Group A *Streptococcus* Endometritis following Medical Abortion

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Case Reports

A 28-year-old female, gravida 2 para 1 (G2P1), was admitted to Antoine-Béclère Hospital for fever and severe metrorrhagia. She had undergone a medical abortion at the gestational age of 7 weeks the week before, with a protocol of mifepristone and misoprostol. After 6 days, massive metrorrhagia occurred with pelvic pain, fever at 39.4°C, chills, and hypotension at 100/50 mm Hg. Complete blood count showed leukocytosis at 2.6 × 10⁹ cells/mm³, hemoglobin at 8.8 g/dl, platelets at 148 × 10⁹/liter, and the C-reactive protein at 170 mg/liter. Empirical intravenous antibiotic treatment was started with amoxicillin-clavulanic acid (1 g three times/24 h) and gentamicin (400 mg/24 h). Despite intensive fluid loading, the hypotension persisted and the patient was referred to the intensive care unit. An ultrasound scan showed a 14-mm thickening of the endometrium wall, prompting surgical endouterine aspiration. Residual intrauterine trophoblastic tissue was removed and sent for culture and histological examination. Gram stain of the single blood culture and the trophoblastic tissue yielded Gram-positive cocci that formed pairs and short chains, secondly identified on the medium as *Streptococcus pyogenes* (group A *Streptococcus* [GAS]) by matrix-assisted laser desorption ionization–time of flight (MALDI-TOF; confidence score of 2.633). Routine antibiotic susceptibility testing was performed on Mueller-Hinton agar with 5% sheep blood (BD Diagnostic) using the disc diffusion method. The organism was susceptible to all antibiotics tested and active against *S. pyogenes*: amoxicillin, di-ameter of inhibition of 40 mm; erythromycin, 31 mm; clindamycin, 29 mm, with no inducible resistance to clindamycin (D-test negative); vancomycin, 26 mm; levofloxacin, 23 mm; tetracycline, 33 mm. The organism was resistant to a low level of gentamicin (34 mm). The antibiotic treatment was switched to oral amoxicillin-clavulanic acid (1 g three times/24 h) for 15 days, with favorable clinical outcome. The isolate was sent to the National Reference Center for streptococci and confirmed to be of *emm*4 genotype harboring the genes encoding the streptococcal pyrogenic exotoxins SpeB and SpeC, the streptococcal superantigen Ssa, and the streptococcal mitogenic exotoxin SmeZ.

The second case occurred in a 21-year-old G1P0 woman admitted to La Conception Hospital, Marseille, France, for fever, chills, and metrorrhagia. The patient had undergone an ambulatory medical abortion with mifepristone and misoprostol at the gestational age of 6 weeks, 4 days before admission. After 3 days, severe metrorrhagia started, with hyperthermia at 40°C. The vital signs and abdominal examination were unremarkable. The leukocytes count was at 0.8 × 10⁹ cells/mm³, hemoglobin at 12 g/dl, and the C-reactive protein at 82 mg/liter. A vaginal ultrasound scan found a residual intrauterine retention of 20 mm. A surgical endouterine aspiration was performed together with an empirical intravenous antibiotic treatment utilizing amoxicillin-clavulanic acid (1 g three times/24 h) and ofloxacin (200 mg two times/24 h). The Gram stain performed on the single blood culture taken prior to antibiotic therapy and on the trophoblastic tissue showed Gram-positive cocci that formed short chains. Both specimens grew *S. pyogenes*, identified on the medium by MALDI-TOF (confiden score of 2.315). The strain was found to be susceptible to amoxicillin (diameter of inhibition of 40 mm), erythromycin (30 mm), clindamycin (29 mm), with no inducible resistance to clindamycin (D-test negative), vancomycin (26 mm), levofloxacin (23 mm), and tetracycline (32 mm). The organism was resistant to a low level of gentamicin (32 mm). Ofloxacin was switched to clindamycin (600 mg three times/24 h), and apyrexia finally occurred on day 3. Oral amoxicillin-clavulanic acid (1 g three times/24 h) and oral clindamycin (600 mg three times/24 h) were maintained for a total 3-week duration, with favorable outcome. The isolate was confirmed by the National Reference Center to be of *emm*4 genotype harboring the genes encoding the streptococcal pyrogenic exotoxins SpeB and SpeC, the streptococcal superantigen Ssa, and the streptococcal mitogenic exotoxin SmeZ.

Overall frequency of infections following medical abortion is...
below 1% (1) and around 0.025% for the protocol associating mifepristone to oral misoprostol (2). Five fatal cases of *Clostridium sordellii* sepsis were reported after medical abortion (3) but, to our knowledge, only one severe case of GAS infection (4). In this case and ours, the patients were young, with no remarkable comorbidities. In the case reported by Daif et al. (4), the clinical signs started 48 h after the procedure (versus 4 to 6 days in our cases), and the necrotizing fasciitis was located to the lower extremity with unfavorable outcome despite antibiotic therapy and surgical debridement, leading to a below-the-knee amputation. Unlike in our report, there was no residual endometrial retention of trophoblastic tissue. As underlined by Daif et al., this last point suggested that the etiology may not be related to the medical abortion itself but perhaps to the relative immune suppression induced by pregnancy and the potent antiglucocorticoid activity of mifepristone. In our cases, two sources of infection can be hypothesized: endometrial migration from a preexisting colonization of the vaginal flora or exogenous contamination during the procedure. Vaginal carriage of GAS is low (0.03%) (5) and has not been formally proven as a risk factor for postpartum or postabortion endometritis. However, the prolonged dilation of the cervix uteri creates favorable conditions for migration of pathogenic vaginal bacteria to the uterus, and blood and necrotic decidual tissue represent an excellent environment for GAS growth. In our two cases, the retention of intrauterine trophoblastic tissue that was evidenced by the postprocedure ultrasound scans certainly played an important role in the occurrence of the infection. Since GAS vaginal screening is not recommended prior to medical abortion in France, vaginal carriage of GAS was not known in our patients. The other possible source of infection is a contamination during the pelvic examination preceding the procedure, via respiratory droplet spread. Several postpartum health care-associated infections related to GAS transmission from health care workers (HCW) have been demonstrated by molecular analysis (6). The carriers are usually colonized in the throat, anus, vagina, or a skin lesion. The unexpected occurrence of these two postabortion infections led to investigations by the local infection control units. No breaks in infection control techniques were noted. In particular, the HCW reported wearing masks during both pelvic examination and endoscopy preceding the medical abortion, as recommended by infection control guidelines (7). Here, since only isolated cases were reported in each hospital, HCW were not screened.

Strains of GAS isolated in our cases were of genotype *emm*89 and *emm*4 and harbored the genes encoding the exotoxins SpeB, SmZe, and SpeC. *emm*4 and *emm*89 GAS strains are responsible for invasive infections and have already been isolated from endometritis and puerperal infections (8, 9). Moreover, *emm*89 is the third most prevalent *emm* type accounting for invasive infections in Europe, *emm*1 and *emm*28 being the first and the second, respectively (8, 9). Apart from strains belonging to *emm*1 and *emm*3, which are clearly more associated with streptococcal toxic shock syndrome, and *emm*28, which are overrepresented among *S. pyogenes* isolated from genital infections, there is no clear correlation between an *emm* genotype and a given infectious presentation. A strict correlation between a given toxinogenic genotype profile and strain virulence has also not been clearly proven and remains controversial. However, all invasive strains have at least M protein and the cysteine protease SpeB, which were clearly demonstrated to play a role in GAS virulence. Lastly it has been established that antibiotics inhibiting protein synthesis, such as clindamycin, should be combined with a beta-lactam in order to decrease the production of bacterial toxins in the case of streptococcal toxic shock syndrome or necrotizing fasciitis, which was not the case in this report.

Antibiotic prophylaxis is routinely administered for surgical abortions and has been proven to decrease postabortion infection rates by 42% (10). The Food and Drug Administration (FDA) does not recommend the use of prophylactic antibiotics for medical abortion, considering that this procedure does not require instruments in the cervix or uterus, but also underlines that data are lacking. The severity of these two cases may raise the question of prophylaxis; however, this should also be balanced with the relatively low incidence of such infections and the potential negative ecological impact of wide antibiotic use.

Two months after these cases, a third one was reported in another French hospital, with similar clinical characteristics due to an *emm*28 GAS strain. GAS is a well-documented cause of puerperal sepsis; therefore, it is not unexpected that this microorganism can also cause invasive infections following abortion. However, very few cases describing GAS infections occurring after nonsurgical abortion have been described. These rare cases should be known by microbiologists, infectious disease practitioners, as well as hygienists. It stresses that precautions and hygienic measures, in particular wearing a mask during pelvic examination preceding such procedures, should be similar regardless of the method used (surgical or medical).

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