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Foodborne outbreaks of hepatitis A in a low endemic country: an emerging problem?

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SUMMARY

This paper describes 2 outbreaks of hepatitis A infection in Finland, a very low endemic area of hepatitis A infection, where a large proportion of the population is now susceptible to infection by hepatitis A virus (HAV). The first outbreak involved people attending several schools and day-care centres; the second employees of several bank branches in a different city. The initial investigation revealed that both were related to food distributed widely from separate central kitchens. Two separate case-control studies implicated imported salad food items as the most likely vehicle of infection. HAV was detected in the stool of cases from both outbreaks using reverse-transcriptase polymerase chain reaction; however, comparison of viral genome sequences proved that the viruses were of different origin and hence the outbreaks, although occurring simultaneously, were not linked. Foodborne outbreaks of HAV may represent an increasing problem in populations not immune to HAV.

INTRODUCTION

The majority of cases of hepatitis A infection in low endemic areas of the world are sporadic and related to household contact with a case, travel or occur in certain risk groups [1, 2]. Outbreaks of hepatitis A virus (HAV) infection have been reported in nosocomial and institutional settings [3–5] and amongst those risk groups such as injecting drug users [6–8], homosexual men [9] and occasionally those exposed to contaminated blood products [10, 11]. A minority of outbreaks are related to food or water-borne spread [12]. Foodborne outbreaks of hepatitis A infection have been reported in association with food contaminated either by infected food handlers [13], or prior to sale. Foods involved include shellfish [14], milk [15], frozen strawberries and raspberries [16–18] and salad [19, 20]. On occasions these foods have been widely distributed [17, 20].

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Currently, Finland and other Nordic countries have a very low incidence of HAV infection. Due to declining population immunity there are an increasing number of adults susceptible to infection; sero-epidemiological surveys show that over 98% of those < 45 years are seronegative for HAV antibodies [21, 22]. Most reported cases in recent years are sporadic and are frequently related to travel to highly endemic areas of the world. However, a marked increase in domestic cases occurred in 1994 with an outbreak of several hundred cases, many of whom were intravenous drug users in the Finnish capital, Helsinki [8]. No foodborne outbreaks of hepatitis A have been described in Finland in recent years.

Over a 1 month period in 1996, two clusters of hepatitis A cases occurred in Finland. Outbreak 1 began in October 1996 when several cases of acute hepatitis A infection were reported amongst students and a food handler at a secondary school in Jyväskylä, a town 270 km north of Helsinki. The school had 550 staff

and pupils aged 7–15 years. The school kitchen was responsible for distributing a total of 2900 meals daily to 8 schools and 8 day-care centres. During 1995, two cases of domestically acquired acute HAV infection had been notified from the Jyväskylä area.

Four days later several cases of acute hepatitis A infection were reported amongst bank employees working in 4 separate branches in Greater Helsinki (outbreak 2). A central kitchen daily distributed 1500 meals to these and 57 other workplaces located in the Greater Helsinki area. During 1993 before the HAV infection outbreak related to injecting drug users, only 5 cases of domestically acquired acute HAV infection were notified from this region.

An investigation was undertaken to determine the magnitude of the outbreaks, define the source and vehicle of infection and any possible link between the clusters.

MATERIALS AND METHODS

Epidemiological investigations

In both outbreaks, a case of acute hepatitis A infection was defined as an individual whose serum was positive for IgM to HAV (anti-HAV) after 1 September 1996. Active case searching for acute cases of HAV infection was undertaken at local hospitals, health-care centres and virological laboratories.

In-depth interviews were conducted with identified cases regarding symptoms and common exposures in the 15 days before the first case and the 50 days before the last case. We elicited potential exposures to food and water, school and work-related gatherings, illicit drug use, overseas travel and contact with recently jaundiced individuals. An unmatched case-control study was conducted in both outbreaks to examine exposures related to disease acquisition amongst primary cases in the 3–5 weeks before disease onset; in particular, consumption of food prepared from the kitchens. Controls were selected by systematic sampling and were defined as a susceptible work or schoolplace colleague who was anti-HAV negative and who had also consumed meals prepared from the central kitchen.

Laboratory investigations

Serum specimens were analysed by EIA for total anti-HAV and IgM anti-HAV using commercially available kits. Stool specimens were collected from acute cases and screened for the presence of viral RNA using reverse transcription and PCR amplification. The cDNA was amplified by primers covering the region coding for the C-terminus of VP1 and N-terminus of 2A polypeptides [23], the amplicons were cloned in pGEM-T vector (Promega Inc., Wisconsin, USA), and the nucleotide sequence was determined by using the dideoxynucleotide chain termination method.

Computer analysis

All data were analysed by Epi Info (version 6.04) with calculation of the odds ratios and 95% confidence intervals for each of the risk factors. Genetic analyses were carried out using the Genetics Computer Group software package [24]. A 168-nucleotide long partial sequence was used in the comparison.

RESULTS

Epidemiological investigations

Outbreak 1

Eighteen cases became ill with fever between 3 and 11 October (Fig. 1). At 2 schools there were 12 cases in pupils aged 12–15 years from 8 different classes and also in 2 food handler-cases and 1 teacher; at a third school there was 1 teacher-case. Sixteen of the primary cases were icteric and 9 were hospitalized for 1–6 days.

Preliminary case interviews indicated no common exposures outside the school; however, all cases ate meals prepared from the main kitchen in the 3–5 weeks prior to illness. A food preference questionnaire was administered to 14 primary cases and the 62 susceptible classmate, teacher and food handler controls. One food handler control was excluded due to previous HAV infection and no asymptomatic cases were detected amongst the controls.

All but one case (93%) compared to 76% of controls (OR 4·1, 95% CI 0·5–90) recalled eating salad. Other food items were equally consumed by cases and controls. Anecdotally, in-depth interviews with 2 cases found that neither usually ate meals prepared from the kitchen, but they had both consumed school salad once at the end of August.

Outbreak 2

Twelve cases became ill with fever between 9 and 24 October (Fig. 1). The median age of cases was 42·5 years (range 26–55 years). All except one were employed by a major bank and worked in 9 different

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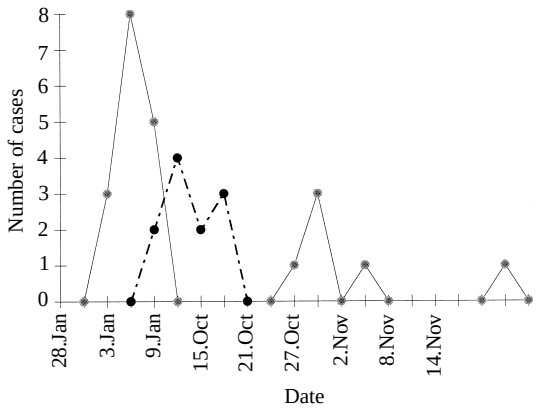

Fig. 1. Number of cases of hepatitis A infection by date of onset, Jyväskylä and Helsinki, Finland, 1996 (--●-- Helsinki, —◉— Jyväskylä).

branch offices around the city. The other case worked in a post office. All but one case were icteric and 3 were hospitalized. No common exposures were found except all cases ate meals prepared from the central kitchen supplying all the workplaces including the post office. A food recall questionnaire was administered to all 12 cases and 33 susceptible workplace controls. Two controls were excluded due to previous HAV infection and no subclinical cases were detected amongst controls.

All the cases and controls had consumed at least one food item listed on the questionnaire. Cases were more likely than controls to have eaten celery (OR 9·8, 95% CI 1·1–221·8) and tomato (OR 8·7, 95% CI 1·0–197·5) served from the central kitchen.

Environmental investigations

All food handlers besides the 2 known primary cases, who fell ill simultaneously with the other cases, at the 2 kitchens were IgM anti-HAV negative. Hygiene standards in both kitchens were adequate. The wholesalers of the suspect salad in the Jyväskylä outbreak were traced. Several of the salad items had been grown in Finland. All 20 workers employed on the farm where they had been cultivated were IgM anti-HAV negative. The other salad items, cucumber and peas, had been imported. In the Helsinki outbreak, several of the suspect salad components were imported.

Laboratory investigations

HAV RNA was detected by PCR amplification in 2 stool specimens from the Jyväskylä outbreak and in a single stool specimen in the Helsinki outbreak. The nucleic acid capsid sequence from the 2 Jyväskylä strains was identical apart from a single base pair difference. The viral capsid sequence from the Helsinki outbreak had 9 base pair differences from the Jyväskylä isolate and so represented a different strain. In addition both strains were significantly different from strains sequenced during the Helsinki drug users' outbreak in 1994 [8].

Control measures

Gammaglobulin was administered to case-contacts; and cases were excluded from schools and day-care centres while symptomatic. Despite these measures in Jyväskylä, 6 secondary cases occurred in the following 2 months. In Helsinki only a single secondary case was reported in December.

DISCUSSION

Our data suggest that 2 unlinked foodborne outbreaks of hepatitis A occurred in Finland during October 1996–January 1997 which were related to consumption of contaminated imported salad. The food was prepared by central kitchens and distributed to a large number of workplaces and schools in 2 Finnish cities.

There are several potential biases associated with our case-control study; the long incubation period of 3–5 weeks produces problems of recall of specific events. Although food menus were available, there were no unique circumstances to help develop a more specific food hypothesis; thus a large number of food items were investigated and some may have approached significance purely by chance. The use of a food preference questionnaire which asks about usual food habits, rather than recalling consumption of foods on a particular date, may be a more practical alternative [19]. In addition the studies suffered from lack of power due to the small number of cases. The high proportion of asymptomatic cases in a young population means that seroepidemiology can play an important role both in case finding to increase power and also in avoiding misclassification of cases as controls. However bleeding of young children is not always acceptable and salivary testing for IgM, a technique we hope to use in future outbreaks, is a suitable alternative in an outbreak [25–27].

Foodborne outbreaks of hepatitis A, including those related to consumption of salad, have been previously documented [19, 20]. Contamination prior to retailing is presumably related to agricultural practices such as irrigation with faecally contaminated

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water in highly endemic areas of HAV infection. This may represent an increasing problem with more international movement of food from these regions to very low endemic areas where a large proportion of the population are non-immune to HAV. The increasing centralization of food preparation and distribution mean that the potential number exposed to contaminated food may be large. In these outbreaks the 2 kitchens were daily responsible for distributing a total of 4400 meals. The small number of cases detected may have been due to sparse contamination of the food.

A low incidence of hepatitis A infection in Finland for several decades has resulted in a large susceptible adult population thus shifting the age distribution of cases. Indeed, the median age of cases in the Helsinki outbreak was 42 years and only 2 of a systematic sample of 35 individuals from the at-risk population were found to have evidence of previous infection. It has been suggested that adults suffer from more severe disease [28]. Certainly in both outbreaks there was significant morbidity, but also amongst the schoolchildren: 9 of the 17 cases in the Jyväskylä outbreak compared to 3 of the 12 cases in the Helsinki outbreak were hospitalized. Many of the cases were absent from work or school for prolonged periods. In the Helsinki outbreak, one adult had prolonged jaundice requiring repeated hospital admissions and another had her cancer chemotherapy markedly delayed due to persistently elevated aminotransferase levels.

Despite the widespread administration of gammaglobulin in both outbreaks a significant number of secondary cases occurred in Jyväskylä. Many of the these latter were related to contact with initially undetected asymptomatic cases from school or day-care settings – a well-documented environment for maintenance of viral circulation [5]. Serological studies amongst adults suggest that 76–96% are symptomatic [28], which confirms the experience in Helsinki where good coverage with gammaglobulin of contacts of symptomatic cases presumably contributed to the low secondary attack rate.

RT-PCR sequence analysis played an important role in defining the epidemiology of these outbreaks. It was suspected that the 2 outbreaks were due to a common source as they were temporally linked and both were probably related to consumption of contaminated imported salad. However, PCR sequence analysis of viral isolates indicated that the 2 outbreaks were associated with different virus strains and so were not linked. Libraries of HAV genomic sequences are now becoming established and these molecular epidemiological techniques should play an increasingly important role in the investigation of these scenarios. These outbreaks may represent an increasing problem with the international movement of foodstuffs and the largely susceptible population in very low endemic areas, with implications for outbreak investigation and control.

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