IDCases 20 (2020) e00721

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

Fatal hepatitis A virus infection in an adolescent

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ARTICLE INFO

Article history:
Received 3 February 2020
Received in revised form 10 February 2020
Accepted 10 February 2020

Keywords:
Hepatitis A virus
Fulminant
Oman

ABSTRACT

Acute hepatitis A infection is largely self-limiting illness, rarely resulting in fulminant course with consequent hepatic failure and death. We present a 13-year old previously healthy Omani with fatal hepatitis A virus infection. This case highlights the critical role of hepatitis A vaccination and argues for consideration of its inclusion in national vaccination programs in order to avert similar devastating consequences of yet another vaccine preventable disease.

Introduction

Hepatitis A is the most common form of acute viral hepatitis in the world [1] especially in endemic areas with poor sanitation infrastructure [2]. It is estimated that hepatitis A virus (HAV) infects approximately 1.4 million persons per year globally [3] and remains one of the most common and rampant causes of acute viral hepatitis in children particularly in resource limited countries [4].

Transmission of HAV follows a fecal-oral route through the consumption of contaminated food or water [5] making it one of the most important causes of food-borne diseases [5]. One of the whole marks of HAV is its capability to cause large community outbreaks both in underdeveloped [2,6] and developed countries [7,8].

The disease spectrum of HAV infection is wide ranging from an asymptomatic self-limited infection to a life-threatening and fulminant hepatitis [9]. Adults with preexisting chronic liver disease tend to have more severe disease course [10]. Contrarywise, clinical course of hepatitis A infection in pediatric population is typically benign [11] with fulminant hepatitis A being exceedingly infrequent in children [12].

We present a 13-year old previously healthy Omani patient with acute hepatic failure due to hepatitis A virus resulting in a fatal outcome. This infection occurred in the context of an outbreak of hepatitis A infection within the family unit. This report highlights the critical role of hepatitis A vaccination and argues for consideration of its inclusion in the national vaccination program in order to avert similar devastating consequences of yet another vaccine preventable disease.

Case presentation

A 13-year old previously healthy adolescent presented to a regional hospital in Oman with a four-day history of fever associated with upper respiratory tract like symptoms for which he was prescribed amoxicillin/clavulanate and acetaminophen. His symptoms worsened as he became extremely lethargic with persistence of fever and development of non-specific abdominal pain, nausea, vomiting, and icterus. He was found to have a severely deranged hepatic enzymes consistent with a diagnosis of acute hepatitis. His clinical course rapidly worsened as he became encephalopathic leading to respiratory depression necessitating urgent endotracheal intubation and mechanical ventilation. A diagnosis of acute hepatic failure was assumed, and the patient was referred to this hospital for further care. Additional history revealed that two of his cousins (whom he had close contacts with) were diagnosed with acute viral hepatitis A infection eight and four weeks respectively antecedent to his illness. Subsequent to this patient hospitalization, a family cluster of laboratory-confirmed acute hepatitis A virus infection afflicting four other cousins was recognized by the public health. All six had uneventful clinical courses.

Examination revealed a critically ill, febrile and deeply icteric child on a ventilator. He was tachycardic (114/minute) and hypotensive (101/84 on noradrenaline). Abdominal examination showed a massively distended abdomen with ascites and hepatomegaly. No ecchymoses or overt bleeding. Rest of the examination was normal.

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https://doi.org/10.1016/j.idcr.2020.e00721

Salient initial laboratory investigations revealed hemoglobin of 9.0 g/dL, platelet count of 57 × 10^3/uL and white cell count of 15.2 × 10^3/uL. Chemistry panel was relevant for alanine aminotransferase (ALT) of 3673 U/L (normal: 0–41 U/L), aspartate aminotransferase (AST) of 2915 U/L (normal: 0–40 U/L), total bilirubin of 28.54 mg/dL (normal: 0-0.99 mg/dL) and ammonia of 198 umol/L (normal: 11–32 u mol/L). Coagulation profile showed prothrombin (PT) of 39.5 s (reference: 9.7–12.3), APTT of 76.8 s (reference: 26.3–38.2), and INR of 3.64 (reference: 0.8–1.2).

Serology for acute viral hepatitis revealed reactive hepatitis A IgM and IgG confirming acute hepatitis A virus infection. Serology for hepatitis B, C and E were non-reactive. Screening for autoimmune hepatitis was negative and acetaminophen level was normal.

Over the subsequent few days, the patient clinical condition continued to worsen rapidly with development of difficult to control seizures, disseminated intravascular coagulation resulting in extensive bleeding, and later severe acute respiratory distress culminating in patient death eight days after hospitalization. This fulminant course occurred despite intensive supportive care including blood products, anticonvulsants, anti-brain edema measures, and cardiopulmonary support. A Computed tomography (CT) of the brain on day three of admission (Fig. 1B) demonstrated diffuse cerebral edema.

Discussion

The epidemiology of acute viral hepatitis A in Oman is largely unknown. We believe that the case presented here is the first published report from Oman of acute viral hepatitis A with a fulminant course.

This case was particularly unusual with regards to its fulminant nature and the rapidity at which this course progressed. Progression of hepatitis A infection to acute liver failure is seldom seen in pediatric population. This fulminant course is reportedly observed in less than 1% of infections and typically occurs in older children and adults [12]. Contrary to this patient, hepatitis A virus infection in children frequently is a subclinical illness. Mild and self-limiting illness with nonspecific symptoms of fever, abdominal pain, nausea, vomiting and jaundice is classic for overt clinical disease in children [9]. This typical mild and self-limiting clinical course was true for the patient contacts where all experienced uneventful outcome.

It is currently unclear as to why some patients with acute viral hepatitis A infection progress to fulminant hepatic failure while others follow a much common and benign course [13]. However, it is hypothesized that a profound host immune response is strongly associated with the development of fulminant hepatitis and severs hepatic damage [14]. In HAV, virus specific CD8 lymphocytes and natural killer cells are the main mediators of the pathogenesis of this process [14]. It is also postulated that genetic predisposition might contribute to the progression of the disease but this concept is not clearly established [14].

Fulminant hepatitis is associated with massive hepatic necrosis which results in development of jaundice, significant rise in liver enzymes, coagulopathy and encephalopathy. This was the case in this patient where an overwhelmingly aggressive course characterized by brain edema, refractory coagulopathy, and cardiopulmonary collapse culminated in his death despite aggressive supportive therapy. This grave consequence is unfortunately consistent with the published literature where mortality rate in children with fulminant hepatitis reaches up to 70 % [12]. Furthermore, literature suggests that development of hepatic encephalopathy in the context of end stage liver disease in children is a significant and powerful prognostic factor for poor outcome [12]. Our search of the literature identified eight cases of fulminant hepatitis A infection in pediatric age group reflecting the rarity of hepatitis A related acute liver failure [15–19]. Five out of the eight identified patients (63 %) died and death was due to extensive liver damage with encephalopathy and cerebral edema.

Treatment of acute hepatitis A infection is mainly supportive as there is no specific treatment. Liver transplantation shall be considered (if feasible) as a treatment option for patients with fulminant hepatitis A infection not responsive to intensive supportive care [20]. The unavailability of liver transplantation program in Oman and the extremely rapid and aggressive course of the disease rendered this intervention unfeasible in this patient management.

Hepatitis A virus infection is a notifiable disease in Oman. Our national Infectious diseases surveillance data reported 1175

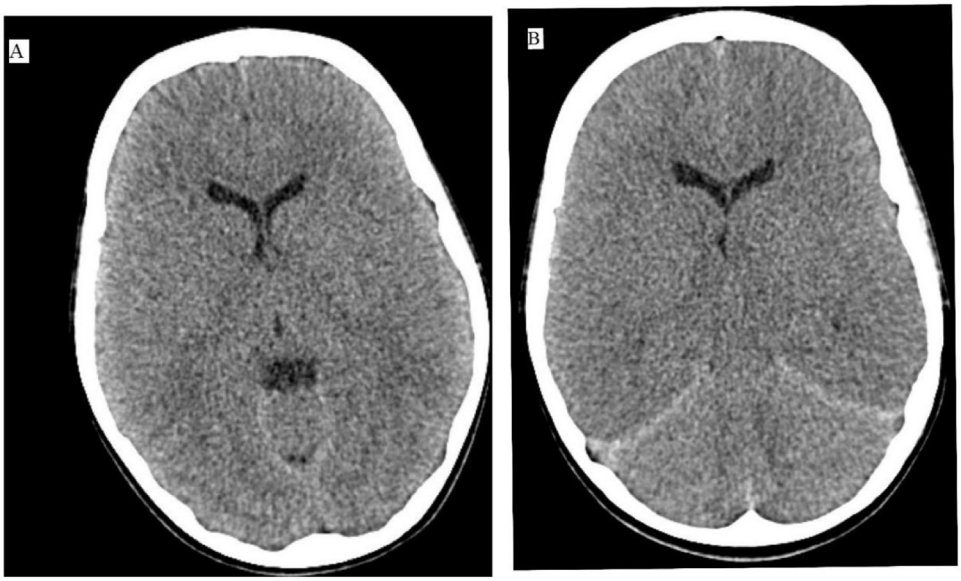

Fig. 1. Computed tomography (CT) of the brain on day of admission **(A)** and three days later **(B)**. **A:** Normal CT of the brain on day of admission. **B**: CT of the brain three days later showing diffuse cerebral edema with effacement of cerebral sulci and poor grey/white matter differentiation. Additionally, the lateral and third ventricles appear smaller and the quadrigeminal and ambient cistern are obliterated features consistent with diffuse hypoxic brain injury.

laboratory-confirmed hepatitis A cases in 2017 including this patient [unpublished data]. To our knowledge-with the exception of this patient- none had a fulminant or a fatal outcome. Improved sanitation, food safety, and immunization are the most effective ways to combat hepatitis A infection [5]. We believe that this case with its devastating outcome coupled with the emergence of a large outbreak of hepatitis A infection in the community plausibly argue for seriously considering inclusion of hepatitis A vaccine in childhood/pre-school vaccination program in Oman. Intuitively, deaths from vaccine preventable diseases shall not be tolerated.

Patient consent

Patient consent was not required for this publication.

Funding

None.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Acknowledgment

We acknowledge that: This work is original and has not been published previously. The manuscript is not under consideration for publication elsewhere. The submission is approved by all authors. First/corresponding author was responsible for the writing and revising the manuscript, and all authors contributed to the clinical care of the patient and to the revision of several drafts before submission. Last author, did a thorough revision of the draft.

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