacteriological investigations were collected from newborns at our hospital to screen for neonatal infection. Such collection was performed systematically at delivery in the following cases: maternal fever, labour > 12 h, meconium-stained amniotic fluid, low Apgar score or respiratory failure. Gram stains were performed on samples from placenta, gastric aspirate and ears. The presence of leukocytes and microorganisms was noted. A vaginal swab was taken from six mothers before delivery.

Samples were cultured on 5% horse blood agar (bioMérieux, France) under aerobic and anaerobic conditions. Chocolate agar plates were incubated in an atmosphere of 5% CO₂ for 48 h. All bacterial strains were identified.

*Streptococcus milleri* forms minute colonies after 24 or 48 h of incubation. Some isolates produce a strong caramel smell on agar plates. Using the API 20 Strep system (bioMérieux), organisms were identified as *Streptococcus milleri*, probably *Streptococcus anginosus*, by their production of acetoin and β-glucosidase, hydrolysis of arginine and esculin, and fermentation of amygdalin, lactose and raffinose.

Because the API 20 Strep system does not contain the tests necessary to differentiate *Streptococcus anginosus* from *Streptococcus intermedius*, we were unable to confirm the identification of *Streptococcus anginosus*, and further tests could not be undertaken. Lancefield serotyping was performed using the Streptex kit (Murex Diagnostics, UK). Antimicrobial susceptibility testing was performed on blood agar using the disk diffusion method and an incubation time of 48 h.

**Results and Discussion.** During the one-year study period, evidence of colonization (2 or more positive samples of the same pathogen) was observed in 127 (5%) of 2,510 neonates. Eleven (0.4%) of the 2,510 infants had neonatal sepsis, as demonstrated by a positive blood or CSF culture. Organisms isolated from colonized neonates were as follows: *Escherichia coli* with or without K1 antigen (30.7%), group B streptococci (27.5%), *Streptococcus milleri* (7.9%), *Enterococcus* spp. (2.3%) and other non-*milleri Streptococcus* spp. (1.6%) (11.8% in all for non-group B streptococci). In 7.9% of the cases *Escherichia coli* K1 and group B streptococci were associated. Other pathogens isolated were *Listeria* spp. (2.3%), *Staphylococcus aureus* (2.3%), *Haemophilus* spp. (1%) and various members of the family *Enterobacteriaceae*.

*Streptococcus milleri* was isolated from swabs (nose, anus, ears, gastric aspirates) obtained from

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nine neonates (7.9 % of the colonizations). In one foetus examined after spontaneous abortion, only Streptococcus milleri was isolated, and microscopic examination of the placenta showed chorioamnionitis. In 8 of the 10 cases Streptococcus milleri was in pure culture; in one case it was associated with Escherichia coli K1, and in the remaining case with Haemophilus influenzae.

A positive blood culture was obtained from one of the nine neonates colonized by Streptococcus milleri. Clinical evidence of sepsis (respiratory distress, temperature instability, tachycardia or bradycardia associated with low Apgar score) was present in seven of nine neonates, five of whom required mechanical ventilation. Neutropenia, thrombopenia and/or high C-reactive protein levels of > 8 mg/l were present in seven of nine neonates. In the two remaining neonates bacterial colonization without invasive sepsis was evident, despite a positive blood culture in one of the mothers. After treatment (amoxicillin 100 mg/kg/day plus netromycin 2 mg/kg/day), all babies recovered without sequellae.

Risk factors for the development of neonatal sepsis (prematurity, maternal fever, maternal bacteremia, prolonged rupture of membranes) were present in eight of the nine mothers of live babies. Preterm labour (33–35 weeks’ gestation) occurred in four cases, and amniotic fluid was meconium-stained in three cases. The mother presenting with abortion was febrile, and three women were febrile during labour. Fever was associated with positive blood cultures in two cases, one with Streptococcus milleri as the only pathogen and one with both Streptococcus milleri and Haemophilus influenzae. Vaginal swabs were taken from six mothers before delivery, four of whom harboured Streptococcus milleri.

None of the Streptococcus milleri strains isolated was β-haemolytic. Five strains (50 %) were found to be Lancefield group F, whereas the other strains were nongroupable. All strains were susceptible to β-lactam agents, aminoglycosides, macrolides and vancomycin.

Streptococcus milleri is usually considered a commensal of the gastrointestinal and genitourinary tracts (3). It is sometimes mistaken for anaerobic streptococci because of its need for carbon dioxide for isolation or for β-haemolytic streptococci with a given Lancefield classification, while nonhaemolytic organisms are identified as viridans streptococci. Conventional biochemical testing remains the method of choice for identification of viridans streptococci, including Streptococcus milleri. Whiley et al. (3) reported that 12 % of the strains of Streptococcus milleri (anginosus) were β-haemolytic, 26 % belonged to Lancefield group F and 48 % were nongroupable. In our study none of our ten strains was β-haemolytic, and 50 % belonged to Lancefield group F.

Streptococcus milleri organisms have been isolated from the vaginae of patients with intrauterine devices associated with vaginal discharge (7) and occasionally are found in obstetrical infections and neonatal sepsis (6). Streptococcus milleri has been reported as a cause of septicemia and pneumonia in premature neonates (8). None of our neonates had pneumonia. In four cases the source of Streptococcus milleri was the vagina. Whether infection follows spontaneous rupture of membranes or whether heavy vaginal colonization predisposes to rupture of membranes is not known. It has been hypothesized that phospholipase A2, produced by infecting bacteria, could cause premature labour by deacylation of arachidonic acid (9).

In our study, in neonates colonized by pathogens at birth, frequency of infection due to non-group B streptococci was 11.8 %, and 7.9 % of infections were due to Streptococcus milleri. In a previous study, the incidence of non-group B streptococci in neonatal infections was reported to be 7.4 % (10). Pneumonia associated with these pathogens may be clinically indistinguishable from uncomplicated hyaline membrane disease (2).

The isolation of Streptococcus milleri is enhanced by elevated carbon dioxide concentrations. This organism is probably often misidentified, resulting in mismanagement of newborns with neonatal sepsis. The frequency of Streptococcus milleri infection seems to be underestimated, thus Streptococcus milleri should be suspected in cases of neonatal sepsis and septic abortion.

References