



Original paper

Acute hepatitis A virus infection in patients hospitalized at the Department of Infectious Diseases, Medical University of Lublin (Eastern Poland) in 2017 – a hospital-based retrospective study

Joanna Małgorzata Krzowska-Firych^{1,2}, Robert Ściślak², Agnieszka Wójtowicz², Krzysztof Tomasiewicz¹, Georgia Lucas², Christiana Lucas²

¹Department of Infectious Diseases, Medical University of Lublin, Poland ²Clinical Research Association for Infectious Diseases, Medical University of Lublin, Poland

Abstract

The aim of our study was to analyze medical records of all adult patients with acute hepatitis A virus (HAV) infection who were hospitalized at the Department of Infectious Diseases, Medical University of Lublin, Poland in 2017. During the studied period acute HAV infection was confirmed in 33 patients. In the study group there were 30 men and 3 women. The mean time of hospitalization was 12 days. All patients recovered with no clinical sequelae.

Key words: hepatitis A virus infection (HAV), epidemiology, clinical course, Lublin Province.

Address for correspondence

Dr. Joanna Małgorzata Krzowska-Firych, Medical University of Lublin, 16 Staszica St., 20-089 Lublin, Poland, e-mail: firychjdr@poczta.onet.pl

Introduction

Hepatitis A virus (HAV) infection is one of the most common causes of acute hepatitis worldwide [1]. Hepatitis A virus belongs to the Hepatovirus genus of the family Picornaviridae. Due to the advances of molecular technology, 7 unique genotypes of HAV have been identified. Genotypes I, II, III, and VII are of human origin, and genotypes IV, V and VI are of simian origin. Genotypes I and III are the most prevalent genotypes identified in humans [2]. The chief mode of transmission for HAV is through the fecal-oral route, including person-to-person spread, and contaminated water or food products, but it has also been associated with outbreaks in injecting drug users and men who have sex with men (MSM) [3]. HAV is endemic in many parts of the developing world, where poor sanitation conditions facilitate transmission of the virus. In areas where HAV infection is endemic, transmission occurs most frequently among close contacts. In the

developed world, the incidence of hepatitis A disease is generally low, and cases occur in the context of community-wide outbreaks transmitted among preschool and school-age children to their adult contacts, or in foodborne outbreaks. In countries with childhood hepatitis A vaccination programs, an increasing proportion of cases occur among travelers returning from endemic areas. Persons who acquire HAV during travel can transmit the infection to susceptible persons upon their return. Several outbreaks of acute HAV infection among communities of MSM and injecting drug users (IDUs) have been reported in several developed countries of low endemicity for HAV infection [2, 4]. HAV vaccination is the most efficient approach to prevent acquisition of HAV infection [5]. Since the introduction of the formaldehyde-inactivated vaccine in the 1990s, drastic changes have been seen in the epidemiology of HAV [6]. In Poland, there has been a shifting epidemiology of HAV. Before 1997, the incidence of hepatitis A in Poland was high, ranging from

155 per 100 000 population to 196 per 100 000 population. Due to progressive improvements in working and living conditions in the country, mainly the gradual introduction of sanitation and hygiene measures, the incidence of hepatitis A has decreased considerably in the years since 1997 [7].

Acute hepatitis A-related morbidity and mortality increase with age. In children aged < 6 years, around 70% of infections are asymptomatic; if the illness does occur, it is typically anicteric. In contrast, in older children, adolescents and adults, infection often leads to clinically overt acute hepatitis. Acute hepatitis A in adults may lead to prolonged incapacitation and rarely also to acute liver failure. There is no specific treatment for acute hepatitis A infection [8].

From January to November 2017, 15 040 cases of hepatitis A were reported by 24 countries, which represents an almost four-fold increase compared to the average 4226 cases reported for the same period between 2012 and 2015.

Aim of the study

The aim of our study was to analyze medical records of all adult patients with acute hepatitis A virus infection who were hospitalized at the Department of Infectious Diseases, Medical University of Lublin, Poland in 2017.

Material and methods

We retrospectively analyzed medical records of all adult patients with acute HAV infection who were hospitalized at the Department of Infectious Diseases, Medical University of Lublin in 2017.

Results

In 2017 (from March to December 2017), acute HAV infection was confirmed in 33 patients. All of these patients were included in our study. In all patients, anti-HAV immunoglobulin M (IgM) antibodies were detected on admission. The serological markers of hepatitis C (HCV) were negative in all patients, and in 1 male patient HBsAg was detected. In patients from the study group symptoms of any sexually transmitted diseases (STD) did not occur and tests for syphilis, herpes simplex and other STDs were not performed. None of them were vaccinated against HAV. In the study group there were 30 men and 3 women, all Polish citizens. All patients were residents of cities, 26 of them (79%) lived in Lublin, and 1 male patient was from Wrocław. From the female group 1 patient

was a Spanish student visiting Lublin. The mean age was 38 years (range: 18-55). Data from the epidemiological history revealed that 3 out of 33 patients before the hospitalization travelled to Greece (1 patient), to the Republic of South Africa (1 patient), and 1 patient to Israel. In our study the biggest group of HAV patients comprised those admitted to the hospital in November (6 cases), in June (5 cases), and in October (5 cases). Four patients were diagnosed in July, and 4 in September. The most frequent risk factor reported in 91% of hospitalized patients was close contact with a person with confirmed HAV infection or a person having symptoms of acute hepatitis. The coexistence of hepatitis A and HIV infection was observed in 2 male patients (6%). In 1 patient (3%) chronic hepatitis B infection was diagnosed.

In all patients abdominal ultrasound performed on admission revealed liver and spleen enlargement in 19 patients with no other abnormalities.

Considering the clinical manifestations of our patients, the duration of the prodromal period ranges from 7 to 14 days, and the most common prodromal symptoms include fever, malaise, nausea/vomiting, poor appetite, and abdominal discomfort, occurring in 26 patients (79%). Other symptoms include arthralgia/myalgia (15%) and chills (6%).

The clinical symptoms include jaundice with mean bilirubin concentration 6.74 mg/dl on admission. The mean bilirubin concentration during hospitalization was 17.88 mg/dl, and the mean bilirubin concentration on discharge was 3 mg/dl. All patients presented abnormal aminotransferase activity. The mean concentration of alanine aminotransferase (ALT) on admission was 4484.4 IU/l, during hospitalization 820 IU/l, and on discharge 281 U/l. The mean concentration of gamma-glutamyl transferase (GGT) was 875 IU/l on admission, 255.4 IU/l during hospitalization, and 197 IU/l on discharge.

The prothrombin index was abnormal in 4 patients, but with no clinical sequelae. The mean time of hospitalization was 12 days (range 3 to 23 days). There were no deaths, complications or hepatitis A relapse in the study group.

Discussion

The annual risk of infection with HAV is associated with indicators of socioeconomic development, hygiene and access to safe water. The World Health Organization (WHO) estimates the level of endemicity based on the age-specific seroprevalence estimates of HAV antibodies in the population. Seroprevalence varies widely among countries. Poland now is consid-

ered as a country with low endemicity [9, 10]. During a 9-year period, 2008 to 2016, 23 patients were hospitalized at the Department of Infectious Diseases, Medical University of Lublin with confirmed HAV infection. In 2017 the peak prevalence was noted with 33 diagnosed cases, and male cases were more frequent (ten times) than female ones (30 vs. 3). The total number of HAV patients hospitalized at the Department of Infectious Diseases, Medical University of Lublin from 2008 to 2017 is presented in Table 1.

From September 2015 to March 2016, hepatitis A notification in Germany increased by 45% to 699 cases. Children aged five to nine years were predominantly affected (22% of all cases). The possible cause of this increase could be the marked influx of asylum seekers in this time period in Germany [11]. Since 2016, an increase in the number of hepatitis A cases affecting mainly men who have sex with men (MSM) has been reported in low endemicity countries in Europe [12]. Since September 2016 an increase of acute hepatitis A cases was noted in central Italy, and the molecular investigation suggested that this outbreak was mainly supported by an HAV variant spreading within MSM communities across Europe [13]. In December 2016, the European Center for Disease Control and Prevention (ECDC) issued a Rapid Risk Assessment reporting of two distinct hepatitis A virus genotype IA strains circulating among MSM in the United Kingdom and Netherlands in 2016. Germany, Italy and Spain had also reported a recent increase in male HAV cases. Since November 2016, 38 cases of hepatitis A have been noted in Berlin. In this group there were 37 male patients and 30 reported having sex with men. Sequencing results and phylogenetic analysis showed three distinct clusters of MSM-related HAV strains circulating in Berlin [14]. Between July 2016 and February 2017, 48 male cases of hepatitis A were noted in the Netherlands. Of these, 17 were MSM [15]. Between July 2016 and 2 April 2017, 266 cases associated with the outbreak had been identified in England. At least 74% of these were among MSM, and 63% of cases were in London. A high proportion of cases likely acquired the infection abroad at the beginning of the outbreak, but transmission now mainly occurs in England. The outbreak comprises three concurrently circulating genotype IA strains, previously not seen in England [16].

An important increase in the number of acute HAV cases in MSM has been also noted in France since the end of 2016. From 1 January 2017 to 30 June 2017, 46 cases of acute hepatitis A infection were diagnosed in Lyon (France). Two cases occurred in children under 15 years of age. Among 44 adult cases, 38 were men, and 33 were MSM including 17 HIV-negative, and 16 HIV-

Table 1. Total number of cases of hepatitis A virus (HAV)-infected patients hospitalized at the Department of Infectious Diseases, Medical University of Lublin from 2008 to 2017

Year	Total number of HAV-infected patients
2008	18
2009	1
2010	1
2011	-
2012	3
2013	-
2014	-
2015	-
2016	-
2017	33
Total	56

infected. In all but one case occurring in MSM, sequencing identified one of the three epidemic strains circulating among MSM in many European countries [17].

From January to November 2017, 15 040 cases of hepatitis A were reported by 24 countries, which represents an almost four-fold increase compared to the average 4226 cases reported for the same period between 2012 and 2015.

In 2017, 3014 confirmed cases of HAV infection were noted in Poland. The largest numbers of cases occurred in Mazowieckie voivodeship (696 cases), Śląskie voivodeship (546), and Wielkopolskie voivodeship (487). In the Lublin Province 38 HAV positive cases were noted [18].

In Europe, the last outbreak of hepatitis A among MSM occurred between 2008 and 2011 [19].

In December 2016, the first hepatitis A case was diagnosed in Tel Aviv district (Israel). By June 2017, 19 cases of HAV infection were noted. Seventeen patients were men, aged 22 to 41 years, who self-identified as MSM. There was 1 female patient with a travel history to India. Of the 15 MSM, 3 had travelled to Europe, and 1 to the United States. Phylogenetic analysis of HAV-positive samples showed that all sequences clustered with two of the three strains identified in the current European HAV outbreak [20].

The epidemiological analysis of this current HAV outbreak reported from many countries indicates that the only preventive and successful measure is vaccination against HAV.

Limitation of this study

Data about sexual orientation among our patients were not obtained and recorded.

Disclosure

Authors report no conflict of interest.

References

- Centers for Disease Control Prevention. Prevention of hepatitis
 A through active or passive immunization: Recommendation of the Advisory Committee on Immunization Practices (ACIP).
 MMWR Recomm Rep 1999; 48 (RR-12): 1-37.
- Robertson BH, Jansen RW, Khanna B, et al. Genetic relatedness of hepatitis A virus strains recovered from different geographical regions. J Gen Virol 1992; 73 (Pt6): 1365-1377.
- Widell A, Hansson BG, Moestrup T, et al. Increased occurrence of hepatitis A with cyclic outbreaks among drug addicts in a Swedish community. Infection 1983; 11: 198-200.
- Bell BP, Shapiro CN, Alter MJ, et al. The diverse pattern of hepatitis A epidemiology in the United States – implications for vaccination strategies. J Infect Dis 1998; 178: 1579-1584.
- Lu P, Byrd KK, Murphy TV. Hepatitis A vaccination coverage among adults 18-49 years traveling to a country of high or intermediate endemicity, United States. Vaccine 2013; 31: 2348-2357
- Lednar WM, Lemon SM, Kirkpatrick JW, et al. Frequency of illness associated with epidemic hepatitis A virus infections in adults. Am J Epidemiol 1985; 122: 226-233.
- Janaszek-Seydlita W, Bucholc B, Wiatrzyk A. Prevalence of anti-HAV antibodies in Warsaw population. Przegl Epidemiol 2007; 61: 675-682.
- 8. Ciocca M. Clinical course and consequences of hepatitis A infection. Vaccine 2000; 18 Suppl 1: S71-74.
- 9. WHO position paper on hepatitis A vaccines June 2012. Wkly Epidemiol Rec 2012; 87: 261-276.
- 10. Gossner CM, Severi E, Danielsson N, et al. Changing hepatitis A epidemiology in the European Union: new challenges and opportunities. Euro Surrveill 2015; 20. pii: 21101.
- 11. Michaelis K, Wenzel JJ, Stark K, et al. Hepatitis A virus infection and outbreaks in asylum seekers arriving to Germany, September 2015 to March 2016. Emerg Microbes Infect 2017; 6: e26.
- European Centre for Disease Prevention and Control (ECDC).
 Hepatitis A outbreaks in the EU/EEA mostly affecting men
 who have sex with men. Stockholm: ECDC; 19 Dec 2016.
 Available from: http://ecde.europa.eu/en/publications/Publications/13-12-2016-RRA-Hepatitis A-United Kingdom.pdf
- 13. Lanini S, Minosse C, Vairo F, et al. A large ongoing outbreak of hepatitis A predominantly affecting young males in Lazio, Italy; August 2016 March 2017. PLoS One 2017; 12: e0185428.
- 14. Werber D, Michaelis K, Hausner M, et al. Ongoing outbreaks of hepatitis A among men who have sex with men (MSM), Berlin, November 2016 to January 2017 linked to other German cities and European countries. Euro Surveill 2017; 22.
- 15. Freidl GS, Sonder GJ, Bovee LP, et al. Hepatitis A outbreak among men who have sex with men (MSM) predominantly linked with the EuroPride, the Netherlands, July 2016 to February 2017. Euro Surveill 2017; 22. pii: 30468.
- Beebeejaun K, Degala S, Balogun K, et al. Outbreak of hepatitis A associated with men who have sex with men (MSM), England, July 2016 to January 2017. Euro Surveill 2017; 22.
- 17. Charre C, Ramiere C, Roque-Alfonso AM, et al. Hepatitis A outbreak in HIV-infected MSM and in PrEP-using MSM despite a high level of immunity, Lyon, France, January to June 2017. Euro Surveill 2017; 22.

- 18. Raport Głównego Inspektoratu Sanitarnego, Departament Zapobiegania oraz Zwalczania Zakażeń i Chorób Zakaźnych u Ludzi. Choroby zakaźne i zatrucia w Polsce w 2017 roku. http://wwwold.pzh.gov.pl/oldpage/epimeld/2017/Ch_2017_ wstepne_dane.pdf
- 19. Bordi L, Rozera P, Scognamiglio P, et al. Monophyletic outbreak of hepatitis A involving HIV-infected men who have sex with men, Rome, Italy 2008-2009. J Clin Virol 2012; 54: 26-29.
- 20. Gozlan Y, Bar-Or I, Rakovsky A, et al. Ongoing hepatitis A among men who have sex with men (MSM) linked to outbreaks in Europe in Tel Aviv area, Israel, December 2016-June 2017. Euro Surveill 2017; 22. pii: 30575.