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Mysterious Case of Severe Acute Hepatitis Affecting Children: About 3 Cases

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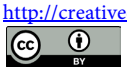

Abstract

Severe acute hepatitis of unknown origin was reported for the first time among children in many countries or regions worldwide. This article describes the first Moroccan cases of severe acute hepatitis admitted for cholestasis jaundice. The biological assessment revealed significantly hepatic cytolysis for our three cases. The viral hepatic serology was negative and the autoimmunity assessment was unremarkable. The cause of this inflammation of the liver is not yet known. The aim of this manuscript is to sensitize young children to this serious disease of unknown etiology.

Subject Areas

Gastroenterology & Hepatology, Pediatrics

Keywords

Acute Hepatitis, Adenovirus, SARS-CoV-2, Adenovirus 41

1. Introduction

Acute hepatitis is said to be severe if the prothrombin (PT) level is less than 50%. The etiologies are variable according to the regions of the world, nevertheless the viral origin is in decline, contrary to the toxic causes, in particular medicinal [1]. We report 3 cases of severe acute hepatitis of unknown origin. The purpose of this article is to describe the clinical presentation in our patients and to raise awareness about this liver disease of still unknown etiology.

2. Observation 1

This is a 10-year-old boy with no history, admitted for cholestatic jaundice evolving 1 month earlier. The clinical examination found a conscious child who

was hemodynamically and respiratory stable, with the presence of extensive pustular lesions on the face with an edematous syndrome. The evolution was marked by an alteration of his neurological state with agitation, hallucinations, asterixis and a disturbance of the hepatic biological assessment indicating his transfer to intensive care unit. After stabilization, the patient is readmitted to our unit for additional care and etiological assessment which was in favor of severe acute hepatitis with a prothrombin rate at 10% and Factor V at 29%; hepatic cytolysis with ASAT at 3668 UI/l, and ALAT at 2288 UI/l; and cholestasis with a direct bilirubin of 77 mg/dl, and a total bilirubin of 112 mg/dl.

Viral hepatitis serology was negative as well as the autoimmunity test. In the context of Wilson's disease, the assessment was negative. The patient underwent an abdominal ultrasound in favor of a heterogeneous liver of normal size. After initial conditioning and stabilization, the child received symptomatic treatment for the hepatic encephalopathy, with large-spectrum antibiotic therapy and corticosteroid therapy given the deterioration of the clinical condition. The liver biopsy could not be performed in our patient because of the prothrombin level which was still low. The evolution was marked by a stabilization of the clinical state, especially neurological, with regression of the jaundice and normalization of the cytolysis assessment.

3. Observation 2

This is an 11-year-old boy with no notable pathological history, admitted with cholestatic-like jaundice evolving 20 days before his hospitalization, in whom the clinical examination found a conscious, jaundiced child, with signs of clinical cholestasis, with slight hepatomegaly, all evolving in a context of apyrexia. The biological assessment showed a disturbed cytolysis assessment, biological cholestasis, and the assessment of hepatic insufficiency with a TP: 74% and Factor V: normal. Abdominal ultrasound was in favor of homogeneous hepatosplenomegaly. NFS showed pancytopenia with neutropenia and lymphopenia, thrombocytopenia and normochromium normocytic aregenerative anemia. Viral serology: IgG HAV: + IgM: − IgG EBV: + IgM: −, COVID serology: IgG positive. CMV and Parvovirus B19 serology: IgG positive IgM negative. The autoimmunity test was negative. In front of the pancytopenia, a myelogram was in favor of a desert marrow. The BOM revealed a histological aspect of aplastic anemia with absence of tumor cells. It should also be noted in this patient that the Hepatic Biopsy could not be performed given the deep thrombocytopenia.

The diagnosis retained was bone marrow aplasia probably post-severe acute liver infection. Therapeutically, the child received corticosteroids and immunosuppressant, with symptomatic treatment of aplastic anemia. The evolution was marked by clinical improvement (disappearance of jaundice and clarification of urine) and biologically normalization liver test.

4. Observation 3

This is a 13-year-old girl, treated for growth retardation, admitted for cholestasis

jaundice evolving for 1 month with bilateral cervical, axillary and inguinal polyadenopathy, and hepatomegaly and splenomegaly. All evolve in a context of asthenia, apyrexia and weight loss.

The biological assessment was in favor of significant hepatic cytolysis at >30 time's normal, biological cholestasis, without hepatocellular insufficiency. The complete blood count objectified bicytopenia with neutropenia and non-regenerative anemia and the bone marrow was desert. The BOM objectified a hypoplastic marrow, affecting the 2 erythroblastic and granular lines with reactive megaloblastic hyperplasia. Abdominal ultrasound revealed discrete homogeneous hepato-splenomegaly with low abundance ascites. For polyadneopathies, a TAP scan was performed, with no particularity. The viral hepatic serology was negative and the autoimmunity assessment was unremarkable. Liver biopsy was performed, returning without abnormalities. Therapeutically, the patient received corticosteroid therapy with antibiotic treatment for febrile neutropenia. The evolution was favorable, with clinical and biological improvement.

5. Discussion

Acute hepatitis refers to a rapid onset inflammation of the liver that can progress to acute liver failure with significant morbidity and mortality. It may affect previously healthy individuals and can be due to several infectious causes, hepatitis A, B and E virus, Epstein-Barr virus and cytomegalovirus being some of the more common, as well as non-infectious causes.

The World Health Organization (WHO) has been informed of several cases of severe acute hepatitis of unknown origin in children under the age of 10 [2]. Typical viruses that are known to cause acute viral hepatitis (*i.e.* hepatitis A, B, C, D or E virus) have not been detected in the patients affected in any of the 15 countries. Interestingly, in England and Scotland, 75.5% and 50% of cases have tested positive for human adenoviruses (HAdVs) [3].

We describe three cases of young children presenting to hospital with severe hepatitis of unknown origin. An infectious aetiology is now considered more likely given the epidemiological and clinical features, and taking into account the additional cases from across the UK and the US cluster. At the time of publication, the leading hypotheses centre around adenovirus—either a new variant with a distinct clinical syndrome or a routinely circulating variant that is more severely impacting younger children who are immunologically naïve. The latter scenario may be the result of restricted social mixing during the COVID-19 pandemic. Adenovirus infection as a cause of severe hepatitis is rare in immunocompetent children but has been reported in case reports and series [4] [5].

Public health specialists, paediatricians and other clinicians should be aware of children presenting acutely with gastrointestinal symptoms and jaundice or elevated serum.

Transaminases > 500 UI/L (AST or ALT) and have a higher index of suspicion and a lower threshold for referral for specialist care. Cases should be reported to

national and international public health bodies for appropriate follow-up investigation and management as well as the WHO for situational awareness. Until the cause of these cases of severe illness is found, standard public health guidance emphasising the importance of hand hygiene should be provided in settings where unexplained hepatitis is detected [6].

6. Conclusion

Currently, around 200 cases of severe acute hepatitis have been reported in around ten countries around the world. This article describes the clinical presentation of severe acute hepatitis in our patients. The cause of this inflammation of the liver is not yet known. In about three-quarters of children with confirmed hepatitis who were tested, a specific human adenovirus called F41 was found. This hypothesis remains probable for the moment in our patients.

Conflicts of Interest

The authors declare no conflicts of interest.

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