Case Report

Hepatitis A related acute liver failure by consumption of contaminated food

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A B S T R A C T

We present a patient with no medical history admitted for jaundice and dark coloured urine. Further investigations revealed hepatitis A related acute liver failure while the patient had no travel history, nor contact with infected individuals. After admission, the patient deteriorated fulfilling the King's College criteria for acute liver failure. Two days after admission, he underwent liver transplantation and recovered. Careful investigation identified imported semi-dried tomatoes as the source of the hepatitis A infection. This patient was part of a foodborne hepatitis A outbreak in the Netherlands in 2010 affecting 13 patients. Virus sequence analysis of our patient's virus showed a strain commonly found in Turkey. Hepatitis A related acute liver failure is rare, but is associated with a poor prognosis. In developed countries, the incidence of hepatitis A is low, but foodborne outbreaks are emerging. Further, we review the literature on recent foodborne hepatitis A outbreaks in developed countries, hepatitis A related acute liver failure, and hepatitis A vaccine.

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1. Why this case is important

The hepatitis A virus (HAV) is a RNA virus transmitted via the faecal–oral route and is the most common cause of acute viral hepatitis in the world. Typically, patients present with non-specific symptoms such as fever, malaise, nausea, vomiting and flu-like symptoms accompanied with dark urine and jaundice [1]. Hepatitis A is a self-limiting disease, but is accountable for an estimated 3.1% of acute liver failures [2].

The incidence of HAV infections is low in developed regions (Western Europe, and North America). Infections are predominantly associated with person-to-person contact with an infected person or travel to high endemic regions (sub-Saharan Africa, and parts of South Asia) [3]. In the last decade, however, hepatitis A outbreaks are emerging in developed countries, mostly caused by imported food contaminated with the HAV. This emergence can be largely attributed to the vast and increasing trade of food products globally. In this case report, we describe a case of hepatitis A related acute liver failure caused by contaminated food and review the literature on this topic.

2. Case report

A 39-year old man with no medical history was admitted to the Erasmus MC University Medical Centre Rotterdam (Rotterdam, The Netherlands) in January 2010. His symptoms started one week earlier with malaise, nausea, and vomiting. Since two days, he noted jaundice and dark coloured urine. He did not have fever, and had not travelled for several months. Nobody in his surroundings was sick. We did physical examination on admission, and found a disorientated man with jaundice and flapping tremor suggesting acute liver failure accompanied with hepatic encephalopathy.

Laboratory results revealed aspartate transaminase 2465 U/L (<34 U/L), alanine aminotransferase 6555 U/L (<44 U/L), bilirubin 209 µmol/L (<16 µmol/L), prothrombin time 79 s, activated partial thromboplastin time 55 s, international normalised ratio 6.6, factor V 0.101 U/mL, and creatinine 208 µmol/L (65–115 µmol/L). Due to the severity of his condition (fulfilling the King’s College criteria for acute liver failure), we immediately placed him on the high-urgency waiting list for liver transplantation and performed...

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a broad range of diagnostics. Initial differential diagnosis for acute liver failure included viral hepatitis (hepatitis A, B, and E), drug-induced liver failure (acetaminophen), autoimmune hepatitis, and Wilson's disease. Liver ultrasonography showed no abnormalities. As for virological results, the patient was negative for hepatitis B surface antigen, anti-HBc, anti-hepatitis C virus, IgM and IgG anti-hepatitis E virus, IgM and IgG cytomegalovirus, and Epstein–Barr virus DNA. However, the test for hepatitis A virus specific IgM and IgG antibodies was positive, and therefore the diagnosis hepatitis A related acute liver failure was made. One day after admission he was transferred to the intensive care unit as his hepatic encephalopathy worsened and his renal function deteriorated. The following day he underwent a successful liver transplantation. The patient recovered and was discharged one month later. The patient is doing well now.

Our patient was part of a hepatitis A outbreak in the Netherlands in 2010. His infection source was unclear as he did not travel in the past months, nor did he have contact with infected individuals. A similar case occurred in the same period in the north of the Netherlands. A 59-year-old man was admitted to the University Medical Centre Groningen (Groningen, the Netherlands) with also a hepatitis A related acute liver failure. This patient had neither travel history, nor contact with infected individuals in the past months. He underwent liver transplantation two days after admission and recovered.

Hepatitis A is a notifiable disease in the Netherlands, and therefore both patients were reported to the national authorities. The National Institute for Public Health and the Environment (the RIVM) recognised a hepatitis A outbreak affecting 13 geographically spread patients in the Netherlands between December 2009 and February 2010. Sequence analysis showed that all 13 patients were infected with an identical HAV strain (HAV genotype 1B). After careful investigation, evidence suggested imported semi-dried tomatoes as the source of the outbreak. Upon further questioning, both our patients reported substantial consumption of semi-dried tomatoes. In addition, we identified a virus sequence in both our patients that was commonly found in infected travellers returning from Turkey and hepatitis A patients in Turkey (Fig. 1).

### 3. Other similar and contrasting cases in the literature

The transmission of HAV by contaminated food or water is known phenomenon, but was considered rare in Western countries [1]. However, a population-based surveillance study from the US showed that food or waterborne outbreaks were responsible for approximately 7.2% of reported hepatitis A cases [4]. One of the largest Western foodborne hepatitis A outbreak affecting at least 601 individuals was reported in the US in 2003 [5]. In this outbreak, contaminated green onions from Mexico were identified as the source, and were responsible for 3 deaths and at least 124 hospitalizations. The first hepatitis A outbreak by semi-dried tomatoes was reported in Australia in 2009 [6]. This foodborne outbreak led to 562 reported hepatitis A cases which was a 2-fold increase of the average annual hepatitis A cases. Furthermore, HAV RNA was detected in samples of imported semi-dried tomatoes. In the following years, semi-dried tomatoes were responsible for multiple foodborne outbreaks: twice in the Netherlands (2010 and 2011) [7,8], France (2010) [9], and the United Kingdom (2011) [10]. In the French outbreak, 59 cases were identified, whereof 28 were hospitalized. Recently, frozen berries were identified as the culprit for hepatitis A outbreaks in Nordic countries and Italy [11,12]. Denmark, Finland, Norway, and Sweden reported 103 cases of hepatitis A between October 2012 and June 2013.

![Fig. 1. Phylogenetic tree of hepatitis A virus sequences of both patients and reference strains. Phylogenetic analysis of HAV sequences of both patients (patient A and B) in relation to samples of other patients in Groningen (GenBank accession number–NL-Gro-year.nr) and reference strains (GenBank accession numbers) of HAV genotype 1A, 1B, 2 and 3. Patient A: 39-year-old man. Patient B: 59-year-old man. For phylogenetic analysis a fragment of 410 bp of VP1–2A were aligned with Clustal W 2.0 and phylogenetic trees were constructed by the neighbour-joining method with bootstrap 1000 using MEGA 4.0 using different reference strains of HAV from GenBank. The HAV sequences derived from this work are submitted to GenBank (accession numbers KM261582–KM261590). *Men who have sex with men.](image-url)
Given the vast volume of imported food and large proportion of susceptible adults in developed countries, foodborne hepatitis A outbreaks are a considerable concern. The benefit of a universal vaccination programme should be assessed by national health authorities of developed countries. The impact of foodborne hepatitis A outbreaks should not be underestimated due to the association of increased severity with advancing age. Both our patients needed liver transplantation after developing hepatitis A related acute liver failure after consumption of contaminated food. Acute liver failure following hepatitis A is uncommon, but its prognosis is poor.

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**Author contributions**

Heng Chi: drafting of the article, and finalising the article. Els Haagsma: patient care, drafting of the article, and finalising the article. Annelies Riezebos-Briman: drafting of the article, virus sequence analysis, drafting of the article, and finalising the article. Arie van den Berg: patient care, and finalising the article. Herold Mertselaar: patient care, and finalising the article. Robert de Knecht: patient care, drafting of the article, and finalising the article.

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