

# A Cytomegalovirus Infection Case Mimicking Total Parenteral Nutrition Associated Cholestasis

## Total Parenteral Nütrisyona İlişkili Kolestaza Benzeyen Bir Sitomegalovirus Enfeksiyonu Vakası

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### Öz

Sitomegalovirus (CMV) erken süt çocukluğu döneminde transplasental geçiş gösteren en sık karşılaşılan virüslerden biridir. Ve non-herediter sensörinöral işitme kaybı nedenleri arasında en sık karşılaşılan enfeksiyöz sebeptir. Burada 29 haftalık aşırı düşük doğum ağırlıklı (ADDA) 460 gr TPN ilişkili kolestaza benzeyen CMV enfeksiyonu geçiren olguyu sunmaktayız. Uzun süre TPN ile beslenen ADDA prematüre bebekte genellikle kolestaz ilk önce TPN ile ilişkili olduğu düşünülür. Direkt hiperbilirubinemi ve kolestaz yeni doğan döneminde sık karşılaşılan problemlerden biridir. Özellikle bu durumlar genellikle sepsis, TPN alımı, doğuştan metabolik hastalıklar ve diğer sebeplerle ilişkili olduğu düşünülür. Özellikle ADDA infantlarda ve uzun süre TPN ile beslenen bebeklerde CMV enfeksiyonları aklımızın bir köşesinde bulunmalıdır.

**Anahtar Kelimeler:** Kolestaz, CMV enfeksiyonları, TPN

### Abstract

A case of cytomegalovirus infection mimicking total parenteral nutrition associated. Congenital cytomegalovirus (CMV) infection is the most common infection that passes through transplacentally in the early infancy period and is the most common infectious cause of the nonhereditary sensorineural hearing loss. We know that most of these cases were asymptomatic in the neonatal period. Especially among the extremely low birth weight infants, CMV prevalence is not known. We present a 29 weeks old 460 gr extremely low birth weight (ELBW) infant with congenital CMV infection mimicking total parenteral nutrition (TPN) associated cholestasis. Usually, when we see the cholestasis in the extremely low birth weight infant feeding with long time TPN, we think that it is associated with TPN. Direct hyperbilirubinemia and cholestasis are the common situations in the newborn period. Especially this is considered to be associated with sepsis, TPN, inborn errors of metabolism and other causes. CMV-associated cholestasis should be kept in mind, especially in cases of premature infants with cholestasis and extremely low birth weight infants have been fed for a long time TPN.

**Keywords:** Cholestasis, CMV infections, TPN

### INTRODUCTION

Congenital CMV infection may cause a lot of clinical signs like intrauterine death, neonatal death, growth restriction, thrombocytopenia, neurological abnormalities, developmental delay, hepatitis, retinitis, hearing loss etc (1). During pregnancy CMV infection can be the form of primary, re activation or re-infection. Virus can be transmitted to anyone by saliva, urine, sexual contact, breastfeeding, solid organ transplantation and vertically. Non primary infections are more common than primary infections and seem to be associated with more neurological disabilities (2). Both primary and non- primary infections may be usually asymptotically in the healthy individuals or pregnant women. Fetus and immunocompromised individuals are severely affected by CMV infections. Prevalence of congenital CMV infection is estimated

to range between 0,2% and 2% ( 3). In country that higher maternal CMV seroprevalence, it is more than this range (4). CMV is most commonly defined virus in the preterm baby less than 32 weeks gestational age and is mainly acquired from breast milk with CMV seropositive mother (5). Postnatal acquired CMV infection is usually asymptomatic. Long term sequelae of postnatal CMV infection have less common neurologic impairment according to the congenital CMV. CMV infection is diagnosed by viral culture or real time polymerase chain reaction (rtPCR) of urine, blood or saliva. The treatment of congenital CMV infections is controversial. Although there is no clinical study with large series about congenital CMV hepatitis, it can be lethally. So we present a ELBW infant that has CMV hepatitis for emphasize the difficulties of diagnosis at the congenital CMV

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infection between perinatally acquired CMV infection.

## CASE

A preterm, extremely low birth weight, growth restricted baby who birth weight was 460 gram (below 10th p), delivered by emergency caesarian section for fetal distress and prolonged rupture of fetal membranes at 29 weeks gestational age. She had no spontaneous breathing at birth and APGAR scores were 2 in one minute and 3 in five minutes. Length, weight and head circumference were 27 cm, 460 gr and 22,5cm, respectively. All of them were below 10th percentile. After the delivery room stabilization, she was admitted to the neonatal intensive care unit. After the surfactant administration and catheterization of the umbilical artery and vein, fluid resuscitation was started. At the postnatal first day minimal enteral nutrition was started by breast milk. But because of abdominal distension and asymmetric IUGR was not achieved nutrition more than minimal enteral nutrition for first 21 days. Total parenteral nutrition (TPN) was continued until day of 39. Until the end of the hospital discharge, she had no proven bacterial sepsis. Several types of antibiotics were used because of suspected sepsis. Erythrocyte suspension was given 3 times. These blood products were irradiated and passed through leukocyte filter. Liver enzymes were increased 3-fold. Initially it was thought to be associated with TPN cholestasis. When cholestasis was apparently seen, tests were planned for etiology of cholestasis. At the follow-up maximum values of alanine transaminase (ALT), aspartate aminotransferase (AST), Gamma-glutamyl transferase (GGT), total bilirubin, direct bilirubin were 327 U/L, 309 U/L, 288 U/L, 11.42 mg/dl, 7.98 mg/dl respectively. Abdominal USG, reducing substances in urine, alpha 1 antitrypsin level, tandem mass spectrometry and urine organic acid profile were normal. Urine culture and blood culture were negative. Thyroid function tests and cystic fibrosis stripe mutation analyze were normal. CMV Ig M and CMV total antibodies were positive and at the postnatal 84th day CMV- DNA rtPCR was 55700 copies /ml from blood sample. No calcification was observed on the cranial computed tomography. Eye examination was not revealed chorioretinitis. Newborn hearing screening test performed by ABR was normal. In Our patient's value of the avidity is slightly higher in 63th of life. Maternal CMV Ig M antibody was negative. Maternal CMV Ig G and avidity were positive highly at the postnatal 70th day. Because of not enough

data about pregnancy, patient's CMV condition was not understood. Is it congenital CMV or postnatal CMV? At the follow-up the values of liver enzymes and bilirubin had begun to fall without any medication. After the 125 days of hospital stay the patient was discharged to come to follow. At the follow-up the patient's value of CMV DNA was negative.

## DISCUSSION

With the advances in technology in NICU, the usage of TPN increased so the survival rate of premature infants increased significantly. Morbidity associated with prematurity increased. Cholestasis and abnormal liver function tests became observed in almost ELBW infants. TPN associated cholestasis has received the most attention due to the liver damage sustained. TPN associated cholestasis became to very important issue in neonatologist.

TPN associated cholestasis is defined that direct bilirubin level of >2.0 mg/dl following a prolonged course of TPN (>2 weeks) and other causes, including surgical and metabolic diseases, have been ruled out. If other specific causes of liver injury are excluded, this disorder is termed parenteral nutrition-associated liver disease or parenteral nutrition-associated cholestasis. Research has revealed that in premature infants, particularly those with very low birth weights, the incidence of TPN associated cholestasis is as high as 50% (6). The cholestasis and liver test abnormalities tend to advance after the parenteral therapy is discontinued, but may continue in some cases. Among infants who developed TPN associated cholestasis in a neonatal intensive care unit, and had conjugated bilirubin >2 mg/dL before two months of age, 17 percent died or went on to liver transplantation (8). Among those with a maximum conjugated bilirubin >10 mg/dL, 38 percent died or went on to liver transplantation.

CMV is a virus seen in worldwide. CMV infections can affect any part of body. The infection is usually asymptotically in healthy people. Population based studies showed that CMV seroprevalence is varied from 45% to 77% in different societies (7). Most newborns with congenital CMV are asymptomatic at birth but as many as 15 percent will develop progressive hearing loss.

There is no wide case series about congenital CMV hepatitis in the literature. One article suggests that congenital CMV hepatitis is a self limited illness, it has favorable outcome and the treatment is not necessary (9). The treatment issue is controversial.

Some authors advocate treatment by the viral load levels (10).

Our patient had received long term TPN and was ELBW infant. Initially we considered that this was a TPN associated cholestasis as a lot of neonatologists. But the situation became more complex; we started thinking about differential diagnosis of etiology of neonatal cholestasis. Majority of congenital CMV infections is considered asymptomatic, urine rt-PCR CMV DNA may be useful first 3 weeks of life particularly ELBW infants. Because these infants cannot achieve full enteral nutrition for a long time. We follow-up clinically the our patient with no treatment. Most of this infants have developed clinical and laboratory findings of cholestasis. The lack of our case was not made liver biopsy because of extremely low birth weight.

Especially neonatal cholestasis was seen most of the ELBW infants. Therefore if the ELBW infant has cholestasis, other causes of neonatal cholestasis must be excluded. CMV infection should be in a particular corner of mind. We suggest that CMV should be investigated for suspicion of the human milk transmission. Particularly ELBW infants should be done urine or blood rt-PCR analyzes for CMV in the first 3 weeks of life.

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