

Diarrhea and Acute Hepatitis in a Two-Month-Old Infant. A Parvovirus B19 infection?

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Abstract

Parvovirus B19 is a single stranded DNA virus whose infection can run in an asymptomatic form or with a wide spectrum of clinical manifestations that includes benign erythema infectiosum, arthropathy, mostly transient aplastic anemia, fetal hydrops.

Acute and chronic hepatitis without a cholestatic component have been reported as isolated cases while with regards to teenagers only one case reported acute hepatitis with cholestasis.

In one patient, severe liver damage required the liver transplantation.

The mechanism underlying hepatic infection involvement is not known. Some authors have shown a better prognosis of the forms of hepatitis associated with acute Parvovirus B19 infection in children aged under 5 years in which lower serum bilirubin values and a more rapid recovery of liver function are observed.

Here is the case of a two-month-old infant with a sepsis like clinical picture, fever, diarrhea for 20 days, dehydration and severe metabolic acidosis, acute hepatitis with hypertransaminasemia without cholestasis. The culture tests (blood, urine, feces), the parasitological examination of the stool sample, the serodiagnosis for salmonella, shigella, brucella, campylobacter, yersinia, the research of the Clostridium toxin, the serology for the main hepatotropic viruses (A, B, C), EBV and TORCH and the search for antigens for rotavirus and adenovirus tested negative. The only positivity regarded IgG and IgM immunoglobulins for Parvovirus B19.

It could be a unique case of diarrhea and non-cholestatic hepatitis due to Parvovirus B19 infection: it has never been described before, particularly in a two-month-old infant.

It confirms the possible association, even if infrequent, between this type of infection and acute hepatitis, suggesting that the research of Parvovirus B19 should be performed in the forms of severe diarrhea with hepatic involvement, which resulted negative to other possible pathogens.

Keywords: Parvovirus B19; Acute Hepatitis; Unexplained Diarrhea

Introduction

Parvovirus B19 is a single stranded DNA virus whose infection can run in an asymptomatic form or with a wide spectrum of clinical manifestations that includes benign erythema infectiosum, arthropathy, mostly transient aplastic anemia, fetal hydrops.

Case Report

A 2 month-old female infant presented at our NICU with diarrhea for 20 days, fever (max value 39°C), dehydration, suffering appearance and irritability. No hepatomegaly. The child was born at term with spontaneous delivery and rupture of membranes < 12 hours, lim-

pid amniotic fluid, negative vaginal swab, Apgar score of 9 at 1 and 5 minutes after birth. No medical history related to the pregnancy. At entry, a severe metabolic acidosis with pH 7.18, EB -18,6 mmol/l, HCO₃ 8,8 mmol/l was detected. Biohumoral tests showed an acute non-cholestatic hepatitis with hypertransaminasemia, the serum alanine aminotransferase level was 967 U/l (normal level: 10 - 35), aspartate aminotransferase level was 1183 U/l (normal level: 5 - 38) and the lactate dehydrogenase level was 272 U/l, γ glutamyl transferase was in the range (82 U/l), direct bilirubin and coagulation tests in the standard, white cell count of 12520/ μ l, thrombocytosis (PLT 1181000/ μ l (n.v. 150000 - 400000), albumin, alpha 1 antitrypsin and ammonia in the limits, altered PCR (4,17 mg/dl). The abdominal ultrasound showed no particular pathologic elements. The ultrasound of kidneys and urinary tract is normal. The culture tests (blood, urine, faeces), the parasitological examination of the faeces, the serodiagnosis for *Salmonella*, *Shigella*, *Brucella*, *Campylobacter*, *Yersinia*, the research of *Clostridium* toxin, the serology for the main hepatotoxic viruses (A,B,C), EBV and TORCH, and the research for antigens for rotavirus and adenovirus resulted negative. The patient was positive for parvovirus B19 IgM and IgG with IgG values 33.70 U/l and IgM 13.40 U/l (pos. > 9). Based on these clinical features and investigations, the patient was finally diagnosed to have parvovirus B 19 infection with diarrhea and acute non-cholestatic hepatitis.

Discussion and Conclusion

Correction of the metabolic acidosis, rehydration, antibiotic (waiting for culture tests), and antipyretic therapy, enteral feeding with hydrolyzed milk, were performed with progressive reduction of hepatic and PCR values that became normal within 10 days and resolution of the clinical picture. The child is taken to pediatric follow-up with a favorable course.

Parvovirus B19 is a single stranded DNA virus belonging to the family Parvoviridae which includes 8 genera: 5 of these contain human parvoviruses (Dependovirus, Erythroparvovirus, Bocaparvovirus, Tetraparvovirus, and Protoparvovirus). Parvovirus B19 is included in the Erythrovirus, a group of virus that use erythroid progenitor cells for propagation and infects human with high specificity. The transmission usually occurs by human contact through respiratory droplets, however, vertical transmission and transmission via blood also occur.

The originality of the case lies in the absolute uniqueness of reporting non-cholestatic acute hepatitis from parvovirus B19 in a one-month-old infant (if we consider the onset of symptoms), as well as the onset with diarrhea never reported before. In effects, the only case of parvovirus diarrhea is described in a single report [1] in which a divergent parvovirus genome was the only eukaryotic viral sequence detected in faeces of a Tunisian child with unexplained diarrhea. To identify other viral infections in this patient, an 18-month-old girl, the Tusavirus-positive sample was individually analyzed by the metagenomic method. A virus belonging to the parvovirus family but not a parvovirus B19. We also report a paper in which during a viral metagenomic analysis of faeces from children with acute diarrhea in Burkina Faso [2], sequences from a highly divergent parvovirus, provisionally called Bufavirus, were detected and four percent of the fecal samples were PCR positive for this new parvovirus.

Systemic features of parvovirus B19 infection are severe in adults, including arthralgia with synovitis and rare manifestations such as aplastic crisis in patients with chronic hemolytic anemia, bone marrow failure in immunocompromised hosts, a transient febrile myasthenia-like syndrome, myositis, and acute heart failure. These occur rarely in infants where the infection can run in an asymptomatic form or with a wide spectrum of clinical manifestations that includes benign erythema infectiosum (the classic fifth disease of childhood), arthropathy, mostly transient aplastic anemia, fetal hydrops.

The cases described on adult patients [3-7], although very few, support an association between parvovirus B19 infection and the development of acute hepatitis. Parvovirus B19 has also been implicated as a cause of liver failure due to fulminant hepatitis [8], although not all studies confirm this association [9,10].

If acute hepatitis in association with parvovirus B19 infection has only rarely been reported in the literature in adulthood, pediatric cases are anecdotal [11-15]. In particular, there are reports of isolated cases of acute and chronic hepatitis without a cholestatic component and only one case of an adolescent with acute hepatitis with cholestasis [11].

In the most important case described [16], severe liver damage required liver transplantation. In this article, authors presented a case of an immunocompetent female child who developed acute liver failure of unknown etiology. The patient was hospitalized to undergo a liver transplantation and died some days after surgery. Therefore, they investigated whether parvovirus B19 might be involved in this clinical manifestation of acute liver failure. They concluded that our study highlights the importance of considering this virus in the differential diagnosis of acute liver failure in patients with hematologic abnormalities, mostly in children, where the disease is usually more severe.

The association of acute hepatitis in parvovirus B19 infection and benign myositis [15] is exceptionally reported with only two cases present in the literature. In particular, a report on a 14-year old male who developed acute hepatitis and benign myositis associated with erythema infectiosum following Parvovirus B19 infection was published.

The youngest pediatric patient with B19 parvovirus hepatitis described in literature [14] is a 9-month-old female infant presented at our hospital with high-grade intermittent fever (39°C) for 6 days, associated with erythematous maculopapular nonpruritic rash. Based on investigations (the serum alanine aminotransferase level was 4745 U/L, the aspartate aminotransferase level was 3428 U/L, and the lactate dehydrogenase level was 825 U/L) and clinical features the patient was finally diagnosed to have erythema infectiosum with acute hepatitis.

The mechanism by which parvovirus B19 infection may result in hepatic injury is not clear. Two possibilities have been proposed [17,18]: hepatic cell damage related to direct viral invasion is one and alternatively cell damage may result as an indirect consequence of the immune response directed against the virus. In another work, it is stated that the case reported supports the hypothesis of the direct cytopathic effect of Parvovirus B19 on liver cells [19]. It is also specified that it seems that all non-erythroid cells are not permissive to the virus, meaning that despite the virus gains entry into the cells, it cannot replicate and that, however, despite the virus inability to replicate within a non-permissive cell, it retains its ability to produce the non-structural protein NS1, which can induce apoptosis of the corresponding infected cell.

Some authors [11] have shown a better prognosis of the forms of hepatitis associated with acute Parvovirus B19 infection in children under 5 years in which lower serum bilirubin values and a more rapid recovery of liver function are observed.

The limitation of this report lies in not having performed the serum PCR for virus detection.

But we believe that it is a significant new case because it reminds that parvovirus B19 can be responsible, though not frequently, for a systemic infection with hepatitis symptoms and this association must also be taken into account in the pediatric and even neonatal age. Probably, because it is a rare occurrence, parvovirus B19 is likely under-diagnosed as a cause of acute hepatic injury in infants while this infection should be considered in the differential diagnosis of patients presenting with acute hepatitis of unknown etiology. The study also suggests, in an unpublished manner, that in the form of severe diarrhea with hepatic involvement which resulted negative to other possible pathogens, the research of parvovirus B19 should be performed.

Bibliography

1. Phan TG., *et al.* "New parvovirus in child with unexplained diarrhea, Tunisia". *Emerging Infectious Diseases* 20.11 (2014): 1911-1913.
2. Tung G Phan., *et al.* "Acute Diarrhea in West African Children: Diverse Enteric Viruses and a Novel Parvovirus Genus". *Journal of Virology* 86.20 (2012): 11024-11030.
3. Aleisha Hatakka., *et al.* "Acute Hepatitis as a Manifestation of Parvovirus B19 Infection". *Journal of Clinical Microbiology* 49.9 (2011): 3422-3424.
4. Diaz F and J Collazos. "Hepatic dysfunction due to parvovirus B19 infection". *Journal of Infection and Chemotherapy* 6.1 (2000): 63-64.

5. Tesapirat L., *et al.* "Parvovirus B19 infection presenting as acute hepatitis and transient anemia in a previously healthy child". *Southeast Asian Journal of Tropical Medicine and Public Health* 46.2 (2015): 226-230.
6. Pinho JRR., *et al.* "Detection of human parvovirus B19 in a patient with hepatitis". *Brazilian Journal of Medical and Biological Research* 34.9 (2001): 1131-1138.
7. Hillings JG., *et al.* "Parvovirus B19 and acute hepatitis in adults". *Lancet* 351.9107 (1998): 955-956.
8. Ho JK., *et al.* "Parvovirus B19 in an immunocompetent adult patient with acute liver failure: an undiagnosed cause of acute non A-E viral hepatitis". *Canadian Journal of Gastroenterology* 19.3 (2005): 161-162.
9. Wong S., *et al.* "Prevalence of parvovirus B19 in liver tissue: no association with fulminant hepatitis or hepatitis associated". *Journal of Infectious Diseases* 187.10 (2003): 1581-1586.
10. Krygier DS., *et al.* "Parvovirus B19 induced hepatic failure in an adult requiring liver transplantation". *World Journal of Gastroenterology* 15.32 (2009): 4067-4069.
11. S Perrini., *et al.* "Parvovirus B19 associated acute cholestatic hepatitis". *La Pediatria Medica e Chirurgica (Medical and Surgical Pediatrics)* 36.5-6 (2014): 224-225.
12. Sokal MS., *et al.* "Acute parvovirus B19 infection associated with fulminant hepatitis of favourable prognosis in young children". *Lancet* 352.9142 (1998): 1739- 1741.
13. Tesapirat L., *et al.* "Parvovirus b19 infection presenting as acute hepatitis and transient anemia in a previously healthy child". *La Pediatria Medica e Chirurgica* 36.5-6 (2014): 102.
14. Beom Joon Kim., *et al.* "Parvovirus B19 Infection Associated With Acute Hepatitis in Infant". *The Pediatric Infectious Disease Journal* 28.7 (2009): 667.
15. Maria Koliou., *et al.* "Acute hepatitis and myositis associated with Erythema infectiosum by Parvovirus B19 in an adolescent". *BMC Pediatrics* 14 (2014): 6.
16. Luciane Almeida Amado Leon., *et al.* "Parvovirus B19 infection in a fatal case of acute liver failure". *The Pediatric Infectious Disease Journal* 36.12 (2017): e355-e358.
17. Lee WM., *et al.* "Brief report: no evidence for parvovirus B19 or hepatitis E virus as a cause of acute liver failure". *Digestive Diseases and Sciences* 51.10 (2006): 1712-1715.
18. Young NS and KE Brown. "Mechanisms of disease: parvovirus B19". *New England Journal of Medicine* 350.6 (2004): 586-597.
19. Poole BD., *et al.* "Parvovirus B19-induced apoptosis of hepatocytes". *Journal of Virology* 78.14 (2004): 7775-7783.

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