

Treatment of Chorioamnionitis with Piperacillin/Tazobactam and Clindamycin

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ABSTRACT

Objective: Chorioamnionitis is a condition that bacteria infects the chorion and amnion and the amniotic fluid which can affect pregnant women. Infections may affect both the mother and fetus. Cervical insufficiency and chorioamnionitis cause preterm birth and perinatal morbidities.

Case: A 37-year-old patient was referred to the clinic with the diagnosis of preterm labor and cervical insufficiency at 26 weeks + 4 days of pregnancy. Cervix was 3 cm dilated, effaced 70%, the amnion membrane intact, and there was a cerclage thread on the cervix. There was a single, viable fetus in the uterine cavity with fetal measurements compatible with 27-28 weeks on ultrasonography. Ampicillin and azithromycin treatments were started. On the seventh day of observation, leukocytes and C reactive protein values had increased, and there was an onset of serohemorrhagic vaginal discharge. Thereupon, intravenous treatment of piperacillin/tazobactam and clindamycin started. Signs of chorioamnionitis were resolved. The patient was delivered on day 38 of admission due to vaginal bleeding. The newborn and patient outcomes were good. Further studies are needed to evaluate the new treatment regime's efficacy in chorioamnionitis treatment.

Keywords: Cervical Insufficiency, Chorioamnionitis, Clindamycin, Piperacillin/Tazobactam, Preterm delivery

INTRODUCTION

Cervical insufficiency is defined as spontaneous softening, shortening, and opening of the uterine cervix without reason, causing miscarriage or preterm labor in the second trimester (1, 2). Occurrence is about 1% in pregnant women and is more prevalent in pregnancies with recurrent second-trimester pregnancy loss (1, 2).

Cervical mucus has an anatomical and preventive function against the development of ascending infection during pregnancy (3). Preterm premature rupture of membranes (PPROM) or cervical insufficiency results in loss of the cervical mucus plug and allows microorganisms to reach the uterus and fetus. That leads to the development of chorioamnionitis, currently termed inflammation or infection or both or Triple I. When cervical insufficiency or PPRM develops, antibiotic therapy is routinely administered to prevent the development of chorioamnionitis. When chorioamnionitis is evident, birth is necessitated.

In the presented case, routine antibiotic treatment was administered in patients with cervical dilatation due to cervical insufficiency. After one week of routine initial antibiotic therapy, chorioamnionitis findings, such as leukocytes and C reactive protein (CRP) values, had increased. These increases were attributed to an early sign of chorioamnionitis. Thereupon, two different antibiotics were administered together. Chorioamnionitis findings regressed during the antibiotic treatment. Birth took place one month after the new antibiotic treatment. This case report aims to present a new antibiotic administration in patients with chorioamnionitis and to pioneer new studies on this antibiotic regime.

CASE

A 37 year-old patient was referred to my clinic with a diagnosis of preterm labor and cervical insufficiency at 26 weeks and 4 days of pregnancy. The previous day, the patient presented at the hospital due to pelvic pain. She was admitted with a diagnosis of preterm delivery and cervical insufficiency. A tocolytic and steroid therapy was administered. One day later, she was referred to my clinic. Upon speculum examination, a cervical cerclage thread was observed on the cervix.

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The amnion membrane was intact, not prolapsed into the vagina. Bimanual examination revealed that cervical dilatation was 3 cm with effacement (70%). The cervical cerclage thread was not removed to prevent sudden cervical dilatation. Upon obstetric ultrasonography evaluation, there was a single, viable fetus in the uterine cavity with fetal measurements compatible with 27-28 weeks. The amniotic fluid volume was in the normal range. There was no uterine contraction as evaluated by a nonstress test (NST). Magnesium sulfate was administered for its neuroprotective effects. The standard clinical routine treatment of ampicillin (4x1 g IV over seven days) and azithromycin (1000 g oral single dose) was started to prevent the development of chorioamnionitis. The leukocytes count of patient was $16.7 \times 10^3/\text{mm}^3$ on admission.

The pregnancy history of the patient was as follows: her first pregnancy occurred after ovulation induction. Labor started in the 25th week of pregnancy. The patient gave a premature birth with a breech presentation. The baby, 650 g weight, died during labor. The second pregnancy occurred by intracytoplasmic sperm injection (ICSI). The patient gave premature birth in the 26th week of pregnancy with breech presentation. The baby, 850 g weight, died during labor. The patient's third pregnancy occurred by ICSI treatment. Preterm labor started in the 26th week of this pregnancy. The patient gave birth to a 950 g baby with cephalic presentation. The baby died after staying 20 days in the neonatal intensive care unit (NICU). The patient's fourth pregnancy, as described herein, occurred spontaneously. A cervical cerclage was performed in the 14th week of pregnancy with the diagnosis of cervical insufficiency.

During inpatient observation, uterine contraction was not observed. Laboratory evaluations on the following day were; leukocyte: $16.8 \times 10^3/\text{mm}^3$ and C reactive protein (CRP): 18 mg/L. Thromboprophylaxis treatment, progesterone, and ampicillin treatment continued during follow-up. Two days later, the leukocyte count was $12.2 \times 10^3 / \text{mm}^3$ and CRP level was 6 mg/L. The patient was continued to observation. Leukocyte count was $14.6 \times 10^3/\text{mm}^3$ and CRP level was 52 mg/L on the 7th day of admission. The values of leukocyte and CRP increased. The patient reported fever, but it was not detected by thermometer.

Vaginal serohemorrhagic discharge started in the patient's 7th day. These findings and symptoms were attributed to the early stage of chorioamnionitis. Thereupon, intravenous treatment of piperacillin/tazobactam (2.25 g four times) and clindamycin (900 mg three times per day) were started. A single dose of steroid (6 mg betamethasone) was administered intramuscularly to decrease inflammation and induce fetal lung maturation. An indomethacin suppository (100 mg) was administered to decrease inflammation severity and prevent uterine contractions' development. During treatment, the patient's vaginal discharge ceased, and preterm labor did not develop. During antibiotic treatment, the leukocytes and CRP values decreased slowly. On the 14th day of treatment, the leukocyte value was $9.5 \times 10^3/\text{mm}^3$ and the CRP value was 9 mg/L. The double antibiotic treatment was stopped on the 15th day. The patient continued to be observed in the hospital. Vaginal bleeding of the patient started on the 38th day of admission.

Uterine contraction and fetal bradycardia were not observed by NST. Since there was no empty ventilator in the NICU of my hospital, the pregnant woman was transferred to a tertiary hospital.

A male baby, 2185 g, was delivered by cesarean section in the transferred hospital. It was observed that the placenta was partially detached (approximately 20%). There was no complication for the mother after birth. The baby was given continuous positive pressure ventilation for two days in the NICU, and then oxygen therapy was given for three days. The baby was discharged on the 21st day of birth at 2575 g weight.

DISCUSSION

According to our knowledge, this is the first time this treatment regimen has been administered to treat chorioamnionitis. This treatment regime prolonged pregnancy duration by about thirty days. Due to United States Food and Drug Administration pregnancy category for piperacillin/tazobactam and clindamycin is group B. When vaginal polymicrobial microorganisms reach the uterus and adnexa, they cause pelvic inflammatory disease. Broad-spectrum antibiotics with anaerobic coverage are used to treat pelvic inflammatory disease. The existence of uterine cervical dilatation, PPROM, or both lead to loss of the cervical mucus plug and supply a way for the same vaginal polymicrobial microorganism to reach the uterine cavity and cause intrauterine chorioamnionitis (4). In light of knowledges, to administration of broad-spectrum coverage antibiotics, these two antibiotics were chosen to treat chorioamnionitis.

When pregnant women with cervical dilatation are detected, routine antibiotic treatment is started to prevent the development of chorioamnionitis (5). Despite antibiotic treatment, chorioamnionitis develops in most patients (5). The initiation of antibiotic treatment in the early period of chorioamnionitis, especially in the early stage, is more effective than starting treatment when the disease becomes severe (6). It has been reported that CRP increases as an inflammatory marker in subclinical chorioamnionitis and may have diagnostic value (7).

The diagnosis of chorioamnionitis in the presented case was established by increased leukocyte and CPR values and the development of serohemorrhagic vaginal discharge. Then a new antibiotic treatment regime was administered. During treatment, leukocyte and CRP values decreased, and serohemorrhagic discharge ceased.

It is shown that 76% of pregnant with cervical insufficiency with microorganisms in the amniotic fluid gave birth within the first 48 hours of their hospitalization (8). Mönckeberg et al. investigated the presence of chorioamnionitis by performing amniocentesis to 70 pregnant women with cervical insufficiency. They found that 19% (13/70) of pregnant women had chorioamnionitis. They found that cervical dilatation and leukocyte and CRP values were higher in pregnancy with chorioamnionitis than pregnancy without chorioamnionitis (8).

They observed that the median time of pregnant women with chorioamnionitis between admission to the hospital and the delivery was 1 d (1-10 days). Of these patients, 69% gave birth within the first 48 hours (8).

It is believed that pregnant women with cervical insufficiency and chorioamnionitis cannot be treated successfully (9). Recently Oh et al. reported that chorioamnionitis could be treated with antibiotic treatment, and the duration of pregnancy could be extended in some of the pregnant women with cervical insufficiency and chorioamnionitis (9).

Gravett et al. reported that antibiotic treatment with immunomodulators (dexamethasone and indomethacin) could threat chorioamnionitis, prevent intra-amniotic infection, placental inflammation, and prolong pregnancy in non-human primate models (10).

In the presented case, the development of subclinical chorioamnionitis in a patient with cervical insufficiency was observed despite routine antibiotic treatment. The findings of chorioamnionitis regressed using the new antibiotic treatment, and the gestation period was prolonged for about one month. More studies need to evaluate the effectiveness of this new treatment modality in patients with chorioamnionitis.

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