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SEVERE HYPERTRANSAMINASEMIA DURING ASYMPTOMATIC COVID-19 INFECTION

Asemptomatik COVID-19 Enfeksiyonu Sırasında Şiddetli Hipertransaminazemi

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ABSTRACT

Although the mechanism of Coronavirus disease 2019 (COVID-19) related liver damage in critically ill children is not well defined yet, it is thought to be related to the hyperinflammation phase (cytokine release). Here, we present a 40-day-old asymptomatic patient with isolated severe liver enzyme elevation associated with COVID-19. A 40-day-old female was admitted to our emergency department for screening after her mother was diagnosed with COVID-19. The patient's vital signs and physical examination were normal on admission. Laboratory findings showed alterations in hepatic function measures. Transaminase levels increased up to 11-fold and 5-fold the upper reference limit for aspartate aminotransferase (AST) and alanine aminotransferase (ALT) on day 6 of admission. No direct bilirubin elevation or coagulopathy was detected, and also the creatine kinase (CK) level was within the normal range. Microbial investigations excluded a superimposed congenital or acquired infection. Ultrasound examination (day 6) found only altered echogenicity in the liver. During the following weeks, AST and ALT levels decreased and resolved to normal range after 14 days from the first biochemical evaluation on admission. Pediatric patients with asymptomatic or mildly symptomatic COVID-19 infection may have severe hepatic enzyme elevation, with or without hepatic failure. A variety of mechanisms, such as direct virus infection may cause liver injury in patients with COVID-19. Clinicians should pay more attention to the occurrence of liver damage in COVID-19 infection and analyze comprehensively the pathogenesis of liver injury in management strategy.

Keywords: COVID-19, Emergency department, Hypertransaminasemia, Pediatric

ÖZET

Kritik hasta çocuklarda COVID-19'a bağlı karaciğer hasarının mekanizması henüz tam olarak tanımlanmamış olsa da hiperinflamasyon aşamasıyla (sitokin salınımı) ilişkili olduğu düşünülmektedir. Burada, COVID-19'a bağlı izole ciddi karaciğer enzim yüksekliği olan 40 günlük asemptomatik bir hastayı sunuyoruz.40 günlük kız hasta, annesine COVID-19 tanısı konulduktan sonra çocuk acil servise tarama amacıyla başvurdu. Başvuru sırasında hastanın vital bulguları ve fizik muayenesi normaldi. Laboratuvar bulguları hepatik fonksiyon ölçümlerinde değişiklikler gösterdi. Başvurunun 6. gününde transaminaz düzeyleri aspartat aminotransferaz (AST) ve alanin aminotransferaz (ALT) için üst referans sınırının 11 ve 5 katına kadar yükseldi. Direkt bilirubin yüksekliği veya koagülopati saptanmadı, ayrıca kreatin kinaz (CK) düzeyi normal sınırlardaydı. Diğer konjenital veya edinilmiş enfeksiyonlar dışlandı. Abdomen ultrasonunda (6. gün) karaciğer ekojenitenitesinde artış saptandı. Takip eden haftalarda AST, ALT düzeyleri düştü ve başvuru sırasındaki ilk biyokimyasal değerlendirmeden 14 gün sonra normal aralığa geriledi. Asemptomatik veya hafif semptomatik COVID-19 enfeksiyonu olan pediatrik hastalarda, karaciğer yetmezliği olsun ya da olmasın, ciddi hepatik enzim yüksekliği görülebilir. COVID-19 hastalarında karaciğer hasarına, doğrudan virüs enfeksiyonu gibi çeşitli mekanizmalar neden olabilir. Klinisyenlerin, COVID-19 enfeksiyonunda karaciğer hasarı oluşumuna daha fazla dikkat etmesi ve tedavi stratejisinde karaciğer hasarının patogenezini kapsamlı bir şekilde analiz etmesi gerekmektedir.

Anahtar Kelimeler: Acil servis, COVID-19, Hipertransaminazemi, Pediatri

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a complex multi-system disease that affects several human systems, mainly respiratory tract infection, also affecting the liver. In critically ill children, COVID-19-related elevated transaminases with or without liver failure have been reported in 60% of the case series (Tian et al, 2020). Although the mechanism of COVID-19-related liver damage in critically ill children is not well defined yet, it is thought to be related to the hyperinflammation phase (cytokine release) (Zippi et al, 2020). Here, we present a 40-day-old asymptomatic patient with isolated severe liver enzyme elevation associated with COVID-19.

CASE

A 40-day-old girl was admitted to our emergency department for screening after her mother was diagnosed with COVID-19. There were no features in the antenatal, perinatal, and neonatal periods, her development was completely normal. Her mother was taking only therapeutic doses of paracetamol for fever. The patient's vital signs and physical examination were normal on admission. COVID-19 infection was confirmed by a positive polymerase chain reaction on nasopharyngeal swabs. Chest X-ray examination was negative. Laboratory findings showed alterations in hepatic function measures. Transaminase levels increased up to 11-fold and 5-fold the upper reference limit for aspartate aminotransferase (AST) and alanine aminotransferase (ALT) on day 6 of admission to the pediatric emergency department, respectively. Gamma-glutamyl transferase (GGT) was 71 U/mL (normal range <204), alkaline phosphatase was 471 IU/L (normal range 60-321). No direct bilirubin elevation or coagulopathy was detected, and also the creatine kinase (CK) level was within the normal range. White blood cell count, and electrolytes were also normal. Microbial investigations excluded a superimposed congenital or acquired infection (HBV, HCV, EBV, CMV, Toxoplasma, and other viral pathogens). Ultrasound examination (day 6) found only altered echogenicity in the liver. During the following weeks, AST and, ALT levels decreased and resolved to normal range after 14 days from the first biochemical evaluation on admission.

DISCUSSION

COVID-19 has a variety of clinical manifestations, with acute respiratory symptoms being the predominant symptoms (Feng et al, 2020). It has been shown to affect affect the extrapulmonary organs, including liver damage (Tian et al, 2020). The incidence of liver injury in patients with severe or critical COVID-19 disease is highly prevalent. Liver damage as the first finding in COVID-19 patients was uncommon, so herein, we report a pediatric case of acute liver injury in the course of COVID-19 asymptomatic infection, notable for the severe increase in serum aminotransferases without liver failure. The exact pathophysiological mechanisms of liver injury during COVID-19 infection remain uncertain (Sgouropoulou et al, 2021). Additional it remains unclear whether COVID-19 has a direct toxic effect on liver function. Several different mechanisms are implicated. It has been reported in previous studies that angiotensin-converting enzyme 2 (ACE 2), which is the receptor of COVID-19 and is mainly found in the lungs, is also widely expressed in liver cells (Tian et al, 2020). So, these might suggest that COVID-19 might directly bind to hepatocytes expressing ACE2 resulting in hepatocyte injury. According to the report by Chai X and Gaun GW et al, bile duct epithelial cells found the ACE2 receptor at a concentration 20 times higher than hepatocytes and suggested that COVID-19 infection may also cause bile duct epithelial cell damage (Chai et al, 2020; Guan et al, 2020). The other mechanisms of liver damage due to COVID-19 are an antibody-dependent enhancement, systemic immune response syndrome and cytokine storms, ischemia and hypoxia reperfusion injury, drug hepatotoxicity, recurrence or aggravation of existing liver disease. Antiviral treatments were recommended during the COVID-19 infection, but many patients were treated with antipyretics, primarily paracetamol (Feng G et al, 2020). As is known, paracetamol can cause significant liver damage or liver failure when it exceeds the toxic dose. Our patient's mother had taken paracetamol as needed during COVID-19 infection and had not reached the toxic dose. The possibility that the liver enzyme elevation was

caused by paracetamol taken through breast milk was also considered to be very low. Few pediatric cases have been reported showing the development of liver damage during COVID-19 infection. In the pediatric case series of Zhou et al., it was reported that mild hypertransaminasemia may be common during acute infection in children aged 0-3 years (Zhou et al, 2020). Palpacelli et al. reported that a case of of liver involvement with transient severe hypertransaminasemia in 30-day-old baby girl with mild COVID-19 infection (Palpacelli et al, 2021). Similarly, transient liver injury without hepatic dysfunction has been reported during a mild SARS-CoV-2 infection in a 5-year-old child (Sgouropoulou et al, 2021). In our case, other liver function tests were preserved despite the findings of severe AST elevation and moderate ALT elevation: albumin, cholestasis parameters (such as bilirubin, GGT, and alkaline phosphatase levels), and coagulation test were always within normal limits for age. We detected incidentally severe liver enzyme elevation in our patient who was positive for a COVID-19 swap scan. Inflammation parameters were normal (absolute neutrophil count, C-reactive protein, immature granulocyte, etc.). There was no indication for hospitalization. There was no need for oxygen support or other medical treatment. These findings indicate that hepatocyte damage was likely independent of immune system involvement, cytokine storm, or hypoxia. Direct viral damage is likely a key contributor to the occurrence of temporary severe liver damage. It is evident that further research is essential to deepen our understanding of this pathophysiological process.

CONCLUSION

Pediatric patients with asymptomatic or mildly symptomatic COVID-19 infection may have severe hepatic enzyme elevation, with or without hepatic failure. In COVID-19 patients, liver damage may result from various mechanisms, including direct viral infection. Clinicians should be aware that liver damage may occur in COVID-19 infection and should incorporate a comprehensive analysis of the liver damage pathogenesis into their treatment strategy.

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