THE MEDICAL BULLETIN OF
SISLI ETFAL HOSPITAL

DOI: 10.14744/SEMB.2018.22605
Med Bull Sisli Etfal Hosp 2020;54(1):113–116

Case Report

Congenital Syphilis Presenting with Prenatal Bowel Hyperechogenicity and Necrotizing

Muhittin Çelik, Ali Bülbül, Sinan Uslu

Department of Pediatrics, Division of Neonatology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey

Abstract

Congenital syphilis is a severe disease that arises from the vertical transmission of Treponema pallidum. Clinical findings are related to the pregnancy stage, fetal gestational week, maternal treatment and fetal immunologic response. Prematurity, low birth weight, nonimmune hydrops fetalis, necrotizing enterecolitis, hepatomegaly, skin eruptions, thrombocytopenia, hemolytic anemia and fever can be detected in the symptomatic newborn. Postnatal respiratory insufficiency, hepatomegaly, anemia and thrombocytopenia were detected in a baby who was born at the 29th week of gestation, weighing 1.160 g and followed due to intestinal hyperechogenicity from the second trimester. Her and her mother's Venereal Disease Research Laboratory titers were positive, confirming test Treponema pallidum hemagglutination was reactive. After penicillin was administered for 10 days, anemia, and thrombocytopenia were regressed. In the 15th day of life, findings of perforated necrotising enterocolitis (NEC) suddenly appeared. The operation was performed due to NEC for three times but nonresponsive laboratory and clinical findings and died in the 54th day of life. We assumed that syphilis is the cause of both bowel hyperechogenicity and necrotising enterocolitis.

Keywords: Bowel hyperechogenicity; congenital syphilis; necrotising enterocolitis; prematurity.

Please cite this article as "Çelik M, Bülbül A, Uslu S. Congenital Syphilis Presenting with Prenatal Bowel Hyperechogenicity and Necrotizing. Med Bull Sisli Etfal Hosp 2020;54(1):113–116".

Congenital syphilis (CS) is a severe infectious disease that arises from vertical transmission of treponema pallidum via the placenta from untreated pregnant women and may result in mortality of the 40% in the postnatal period.[1,2] Although all the organs are affected by this spirochete, the effects on the fetus range from diffuse organ involvement to nonspecific presenting signs and symptoms. More than 50% of all infected infants are asymptomatic at birth. Clinical manifestations of CS can be classified as follows: gestational (stillbirth, prematurity, and small for gestational age), reticuloendothelial (anemia, white blood cell count abnormalities, and/or thrombocytopenia may result in hepatomegaly with or without spleen involvement), mucocutaneous (rhinitis, dermal rash), skeletal (symmetrical long bone lesions, metaphyseal lesions, osteochondritis, osteitis, dactylitis), neurologic (acute meningitis, hydrocephalus, cerebral infarcts), and ocular (glaucoma, chorioretinitis.[3,4] CS is continuing to be a public health burden in both developed, especially in developing countries and is still a severe cause of infant mortality. Thus, prenatal screening and penicillin treatment are strongly recommended for the prevention of the CS.[5]

Address for correspondence: Muhittin Çelik, MD. Sisli Hamidiye Etfal Egitim ve Arastirma Hastanesi, Cocuk Sagligi ve Hastaliklari Anabilim Dali, Neonatoloji Bilim Dali, Istanbul, Turkey
Phone: +90 533 680 73 76 **E-mail:** mehdincelik@hotmail.com

Submitted Date: August 27, 2018 **Accepted Date:** September 12, 2018 **Available Online Date:** March 25, 2020

Case Report

A female infant with birth weight of 1.160 g (50 percentile) was born to a 21 years old mother via cesarean section at 29 weeks' gestation because of fetal distress. The prenatal course was benign except for fetal bowel hyperechogenicity noted at 16th gestational week. Since neither hemorrhage nor any abnormality was detected, it was followed up. More investigations [Toxoplasmosis, other (parvovirus B19, hepatitis B virus, hepatitis C virus, human immunodeficiency virus), rubella, cytomegalovirus (CMV), and herpes serology (TORCH) and chromosomal analysis] had not done for fetal bowel hyperechogenicity. After initial stabilization at the delivery room, she was admitted to the neonatal intensive care unit because of respiratory distress, very low birth weight, and distended abdomen. She was pale and had hepatomegaly. The other physical and neurologic examinations were unremarkable. Respiratory distress was managed with nasal continuous positive airway pressure. A septic evaluation was performed, and empiric ampicillin and gentamicin treatment were started. A complete blood count revealed a hemoglobin level of 9 g/dl, platelet count of 79.000/mm^3 and peripheric smear revealed hemolysis findings. Her blood biochemistry was normal, but transaminase levels were mildly elevated (aspartate aminotransferase 182 U/L, alanine aminotransferase 105 U/L). There was no ABO incompatibility and direct Coombs test was negative. All the culture samples were sterile. TORCH was negative except for high serum titers of VDRL (Venereal Disease Research Laboratory), which was 1/16. Maternal VDRL titers were as high as 1/1280, without previous any clinical findings. Treponema pallidum hemagglutination (TPHA) as a confirmatory test was also reactive. The further evaluation of the infant for other organ involvements, including cerebrospinal fluid analysis (VDRL negative and cells not detected), ophthalmic examination and long bone radiographs, neuroimaging, abdominal ultrasonography, was unremarkable except hepatomegaly and mild ascites. A full 10-day course of penicillin was administered. In the following days, hematological abnormalities were gradually resolved.

By the second week of life, while the infant was clinical stable, on full enteral feeding (breast milk) and gaining weight, she suddenly deteriorated with the signs of bilious vomiting and abdominal distention. The abdominal radiograph showed subdiaphragmatic free air and pneumatosis intestinalis, which consisted of perforated NEC (Fig. 1). Surgical exploration of the abdomen revealed ileal necrosis with perforation. After resection of necrotic sections, end-to-end anastomosis was done. Pathological examination of bowel revealed transmural necrosis. Subsequently, she undergone two more exploratory laparotomies because of serial radiography indicated persistent ileus, and attempts to restart feeds failed. Unfortunately, the infant died on day 54.

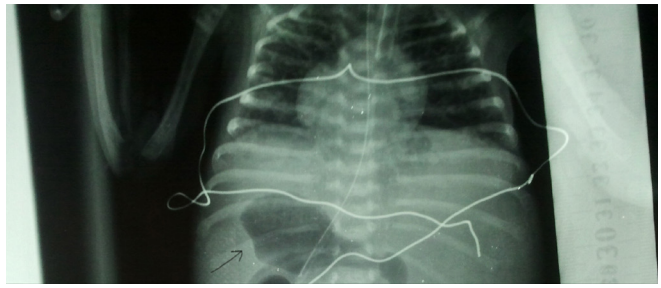

Figure 1. Postoperative supine plain X-ray of the abdomen shows that a specific distension of small bowel loops (Arrows).

Written consent for publication of this case report and image were obtained from the parents of the patient.

Discussion

This case was diagnosed CS based on clinical findings and confirmatory serological tests. Demonstration of T. Pallidum by darkfield microscopy or fluorescent antibody stains in specimens was not possible due to limited facilities. Detection of fetal echogenic bowel needs to a further evaluation in case of coexisting abnormalities, but because it was not done so, the diagnosis is delayed. The infection may cause echogenic bowel by direct damage to the fetal intestine or as a result of the inflammatory response. This case suggests that prenatal-onset inflammation of bowel may be a contributing factor in the development of NEC.

The possibility of vertical transmission of Treponema Pallidum from pregnant women to the fetus is possible in every week of pregnancy in which is high in late weeks. Transmission rates of maternal primary and secondary infection are 60% and 90%, respectively, but it is less than 10% in latent infection. Clinical manifestations of syphilis can be seen in the early stage (first two year) or late stage (after two years).[1,4] All fetal organ systems can be affected by widespread inflammation due to spirochetes. Prematurity, low birth weight, nonimmune hydrops fetalis, necrotizing enterocolitis, hepatomegaly, jaundice, high transaminase levels, skin eruptions, bone deformities, thrombocytopenia, hemolytic anemia, lymphadenopathy, central nervous system abnormalities and fever can be detected in symptomatic newborn. Late stage findings are related to bone, teeth and central nervous system due to chronic inflammation.[4] In our case, prematurity, hepatomegaly, thrombocytopenia and anemia as findings are correlated with literature.

Diagnosis of CS is multidisciplinary and includes a physical examination, radiological tests, serological tests and also microbiological findings. It is difficult to show bacte-

rial pathogens directly; therefore, such nontreponemal tests like VDRL and Rapid Plasma Reagin (RPR) are highly preferable. For certain diagnoses of non-treponemal tests, it must be confirmed by Fluorescent Treponemal Antibody Absorption Test (FTA-ABS) and microhemagglutination test Treponema Pallidum (MHA-TP).[3,4] In our case, hepatomegaly, titers of 1/16 seropositivity of VDRL, 1/1280 maternal seropositivity of VDRL are all send us to suspect from congenital syphilis. Diagnosis is confirmed by TPHA positivity and ensured with no maternal treatment for syphilis. According to WHO, the Centers for Disease Control and Prevention (CDC) guideline, penicillin regimen for 10 days is the first choice of antibiotics.[5,6] Clinical response to this regimen and improvement of laboratory findings were totally successful.

Fetal echogenic bowel is a nonspecific finding that is defined similar to or more than bone echogenity seen in ultrasound and is detected 0.4-1/100 of pregnant women.[7] Most common causes are swallowed blood, aneuploidies (trisomy 21,13 and 18), cystic fibrosis, growth retardation, intrauterine infections (TORCH, parvovirus) and gastrointestinal obstructions (anatomic or functional).[8] Narducci et al. stated that the increase of bowel echogenicity might be related to congenital syphilis in pregnant women with seropositivity.[9] In the presented case, the presence of prenatal bowel hyperechogenicity seems to be the first finding of CS, but probably due to the isolated finding, a further investigation had not been conducted.

The host immune response begins with lesional infiltration of polymorphonuclear leukocytes, which are soon replaced by T lymphocytes.[10] Compared with peripheral blood, lesional fluids were enriched for CD4+ and CD8+ T cells, activated monocytes, macrophages, and dendritic cells. Because Treponema spp. enter the fetal bloodstream directly, the primary stage of infection is completely bypassed. There is no chance and no local lymphadenopathy. Instead, the liver, the immediate target of the invasion, is flooded with an organism that than penetrate all the other organs and tissues of the body to a lesser degree. Necrosis follows fairly regularly in bone but only rarely in other tissues. Extramedullary hematopoiesis in the liver, spleen, kidneys, and other organs can be seen.[11]

Necrotizing enterocolitis is continued to be the first reason in premature infants for gastrointestinal system sourced mortality. Prematurity, formula feeding and colonizing with nonsuitable microorganisms can be counted as reasons. It is believed to be a result of translocation of microorganism through the weakened gastrointestinal barriers with destructive and overactive immune responses in the perinatal period.[12] In recent years, it is believed that the process firstly initiates in the prenatal period and trigger an immune response by hematogenous dissemination of gastrointestinal and vaginal microorganisms or swallowing amniotic fluid through the gastrointestinal system.[13] Shorta et al.[14] reported two cases of CS among a group of term infants with developed NEC. It is thought that fetal echogenic bowel may be a result of activation of the immune system of the fetus with inflammation of intestinal wall by intrauterine spirochete migration, necrosis of intestinal layers by immune mediators and cell infiltration. Thus, these changes may be a contributing factor for development of NEC. Penicillin treatment may give rise to the release of endotoxin-like compounds from spirochetes, and subsequently increase in inflammation. However, all of these points needs further research.

In conclusion, fetal echogenic bowel needs to be carefully evaluated for the appearance of additional findings on following–up, and basic screening tests should be carried out. It seems like intestinal wall invasion by spirochetes or inflammatory response during the intrauterine period leads to gastrointestinal findings that will develop later.

Disclosures

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – M.Ç.; Design – M.Ç., A.B.; Supervision – S.U.; Materials – M.Ç.; Data collection &/or processing – M.Ç.; Analysis and/or interpretation – A.B., S.U.; Literature search – M.Ç.; Writing – M.Ç.; Critical review – A.B.

References

1. Boyer SG, Boyer KM. Update on TORCH infections in the newborn infant. Newborn Infant Nurs Rev 2004;4:70–80.
2. Rawstron S. Treponema pallidum (Syphilis). In: Long S, Pickering L, Prober C, editors. Principles and Practice of Pediatric Infectious Disease. NewYork: Churchill-Livingston; 2003. p. 954–65.
3. Can E, Bülbül A, Cömert S, Bolat F, Okan F, Nuhoğlu A. Congenital Syphilis Presenting With Skin Lesions: A Case Report. Çocuk Enf Derg 2009;3:31–4.
4. Follett T, Clarke DF. Resurgence of congenital syphilis: diagnosis and treatment. Neonatal Netw 2011;30:320–8.
5. World Health Organization. Investment case for eliminating mother-to-child transmission of syphilis promoting better maternal and child health and stronger health systems. Available at: https://www.who.int/reproductivehealth/publications/rtis/9789241504348/en/. Accessed Jan 28, 2020.
6. Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015.

MMWR Recomm Rep 2015;64:1–37.
7. Al-Kouatly HB, Chasen ST, Streltzoff J, Chervenak FA. The clinical significance of fetal echogenic bowel. Am J Obstet Gynecol 2001;185:1035–8.
8. Simon-Bouy B, Satre V, Ferec C, Malinge MC, Girodon E, Denamur E, et al. Hyperechogenic fetal bowel: a large French collaborative study of 682 cases. Am J Med Genet A 2003;121A:209–13.
9. Narducci F, Switala I, Rajabally R, Decocq J, Delahousse G. Syphilis maternelle et congénitale [Maternal and congenital syphilis]. J Gynecol Obstet Biol Reprod (Paris) 1998;27:150–60.
10. Baker-Zander S, Sell S. A histopathologic and immunologic study of the course of syphilis in the experimentally infected rabbit. Demonstration of long-lasting cellular immunity. Am J Pathol 1980;101:387–414.
11. Sanchez PJ, Patterson JC, Ahmed A. Toxoplasmosis, syphilis, malaria, and tuberculosis. In: Gleason CA, Devaskar SU, editors. Avery's Diseases of the newborn. 9th ed. Philadelphia: Elsevir Saunders; 2012. p. 513–37.
12. Grishin A, Bowling J, Bell B, Wang J, Ford HR. Roles of nitric oxide and intestinal microbiota in the pathogenesis of necrotizing enterocolitis. J Pediatr Surg 2016;51:13–7.
13. Neu J. Preterm infant nutrition, gut bacteria, and necrotizing enterocolitis. Curr Opin Clin Nutr Metab Care 2015;18:285–8.
14. Short SS, Papillon S, Berel D, Ford HR, Frykman PK, Kawaguchi A. Late onset of necrotizing enterocolitis in the full-term infant is associated with increased mortality: results from a two-center analysis. J Pediatr Surg 2014;49:950–3.