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Intrauterine *Helicobacter cinaedi* Infection Presenting with Fetal Distress and Mucous Diarrhea at Birth

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Abstract

Helicobacter cinaedi infection is well documented in immunocompromised individuals but is a rare pathogen in fetuses and neonates, with only a few cases of newborns with sepsis caused by *H. cinaedi* reported since 1993. We herein report a case of fetal *H. cinaedi* infection. A 2,257-g female was born via Caesarean section delivery because of fetal distress at 34 weeks' gestation. Her mother showed no signs of illness or diarrhea during pregnancy, although her amniotic fluid was cloudy. The baby excreted mucoid feces immediately after birth. Since *H. cinaedi* was isolated in the amniotic fluid, we concluded it to be the organism that caused the intrauterine infection. Although *H. cinaedi* is rarely isolated in a routine culture, it is important to be aware that *H. cinaedi* can be the causative pathogen for fetal and neonatal infections.

Key words: Gram-negative spirillum, perinatal infection, premature labor, human immunodeficiency virus, neonatal sepsis

Introduction

The *Helicobacter* species is a Gram-negative spirillum that has been isolated from the stomach or intestinal tract of various mammals[1)]. *H. pylori*, a member of this species, is best known as a gastritis pathogen and is, in terms of its global impact, the most important. *H. cinaedi* was first isolated in 1984 from the rectum of homosexual men with proctocolitis and colitis and has been found predominantly in immunocompromised adults, such as those with human immunodeficiency virus (HIV) or immunosuppressed status[2)-4)]. On rare occasions, *H. cinaedi* has also been isolated from the blood and feces of immunocompetent children and adults; indeed, it may be more widespread in the global community than previously believed[5)].

As a reservoir, *H. cinaedi* has been identified in many animals, including rats, cats, dogs, monkeys and hamsters[6)]. Hamsters in particular are known to be a common natural reservoir[7)]. As such, contact with animals is thought to be the most common route of *H. cinaedi* transmission, although a recent report suggests that one outbreak of *H. cinaedi* infection may have been caused by person-to-person contact[8)].

H. cinaedi infection in newborns is rarely reported. The first report of a newborn with sepsis and meningitis caused by *H. cinaedi* was made in 1993[9)]. We herein report a case of fetal *H. cinaedi* infection.

Materials and Methods

Bacteria isolation

Blood culture was performed using a Bact/Alert Microbial Detection System pediatric blood culture vial (Organon Teknika Corp., Durham, NC, USA). The cerebrospinal fluid (CSF), amniotic fluid, and feces were cultured on an agar-plate medium (chocolate, blood, Brucella) and an isolate medium (pleston and HP). Using amniotic fluid, four colonies grew on the HP isolate medium (Eiken Chemical Corp., Taito, Tokyo, Japan) after eight days of incubation. The bacteria obtained from

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the colonies then underwent microbial characterization.

Microbial characterization

The characterization of the isolated bacteria was done by Dr. Yoshiaki Kawamura of Aichi Gakuen University. *H. cinaedi* was confirmed based on its 16S rRNA nucleotide sequence homology[10].

Case

Perinatal period

The patient's mother was transferred to the gynecology department of our hospital due to threatened preterm labor at 32 weeks' gestation. A physician's examination revealed signs of infection in the mother (WBC 12,800/μL, CRP 4.4 mg/dL), and an ultrasound examination showed distension of the fetal intestine. Sudden fetal distress resulted in giving birth to a female infant by Caesarean section at 34 weeks' gestation. Her weight at birth was 2,257-g and her Apgar scores were 8 and 9 at 1 and 5 minutes after birth, respectively. The amniotic fluid was cloudy (meconium-stained). The baby defecated mucus diarrhea (yellow color, five times per day) immediately after birth.

Maternal record

The mother was a 31-year-old woman (gravida 1 para 1). She was healthy and seronegative for human immunodeficiency virus (HIV). She had no diarrheal illness during pregnancy, although she did eat raw chicken at 30 weeks of gestation and also owned a cat. Postpartum, she was administrated intravenous piperacillin for three days followed by oral amoxicillin for seven days. She was afebrile throughout the postpartum course and discharged on post-delivery day 7. The histopathological findings of the placenta revealed necrotizing chorioamnionitis (Blanc stage III). *H. cinaedi* was not detected on the placenta.

Condition after birth

The baby's body temperature was 36.8 ºC, heart rate 160/min, respiratory rate 62/min, and blood pressure 60/30 mmHg. She cried lustily. There was no distension in the anterior fontanelle, and there were no neurological abnormalities. Her respiratory sounds were weak, and she had mild retraction, although no cyanosis was present. Her heart sounds were normal. She had no distension of the abdomen, no hepatomegaly, and no acceleration of bowel sounds.

Laboratory findings

The infant's leukocyte count was 8,900/μL, CRP value was 2.9 mg/dl, and IgM value was 8mg/dl. Her CSF contained 4 leukocytes per mm^3, and bacteria were not detected in a Gram-stained smear of the CSF. *H. cinaedi* was isolated later from the amniotic fluid, although it was not detected in the baby's blood, CSF, or feces.

Clinical course (Fig. 1)

After birth, we thought the focus of the neonate's infection was the intestines, but we could not identify the pathogen from the neonate. The neonate was empirically

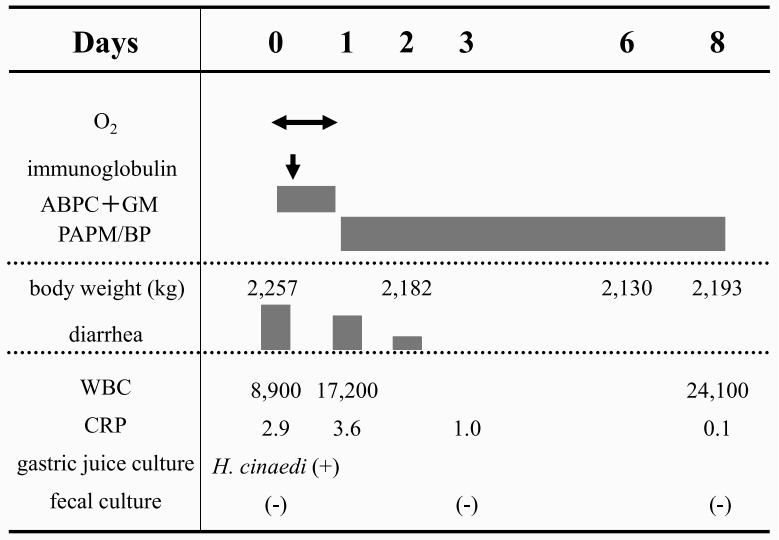

Fig. 1 Clinical course

given intravenous ampicillin (75 mg/kg per day) and gentamicin (5 mg/kg per day) with immunoglobulin. On day 1, a microscopic examination of the amniotic fluid (Fig. 2) and the baby's gastric juice revealed many helicoid Gram-negative bacilli. Accordingly, we suspected infection caused by the genus *Campylobacter*, and intravenous panipenem/betamipron (PAPM/BP) was administered from day 1. Mucous diarrhea disappeared on day 3 and the CRP became negative on day 8. Finally, no meconium excretion was ever observed after birth. The bacteria in the amniotic fluid growth were extremely dysgenic; after eight days of culture, we found only four colonies in the HP isolate medium (Eiken). We identified the bacteria as *H. cinaedi* based on the findings of 16S rRNA sequencing. The patient was treated with antibiotics for 9 days and discharged on day 34 without any sequelae. Her growth and development has been normal for the last 11 years.

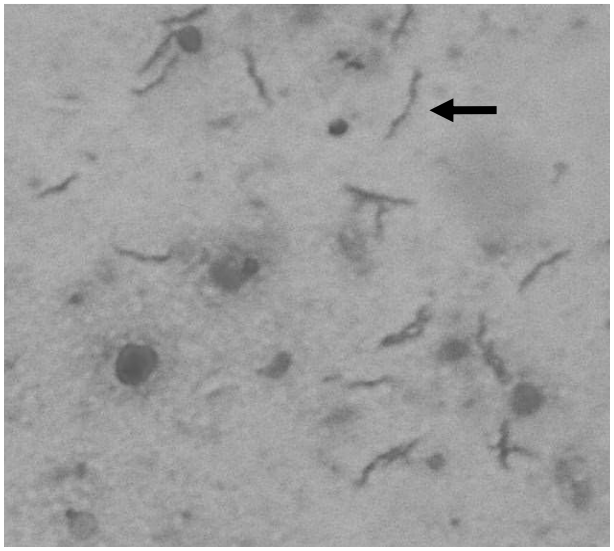

Fig. 2 Microscopic amniotic fluid findings
Arrow indicates Gram-negative spiral bacilli (Gram stain, × 1000).

Surveillance culture

Cultures from the vagina, blood and feces of the mother were negative for *H. cinaedi* and other pathogenic bacteria. *H. cinaedi* was not detected in the pharynx or feces of the mother's cat.

Discussion

In the present case, intrauterine *H. cinaedi* infection was attributed to fetal distress and premature labor. Distension of the fetal intestine and the mucous diarrhea at birth supported our diagnosis of fetal colitis. Intrauterine fetal colitis might also have led to fetal distress. We have two reasons for regarding this case as one of fetal *H. cinaedi* infection: the first is that the birth was via Caesarean section and that diarrhea was noticed immediately after the operation; the second is that chorioamnionitis (Blanc stage III) of the placenta was proven pathologically. *H. cinaedi* was not detected in the pharynx or feces of the mother's pet cat, a species that can host the bacteria. As such, the origin of the *H. cinaedi* is still unclear. Since the mother's bacterial cultures (vagina, blood, feces) were negative except for the amniotic fluid, whether hematogenous transplacental infection or ascending transamniotic infection had occurred could not be determined.

H. cinaedi was not isolated from the baby's feces or blood, possibly because of the difficulty growing *H. cinaedi* using conventional laboratory cultivation techniques. It is known that *H. cinaedi* is extremely dysgenic and can be overlooked in clinical specimens[4]. In fact, after eight days of culture, we identified only four colonies in the HP isolate medium (Eiken). *H. cinaedi*, as well as other *Helicobacter* genera, are microaerophiles (5% O_2). In addition, *H. cinaedi* needs to be grown in the presence of hydrogen (5% to 10% H_2)[2]. In Japan, however, the *Campylobacter* genus is generally isolated in a microaerophile culture that contains no hydrogen. Furthermore, Skirrow's medium, a common culture medium, contains polymyxin B, which kills some of the *Helicobacter* genera. *H. cinaedi*, therefore, might not grow under such culturing conditions.

Most antibiotics are effective in treating *H. cinaedi*. It has been reported that penicillin, tetracycline, and aminoglycoside have better therapeutic effects than cefem and fluoroquinolones[4]. Due to its tendency to recur, the reported duration of antibiotherapy for *H. cinaedi* septicemia is more than two weeks[6]. In our case, the patient was first given intravenous ampicillin and gentamaicin. These medications, however, were discontinued, and she was given intravenous panipenem/betamipron (PAPM/BP) one day after birth because we suspected *Campylobacter* infection. She was given PAPM/BP for one week and recovered without any sequelae, and there was no recurrence after antibiotic treatment.

H. cinaedi infection in newborns as well as in fetuses is rarely reported. There is one report of neonatal *H. cinaedi* infection manifesting with meningitis and sepsis[9]. In

contrast to our case, it originated via spontaneous vaginal delivery at term. The female baby showed symptoms six days after birth. Her clinical course was relatively benign, despite having 10,000 leukocytes in the CSF before the administration of antibiotics. Her only presenting symptoms were a mild fever and irritability. Her 19-day hospital course was uncomplicated, and at the time of hospital discharge, she had a normal neurological exam. Her mother was healthy and HIV seronegative, but the mother had been exposed to hamsters during the first and second trimesters of her pregnancy. The source of the bacteria was thought to be the hamsters, which were pets in her home. There is another report of intrauterine *H. cinaedi* infection, which might have caused preterm birth and neonatal sepsis[11]. The case was a 446-g male baby born at 22 weeks of gestation via vaginal delivery, in contrast to the present case of Caesarean delivery. There were no symptoms of infection, such as body temperature changes, tachycardia, or diarrhea, but the baby died due uncontrollable hyperglycemia and ketoacidosis at 15 days of life. His mother was healthy and HIV seronegative. Cultures from the vagina, blood, and feces of his mother were negative for *H. cinaedi*; therefore, the origin of the bacteria in this case was unclear. Given the present and previous findings, *H. cinaedi* seems to cause intrauterine infection during pregnancy and may lead to preterm labor.

As mentioned above, it is difficult to isolate *H. cinaedi* in a routine culture. As such, perinatal *H. cinaedi* infections, including neonatal and fetal infections, run the risk of being overlooked. It is therefore important to be aware that *H. cinaedi* may be a causative pathogen for fetal and neonatal infections. In recent years, a serodiagnosis technique for *H. cinaedi* has been developed using an enzyme-linked immunosorbent assay (ELISA)[10]. We expect this will allow for earlier detection and better antibiotic selection.

Conclusion

H. cinaedi should be added to the list of rare organisms causing intrauterine infection, and fetal colitis should be suspected when a neonate has diarrhea immediately after birth in order to institute a prompt and suitable treatment.

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