

Outbreak of severe Hepatitis A in Eastern Piedmont, Italy

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SUMMARY

Hepatitis A (HA) is caused by a hepatovirus from the family *Picornaviridae* (Hepatitis A Virus, HAV). Transmission occurs mainly by the orofaecal route through food or water contaminated by faeces. Sexual transmission has also been reported among men who have sex with men (MSM). From February to May 2017, 14 patients with HA were hospitalized at the University Hospital "Maggiore della Carità", Novara (Eastern Piedmont), Italy. One patient was two years old and was

therefore admitted to the Paediatric Unit, the remaining 13 to the Infectious Disease Unit. Two of the adults were female and the rest (11) were male. The male patients were MSM, and contracted the infection sexually; three of them were known to be HIV positive, while two had a new diagnosis of syphilis infection. Women contracted the infection from contaminated food.

Keywords: outbreak, hepatitis A.

INTRODUCTION

Hepatitis A (HA) is caused by an hepatovirus from the family *Picornaviridae* (Hepatitis A Virus, HAV). Transmission occurs mainly by orofaecal route through food or water contaminated by faeces. Sexual transmission has also been reported among men who have sex with men (MSM).

Even though HA has usually a benign outcome with full recovery, fulminant form with massive hepatic necrosis is possible and Centres for Disease Control and Prevention estimate case-fatality range from 0.3-0.6% for all ages and up to 1.8% among adults aged above 50 years [1].

Six genotypes of the virus have been described. Only genotypes from I to III infect man and are subdivided into subgenotypes A and B. The predominant subgenotype in Europe is IA [2, 3].

Estimated incidence of HA by the World Health Organization is about 1.4 million cases each year. The prevalence of Hepatitis A in Europe is variable and depends on the socio-economic level of the country. It is very low in Western Europe, intermediate or low in Eastern and Central Europe. Italy is a country with an intermediate endemic level, although in the last decade the incidence has decreased from 10 to 3.6 cases per 100.000 inhabitants per year between 1985 and 2004 and to 1.1 cases per 100.000 inhabitants in 2010 [4].

The incidence is higher in southern regions than in northern, because of the habit of eating raw seafood and for greater fecal contamination of the environment. The cases reported in Italy occur both as sporadic cases and in endemic-epidemic clusters. Some regions such as Puglia and Campania are considered endemic.

The most recent largest food borne epidemic of HAV infection, involved a wide geographic area in Europe with 1.589 cases in 13 EU/EEA countries. Cases associated with this epidemic have been described from 1 January 2013 to 31 August 2014. The epidemic was attributed to the con-

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sumption of contaminated frozen berries, especially Bulgarian blackberries and Polish redcurrants. During this epidemic 1.438 cases have been reported in Italy. The sequence GenBank number of the outbreak strain isolated in Italy in May 2013 was KF182323 and the subgenotype was IA [5]. A previous epidemic in Italy was described in Rome between 2008 and 2010. Virological analysis showed that it was caused by a monophyletic genotype IA HAV strain, circulating around the same period also in other European countries. During this epidemic, proportion of MSM was high, and among these 25% were HIV positive [6]. Since February 2016, three distinct strains of the same sub-genotype IA caused 287 cases of HA in Europe, as reported by 13 EU countries [7]. The Italian Surveillance System of Acute Hepatitis (SEIEVA: Integrated Epidemiological System for Acute Viral Hepatitis) has collected 583 cases of HA between August 2016 and February 2017 [8]. In this study we compare epidemiological, clinical and laboratory features of patients admitted for HA to University Hospital “Maggiore della Carità”, Novara during 2017 to historical cases collected from 2010.

PATIENTS AND METHODS

All patients with a diagnosis of HA admitted to our University Hospital were included in the analysis, recording clinical, epidemiological and laboratory data. A comparison with historical cases from 2010 was performed. Epidemiological data were retrieved from Public Health Department notification. Clinical and laboratory data were collected from laboratory records.

RESULTS

From February to May 2017, 14 patients with HA have been hospitalized at the University Hospital “Maggiore della Carità”, Novara (Eastern Piedmont Region), Italy. One patient was 2 years old and was therefore admitted in Pediatric Unit, the remaining 13 in Infectious Disease Unit. Among the adults two were female and 11 were male. Male patients were MSM, and contracted the infection sexually; three of them were known to be HIV positive, while two had a new diagnosis of syphilis infection. Women contracted the infection from contaminated food as well as the youngest patient admitted in Paediatric Unit.

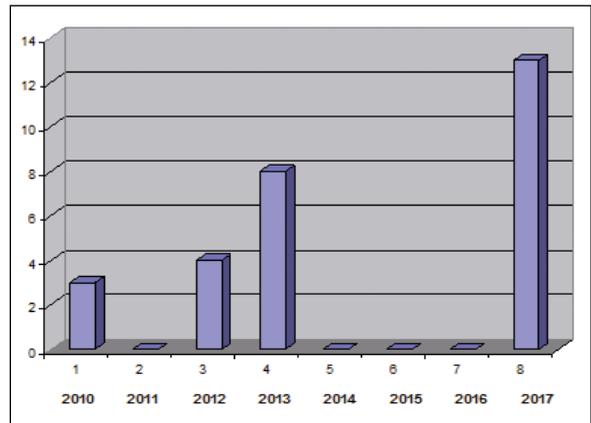


Figure 1 - Cases of HA in adults admitted at University Hospital “Maggiore della Carità”, Novara.

In the same hospital 15 cases of HA in adults have been admitted from 2010 to 2013 (three in 2010, four in 2010, eight in 2013), while no cases have been reported in 2014, 2015, 2016. Five paediatric cases have been also reported in the same period (two in 2013, three in 2014) (Figure 1).

Demographic and clinical differences between adult patients with HA in 2010-2013 and 2017 are summarized in Table 1. While the way of transmission of recent cases was predominantly sexual in MSM, in the previous it was food borne in 11 out of 15 cases and unknown in 4 cases. Mean age was 42 years in 2017 (range 25-55), and 38 in 2010-2013 (range 16-59). Recent cases had more severe

Table 1 - Demographic and clinical characteristics of patients with HA.

	2010-2013	2017
No. cases	15	13
Sex		
Male	12	11
Female	3	2
Mean age (years)	38	43
Risk factor		
MSM	0	11
Foodborne	11	2
Unknown	4	0
Mean AST peak (U/mL)	2399	3902
range	(4854-132)	(8391-1196)
Encephalopathy	0	2
Mean INR peak	1.14	1.42
range	(0.95-1.33)	(1-2.49)

clinical presentation than those in 2010-2013 with higher transaminase peak mean ALT value 3902 U/l (range 8391-1196 U/l) and 2399 U/l (range 4854-132 U/l) respectively, and more frequent alteration of coagulation. In fact, in 2017 mean INR was 1.42 (range 1-2.49) and 6 patients out of 13 had INR above 1.2, in 2010-2013 mean INR was 1.14 (range 0.95-1.33) and only 3 patients out of 15 (20%) had INR above 1.2. Mild symptoms of encephalopathy with hyperammonemia has been documented in 2 out of 13 patients in 2017. None of the patient died or had a fulminant form and everyone had a full recovery. All the patients in 2010- 2013 were HCV and HBsAg negative. In 2017 all were HCV negative and one HBsAg positive (Table 1).

Blood samples were collected and sent to National Health Institute (Istituto Superiore della Sanità, ISS) for the identification of the strains involved and comparison with strains circulating in other Italian regions.

DISCUSSION

Recently, the improvement of hygiene conditions has changed HA epidemiology. In fact, sexual transmission, and in particular in MSM, is overcoming the traditional way of transmission through contaminated food and water.

Therefore, it's important to increase prevention measures for HAV infection by testing for HAV antibodies subjects in care in sexually transmitted infections (STI) centres or who live with HIV infection. HAV vaccination provides protection in more than 90% of subjects vaccinated with a single dose and in more than 95% of subjects completing the vaccine schedule it is therefore a highly effective intervention [9-11].

Viral infections, which were once confined to small areas of high prevalence, spread across Europe with work and touristic travels. Subjects who are at risk of STI should be adequately informed about areas with ongoing epidemic outbreaks. Systems of infectious diseases notification and reporting and genotype analysis are necessary in order to identify epidemic clusters or outbreaks especially if a viral disease shows more severe clinical features and if a more aggressive viral strain is suspected.

Finally, acute infections such as HA may represent

a sentinel pathology highlighting the increase of other sexually transmitted infections (STI) circulation, and may offer the chance to diagnose early chronic and silent infections such as syphilis and HIV.

Conflict of interest

The authors have no conflicts of interest to disclose.

REFERENCES

- [1] Centers for Disease Control and Prevention. Hepatitis A In *Epidemiology and Prevention of Vaccine-Preventable Diseases* (Hamborsky J., Kroger A., Wolfe C., Eds). 135-148, 2015. Public Health Foundation, Washington D.C.
- [2] Vaughan G., Goncalves Rossi L.M., Forbi J.C., et al. Hepatitis A virus: host interactions, molecular epidemiology and evolution. *Infect. Genet. Evol.* 21, 227-243, 2014.
- [3] Desbois D., Couturier E., Mackiewicz V., et al. Epidemiology and genetic characterization of hepatitis A virus genotype IIA. *J. Clin. Microbiol.* 48, 3306-3315, 2010.
- [4] Gallone M.F., Desiante F., Gallone M.S., Barbuti G., Tafuri S., Germinario C. Serosurveillance of hepatitis A in a region which adopted the universal mass vaccination. *Medicine.* 96, e5884, 2017.
- [5] Severi E., Verhoef L., Thornton L., et al. Large and prolonged food-borne hepatitis A outbreak in Europe associated with consumption of frozen berries, 2013 to 2014. *Euro Surveill.* 20, 21192, 2015.
- [6] Bordi L., Rozera G., 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.* 54, 26-29, 2012.
- [7] Beebejaun 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.* 22, 30454, 2017.
- [8] EpiCentro - Istituto Superiore di Sanità. Epatite virale. Retrieved from <http://www.epicentro.iss.it/problemi/epatite/EpatiteAMsm.asp> Last accessed June 25, 2017.
- [9] André F.E. Universal mass vaccination against hepatitis A. *Curr. Topics Microbiol. Immunol.* 304, 95-114, 2006.
- [10] Cotter S.M., Sansom S., Long T., et al. Outbreak of hepatitis A among men who have sex with men: implications for hepatitis A vaccination strategies. *J. Infect. Dis.* 187, 1235-1240, 2003.
- [11] Friedman M.S., Blake P.A., Koehler J.E., Hutwagner L.C., Toomey K.E. Factors influencing a communitywide campaign to administer hepatitis A vaccine to men who have sex with men. *Am. J. Public Health.* 90, 1942-1946, 2000.