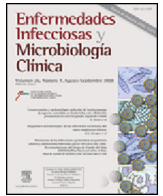




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Original article

Hepatitis A outbreak associated with a food handler in Bizkaia, 2017[☆]

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ABSTRACT

Introduction: The reporting of one case of hepatitis A in a food handler at a bakery and five cases in employees of a company after consuming products from the same bakery prompted an outbreak investigation.

Methods: Outbreak cases were defined as individuals with laboratory-confirmed hepatitis A (HAV) infection, with symptoms which started in June and who, during the incubation period, worked with the food handler and/or had close contact with him and/or consumed products from the bakery. Epidemiologic questionnaires were performed and blood samples were obtained to be tested for the presence of anti-hepatitis A antibodies. Molecular characterisation was carried out by PCR, sequencing of the VP1/2A region and phylogenetic analysis with the maximum likelihood estimation method, bootstrap 1000 (MEGA 7.0 software).

Results: A total of 14 primary hepatitis A cases were identified: eleven cases related to the consumption of products from the bakery, two cases among co-workers of the food handler, and one case was a household contact. All 12 sequenced viruses were genotype IA, matching one of the strains (RIVM-HAV16-090) responsible for the outbreaks occurring at that time in Europe, mostly affecting men who have sex with men.

Conclusions: HAV vaccination of at-risk groups should be reinforced in order to prevent future outbreaks. Increasing the use of molecular typing in hepatitis A cases could improve the investigation of outbreaks, which can be expected to increase in the future because of decreasing immunity in the population.

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Brote de hepatitis A asociado a un manipulador de alimentos en Bizkaia, 2017

RESUMEN

Introducción: La notificación de un caso de hepatitis A en un manipulador de alimentos de una pastelería y de 5 casos en trabajadores de una empresa tras consumir productos de la misma dio lugar a una investigación de brote.

Métodos: Se definieron como casos las personas con infección por el virus de la hepatitis A (VHA) confirmada por el laboratorio, con comienzo de síntomas en junio y que, durante el periodo de incubación,

Palabras clave:

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trabajaron con el manipulador y/o tuvieron contacto estrecho con él y/o consumieron productos de la pastelería. Se realizó una encuesta epidemiológica y se tomaron muestras de sangre para analizar la presencia de anticuerpos anti-hepatitis A. Se realizó la caracterización molecular por PCR, secuenciación de la región VP1/2A y análisis filogenético con el método de máxima verosimilitud, *bootstrap* 1000 (*software* MEGA 7.0).

Resultados: Se identificaron 14 casos primarios: 11 relacionados con el consumo de productos de la pastelería, 2 compañeros de trabajo del manipulador y un contacto familiar. Los 12 virus secuenciados eran genotipo IA, coincidiendo con una de las cepas (RIVM-HAV16-090) responsable de los brotes producidos en ese momento en Europa y que afectaban fundamentalmente a hombres que tienen sexo con hombres.

Conclusiones: Se debería reforzar la vacunación frente al VHA de grupos de riesgo para prevenir brotes futuros. La implementación del uso del tipado molecular en casos de hepatitis A podría mejorar la investigación de brotes, que se puede esperar que aumenten en el futuro debido al descenso de inmunidad en la población.

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Introduction

Hepatitis A is a disease of the liver caused by Hepatovirus A (hepatitis A virus [HAV]), an RNA virus belonging to the *Picornaviridae* family with only one serotype and 6 genotypes (genotypes I to VI).^{1,2} Genotypes I, II and III are divided into subtypes A and B and infect humans.¹ Genotype I is the most frequently reported worldwide and subgenotype IA is more common than IB.^{1,3}

HAV is transmitted by the faecal–oral route, either by ingesting contaminated food or water or by direct contact with an infected person. Almost all patients recover fully and acquire life-long immunity.⁴ The mean incubation period is 28 days (range: 15–50 days). Children are often asymptomatic and the severity of disease generally increases with age. Symptoms can include fever, nausea, choluria and jaundice. The period of peak infectivity corresponds to the second half of the incubation period and rapidly decreases after the onset of symptoms.⁵

In developed countries with good sanitary and hygienic conditions, infection rates are low and most cases occur in high-risk groups, such as injecting drug users and men who have sex with men (MSM), and in people who travel to areas of high endemicity. Food safety, hand washing and the hepatitis A vaccine are the most effective ways to combat the disease.^{4,5} In Spain, the vaccine is recommended to prevent infection in sexual contacts of infected individuals and for high-risk groups, including people infected with the human immunodeficiency virus (HIV) and MSM.

HAV is stable in the environment, especially when associated with organic matter, and is resistant to low pH and heating. These characteristics facilitate the likelihood of transmission by contamination.³ The source of most reported foodborne hepatitis A outbreaks has been infected food handlers. Contamination of a food product can occur at any point during cultivation, harvesting, processing, distribution or preparation.⁶

Recognising foodborne transmission may be difficult because patients may have difficulty recalling food products consumed during the 2–6 weeks before illness, some exposed persons may have subclinical infection and others may have preexisting immunity.⁶

The seroprevalence survey conducted in the Basque Country in 2009⁷ found a prevalence of anti-HAV antibodies of <10% in individuals under the age of 24 years, 23% in the 25–29 age group, 38% in the 30–39 age group and 76% in the 40–59 age group. According to WHO, the level of endemicity in our country is classified as very low (<50% are immune by age 30 years), which may make foodborne outbreaks possible.⁸

Several outbreaks of hepatitis A have been associated with bakeries. In the US, outbreaks in 1968, 1976 and 1994 were associated with bakery employees responsible for applying sugar glaze to baked goods.^{9,10} In Germany, two outbreaks in 2004 and 2012 were

also associated with bakery employees who contaminated the bakery products implicated in the outbreak.^{10,11}

In Biscay, which had a population of almost 1,140,000 in 2016, 10–32 cases of hepatitis A were reported each year between 2010 and 2016 (incidence rate: 0.88–2.96 per 100,000 people). However, between January and May 2017, 32 cases had already been reported. This increase was associated with a major outbreak in Europe affecting several countries that started in June 2016 and mostly affecting MSM.^{12,13}

On 1 June 2017, the Preventive Medicine Department of a hospital in Biscay informed the Epidemiology Unit of Biscay of a case of hepatitis A affecting a person who worked as a food handler at bakery “A”. The patient first experienced symptoms (fever, loss of appetite, nausea, choluria, vomiting, abdominal pain) on 20 May and then developed jaundice on 27 May and was hospitalised from 30 May to June 2. Blood tests revealed the presence of anti-HAV IgM and IgG antibodies and high levels of aminotransferases. The patient, who had been working at the bakery until 28 May, was a HIV-positive MSM who had not been vaccinated against hepatitis A.

Subsequently, on 21 June 2017, the machining company “B”, located in another town in Biscay, reported that 5 of its employees had been hospitalised with hepatitis A after consuming cream-filled doughnuts made by bakery “A” on 15 May. This prompted an investigation to determine the source and extent of the outbreak and to prevent further cases.

Methods

Primary cases of the outbreak were defined as those individuals with laboratory-confirmed hepatitis A infection (presence of hepatitis A-specific IgM antibodies in serum) whose symptoms had started in June and who, during the incubation period: (a) had worked with the food handler at bakery “A”, and/or (b) had been in close contact with the food handler, and/or (c) had consumed products made at bakery “A”.

Secondary cases were defined as those individuals with laboratory-confirmed hepatitis A infection who had not been in contact with the food handler or consumed products made by the bakery but had been in contact with a primary case during the incubation period. All patients were asked to complete a standard hepatitis A questionnaire and were asked about their consumption of bakery products.

Blood samples were taken from the bakery and machining company employees to test for the presence of anti-hepatitis A antibodies. Serum samples of hepatitis A-positive patients were sent to the Hepatitis Unit of the National Centre of Microbiology, Instituto de Salud Carlos III, Majadahonda (Madrid) for PCR-based molecular

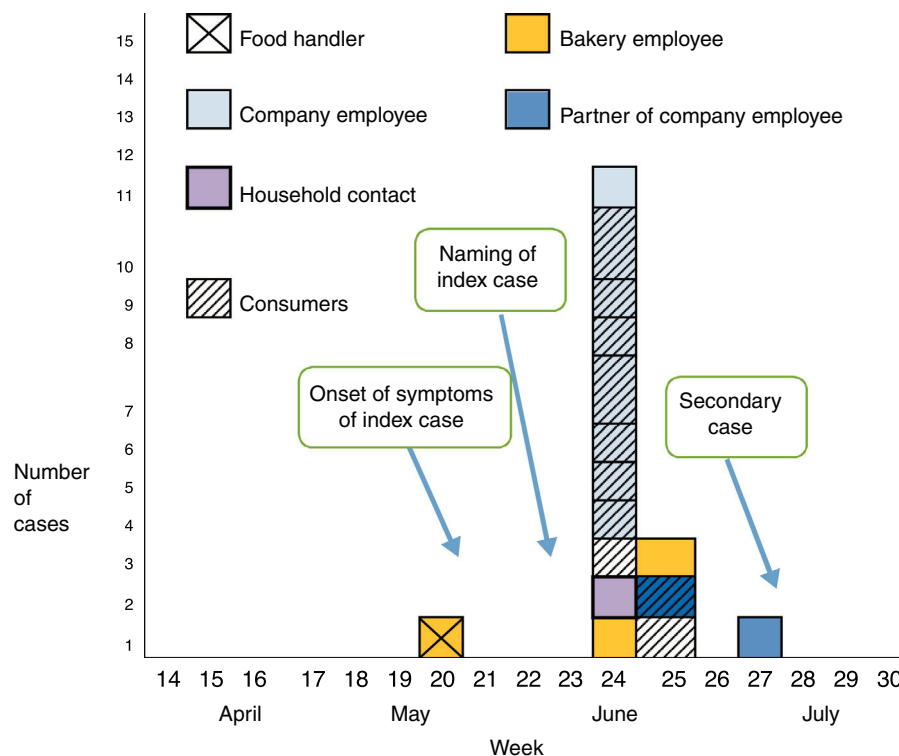


Fig. 1. Week of onset of symptoms of hepatitis A cases.

characterisation, sequencing of the VP1/2A region and phylogenetic analysis using the maximum likelihood method, *bootstrap* 1000 (MEGA 7.0 software). Public Health technicians inspected bakery “A” on 21 and 23 June.

Results

Description of the outbreak

Sixteen cases of hepatitis A were identified in this outbreak: the index case, 14 primary cases and one secondary case. The index case first began to experience symptoms on 20 May but continued to work at the bakery until 28 May. Ten of the primary cases had consumed products made at the bakery (8 from the machining company plus 2 others), three had direct contact with the index case (2 at work and 1 was a household contact), and one case worked at the machining company but stated he had not consumed any bakery products. The onset of symptoms occurred between 12 and 23 June for the primary cases. The secondary case, who was the partner of one of the affected employees from company “B”, started to experience symptoms on 6 July, 24 days after the primary case’s onset of symptoms.

The age of the cases ranged between 15 and 50 years (mean: 34; median: 36). Ten cases were male (64%) and 6 were female.

Fig. 1 shows the progress of the cases over time. Symptoms started in epidemiological week 20 for the index case, in weeks 24–25 for the primary cases and in week 27 for the secondary case.

Of the other 4 employees who worked at the same bakery as the food handler, 2 contracted hepatitis A and 2 were immune (IgM-negative and IgG-positive).

At the machining company, 19 people stated that they had consumed doughnuts made by bakery “A”. Of these, 7 contracted hepatitis A and 5 of the remaining 12 were immune (IgM-negative

and IgG-positive). In other words, 7 of the 14 susceptible individuals who had consumed the doughnuts developed hepatitis A. One of the 10 employees who stated that they had not consumed the doughnuts developed hepatitis A. The partner of one of the cases, who had eaten the same doughnuts at home, also developed hepatitis A. All of the individuals whose blood tests showed they were immune were over the age of 50 years. Blood samples were taken for sequencing and phylogenetic analysis in 12 cases. All sequenced viruses were genotype 1A, with high homology to the RIVM-HAV16-090 sequence (Fig. 2).

Outbreak control measures

An initial inspection of the bakery was conducted on 21 June, which recommended improving hygiene measures, including hand washing, use of gloves and tongs, and surface cleaning. On 23 June, after more cases were reported, food preparation was suspended as a precautionary measure and the facilities were thoroughly cleaned and disinfected. All products that could have been infected were also destroyed. Two employees from the bakery (susceptible cases) were vaccinated against hepatitis A and a new employee who began to work at the bakery at a later date was also vaccinated.

Two technicians from the Epidemiology Unit visited machining company “B” on 26 June to inform workers of the situation, conduct surveys and blood draws and administer the hepatitis A vaccine.

All of the individuals affected were given information on how to prevent secondary cases. With regard to the household contacts of those affected, individuals under the age of 50 years were advised to get the hepatitis A vaccine, while those aged 50–70 years were advised to have a blood test and to get the vaccine if their blood test results were negative. Those aged 70 years and over were deemed to have natural immunity.

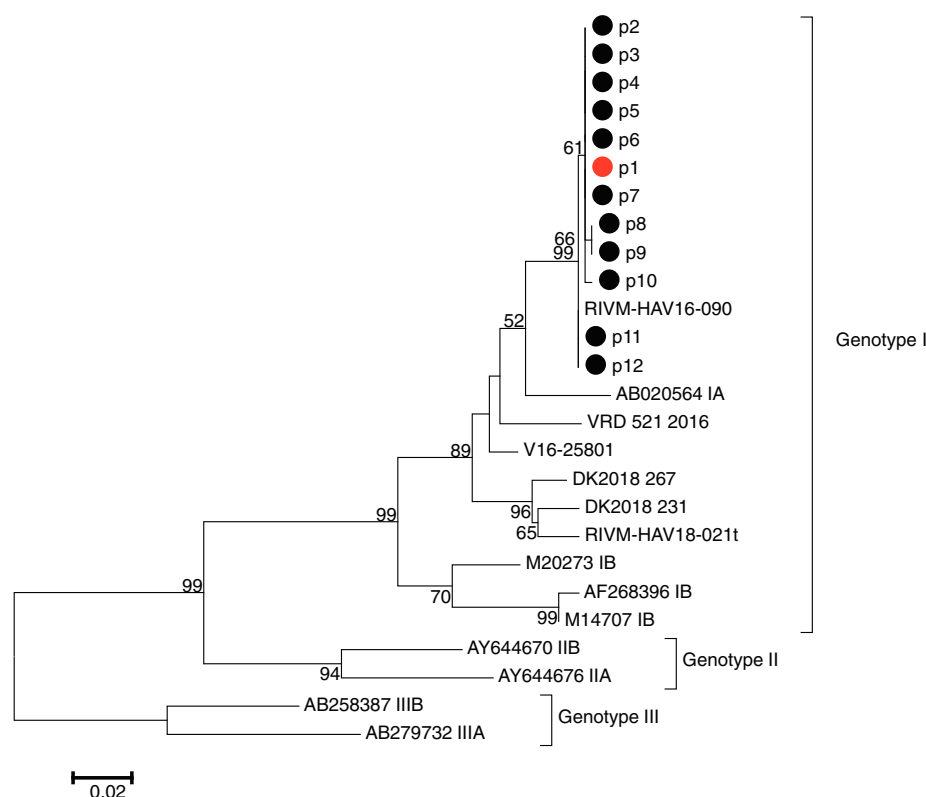


Fig. 2. Phylogenetic tree of 12 sequences from patients 1 (index case, red dot) to 12. VP1/2A region (maximum likelihood method, bootstrap 1000, MEGA 7.0 software).

Discussion

This report describes an outbreak of hepatitis A associated with a food handler from a bakery in Biscay, with 16 cases developing symptoms between 20 May and 6 July 2017. Due to the long incubation period of hepatitis A, some cases related to the outbreak may have been overlooked due to a lack of recall regarding food consumption. The food handler first experienced symptoms on 20 May and developed jaundice on 27 May. However, he continued to work until 28 May. In other words, he was working during the period of peak infectivity.

This outbreak was associated with an increase in cases of hepatitis A in Europe, which started in June 2016, with 3 distinct hepatitis A genotype IA strains (RIVM-HAV16-090, VRD 521 and V16-25801), predominantly affecting MSM. At that time, hepatitis A transmission was not limited to MSM but had affected the entire population.

The viruses responsible for this outbreak were genotype IA strains with the RIVM-HAV16-090 sequence, which matched one of the strains responsible for the European outbreaks. This strain, which is associated with the EuroPride event that took place in Amsterdam in 2016, has caused outbreaks in several European countries^{14–17} and is identical to the strain that has caused a major outbreak among MSM in Taiwan since June 2015.^{18,19}

Of the 113 cases reported in Biscay in 2017, molecular analyses were performed in 67 cases. All were genotype IA, 47 (70%) had the RIVM-HAV16-090 sequence and 20 (30%) had the VRD 521 sequence (UK). Both sequences match the cases detected in the European outbreaks.

In countries of low endemicity, HAV outbreaks among MSM have been reported since the early 1980s.^{20–22} Hepatitis A outbreaks among MSM were also reported in several European countries in 2008 and 2009.^{23–26} With regard to these outbreaks,

82 cases of hepatitis A were reported in Biscay in 2009 and almost 90% of these affected men aged between 20 and 50 years.

The food handler responsible for this outbreak was not vaccinated against hepatitis A, despite belonging to a group for which vaccination is recommended.^{12,22} The importance of HAV vaccination must be reinforced in high-risk groups to prevent future outbreaks. Nevertheless, it is also important to take into account vaccine availability, which may have an impact on the ability to vaccinate a large number of individuals over a short period of time.¹⁴

Increasing the use of molecular typing in cases of hepatitis A and comparing sequences with those found regionally, nationally or internationally could improve the investigation of outbreaks, which can be expected to increase in the future due to decreasing immunity among the population.

Conflicts of interest

None.

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