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Outbreak of Hepatitis A caused by Groundwater Contamination in a Long-term Psychiatric Hospital in Korea

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장기 요양 정신병원에서 지하수 오염에 의하여 발생한 A형간염 집단발병

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= Abstract =

목적: 2017년 지하수를 식수로 사용하고 있는 한 장기요양 정신병원(H병원)에서 A형간염 환자가 집단 발병하여 이에 대한 역학조사를 실시하고 조치 결과를 기술하고자 하였다.

방법: 노출기간 동안 H병원의 근로자 및 재원 환자 234명을 대상으로 사례군 조사 디자인으로 역학조사를 실시하였고, IgM, IgG 혈청검사 및 A형간염 바이러스(HAV)에 대한 PCR검사를 시행하였다. 또한 오염원으로 의심되는 지하수, 병원에서 제공되는 식품 및 인근 저수지의 물에서 HAV 검사를 실시하였고, 검출된 HAV는 유전형 검사를 진행하였다.

결과: H병원 환자 및 직원 234명 중 IgG 양성인 168명을 제외한 66명 중 19명이 최종적으로 HAV 감염자로 확인되어 감수성자 중 발병률은 28.8%로 나타났다. 환자, 지하수, 식품(석박지) 및 저수지에서 동일 유전형의 HAV가 검출되어 지하수 오염에 의한 집단발병으로 결론 내렸으나, 최초 오염원은 확인하지 못하였다. 유행 종결 선언 이후 지하수에 대한 관리로 염소소독과 UV 조사를 하였음에도 불구하고 6개월 동안 지속적으로 HAV가 검출되어 새로운 관정을 개발하여 상황을 종결하였다.

결론: 본 연구에서 지하수를 식수로 사용하는 장기요양 정신병원에서 지하수 오염에 의한 19명의 HAV 집단발병을 조사하였다. HAV 항체가 없는 대상자 중에서 HAV의 높은 발병률을 확인하였다. 지하수 수질검사에서 바이러스 검사는 포함되어 있지 않기 때문에 지하수가 HAV에 오염 시 HAV 집단발병 가능성이 높고 상당기간 지속적으로 검출되기 때문에 지하수에 대한 관리지침에 바이러스 검출을 위한 방안을 추가하고 관련 법을 정비할 필요가 있다.

키워드: A형간염, 집단발병, 지하수

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INTRODUCTION

Hepatitis A virus (HAV) is a positive-strand RNA virus that causes infection through a fecal-oral transmission pathway. After the virus enters the bloodstream through the intestinal tract, it proliferates in hepatocytes. The virus is secreted into the intestines through bile and is discharged through stool. HAV is resistant to treatment with heat, acid, and various chemicals and can propagate through contaminated water and food [1, 2]. HAV has a minimum incubation period of 15 days and a maximum incubation period of 50 days(average 28), a relatively longer incubation period than other food- and water-borne pathogens [3]. Patients with HAV often describe a mild illness, 1 to 7 days before the onset of dark urine. In the early stages, flu-like symptoms are common (fever, mild headache, malaise, and fatigue). Loss of appetite is a common, nausea and vomiting may occur. Within several weeks or months, most patients recovered from infection [4]. Patient of an HAV defined as a person whose has HAV relevant symptoms and whose confirmed through a diagnosis by the test of a specific immunoglobulin M antibodies to hepatitis A virus in blood or by using the nucleic acid amplification assay for HAV genes in blood or stool [5].

According to studies conducted by Hong et al. on the seroprevalence of HAV during 1979-1981 in Korea, the positive rate of anti-HAV IgG antibodies gradually increased beginning at one year of age, and about 100% of adults in their 20s and 30s have antibodies [6]. However, changes in sanitary and residential environments have led to changes in antibody seroprevalence [2]. A comparison of antibody positivity rates between 2005 and 2014 reported less than 30% seroprevalence in the 20-30s age group [7]. The number of cases of hepatitis A has been reported to be around 1,000 each year since 2012, but this increased to 4,679 and 4,419 cases in 2016 and 2017, respectively. In particular, patients with HAV are most common in the 20 to 40 year age group [8].

In Korea, the sentinel surveillance system for hepatitis A has operated since 2001. Because the number of patients greatly increased in 2009, HAV was included in the mandatory surveillance system after 2010. A national immunization program for children between 12 to 23 months was introduced in 2015.

In contrast to the annual number of patients with HAV, outbreak reports were relatively rare. In 2007, one outbreak of HAV was reported in military personnel, and a 2016 outbreak related to ingestion of oysters in Sasang-gu, Busan was reported [9, 10].

On December 25, 2017, there was an epidemic hepatitis A outbreak related to groundwater contamination in a long-term psychiatric hospital (H hospital) in Jeollabuk-do, Korea. The authors and officers in charge of public health departments visited H hospital and investigation for this outbreak.

We present the results of the epidemiologic investigation and implementation of remedial techniques for groundwater disinfection to provide safe water.

METHODS

1. Case definition

In this outbreak, the case was defined as positive anti-HAV IgM in serum among patients and staff from 50 days before the first case (November 6, 2017) to the end of the epidemic (March 12, 2018). This definition was determined considering the maximum incubation period of hepatitis A as a 50 days and the twice of the average incubation periods as a 56 days [3].

2. Personal factor investigation

Epidemiologic investigation was conducted with a case series study about symptom onset, serologic test results, and medical record review. From December 25, 2017 to March 12, 2018, a total of 234 patients or employees in H hospital was investigated. The status of hospitalized and discharged patients in this period was analyzed and compared with the HAV report in the National Notifiable Infectious Disease Surveillance System (NIDSS) of the Korean Center for Disease Control and Prevention. The occurrence of HAV was monitored until the end of this outbreak.

To confirm asymptomatic infection, subjects were tested for serum immunoglobulin M antibody to HAV (anti-HAV IgM). In each case of a seropositive patient, fecal examinations were performed for phylogenetic analysis. Subjects who had negative results were monitored for serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) three times at intervals of 15 days to identify additional cases. The samples of patient serum for diagnosis of HAV and liver function test were transferred to the commercial diagnosis institutes.

3. Environmental factor investigation

To investigate the possibility of person-to-person transmission, the admission environment and treatment program of H hospital were assessed. The origin of infection was determined by examining potential sources such as water or food, food service, cooking facilities, food distribution systems, and surrounding environmental factors. At the time of the first field survey on January 2, 2018, four food samples were collected. Since H hospital uses groundwater as the domestic and cooking water supply, one groundwater sample from the shower room was obtained by filtration water sampling. Samples from eight water purifiers in the hospital were also collected and tested for 16 bacteria and six virus species, including Salmonella spp., Pathogenic *Enterobacter* C*oli*, *Campylobacter* spp., Norovirus, and HAV.

After detecting HAV in the groundwater sample obtained from the shower room, additional samples were collected from two underground water pipes of H hospital, three nearby reservoirs, and 12 private underground water pipes from a village located about 900 meters from H hospital to identify the contamination status and cause of HAV.

Phylogenetic analysis of HAV detected in human and environmental samples was performed at the Jeollabuk-do Institute of Health & Environment Research. The nucleotide sequence of the VP3 / VP1 region was compared with the GenBank database using BLAST (http://blast.ncbi.nlm.nih.gov). The nucleotide sequence was analyzed, aligned, and edited using the Bioedit 7.26 sequence alignment editor. Sequence diagram analysis was performed using the neighbor-joining method via the MEGA 6.06 program. After the epidemic outbreak, the presence or absence of HAV in the groundwater supply of H hospital was continuously monitored through real-time PCR until June 2018.

4. Ethical statement

This study was approved for research review exemption by the Jeonbuk National University Hospital Institutional Review Board (CUH 2022-11-045).

RESULTS

1. Personal factor investigation results

The first symptom of the primary case began on December 25, 2017, but this outbreak was recognized January 2, 2018 with 5 patients of HAV infection. As of January 3, 2018, field investigation estimated the number of exposed persons as 234 (76 open wards, 100 closed wards, 58 employees). Since one subject refused the serologic test and five subjects were previously confirmed to have HAV, the remaining 228 subjects were tested for serum anti-HAV IgM and anti-HAV IgG. Thirteen persons were confirmed to have HAV infection (seropositive anti-HAV IgM), and six of them were asymptomatic. Additionally, one additional person who had been seronegative for anti-HAV IgM and IgG on January 3 was identified as having HAV infection by NIDSS monitoring on January 16. Finally, 66 subjects had no immunity to HAV in the point of outbreak, and 19 (5 previously confirmed cases, 13 seropositive for anti-HAV IgM cases and 1 delayed confirmed case at January 16) of these were confirmed as having HAV infection during the outbreak. The attack rate was calculated as 28.8% (19/66) and pathogenicity was 68.4%(13/19) (Fig. 1 and 2). Overall attack rate includes non-susceptible persons was 8.1% (19/234) and the attack rate of 2nd floor patient (15.0%, 15/100) was higher than 1st floor (2.6%, 2/76) and health care workers (3.4%, 2/58). Among the age groups, the 30-39 age group was higher overall attack rate (25.0%, 6/24) compared with other age groups (Table 1).

The 66 subjects who were not immune to HAV were vaccinated and monitored by serum AST and ALT. Symptomatic patients were treated, and six cases without symptoms underwent cohort isolation until the end of the epidemic in H hospital. The most common symptoms were jaundice (47.4%), fatigue (42.1%), nausea, vomiting, and fever. There was no disease-related death or fulminant hepatic failure (Table 2).

Figure 1. Diagram of the study population and serum antibody to Hepatitis A virus test results.

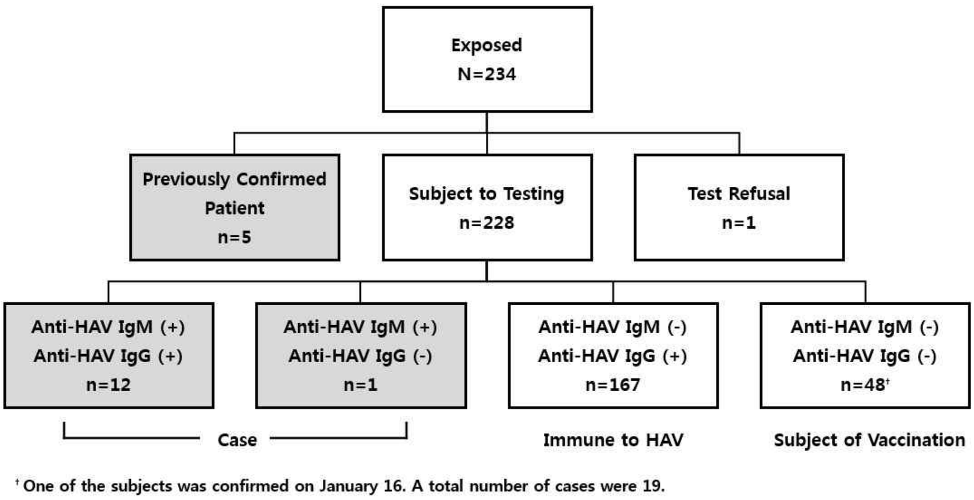


Figure 2. Epidemic curve of Hepatitis A virus outbreak in long term care hospital.

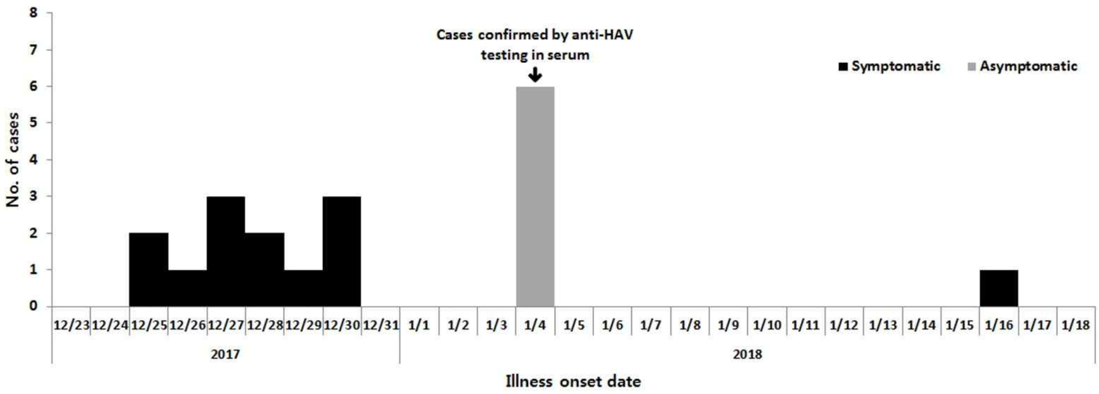


Table 1. Demographic of hepatitis A outbreak in long term care hospital

Characteristic		Total	Case
Total		234 (100.0)	19 (8.1)
	Health care workers	58 (24.8)	2 (3.4)
	Patient(ward)	176 (75.2)	17 (9.7)
	1st floor	76 (32.5)	2 (2.6)
	2nd floor	100 (42.7)	15 (15.0)
Age(years)			
	≤19	5 (2.1)	3 (60.0)
	20-29	27 (11.5)	5 (18.5)
	30-39	24 (10.3)	6 (25.0)
	40-49	36 (15.4)	3 (8.3)
	50-59	60 (25.6)	0 (0.0)
	60-69	41 (17.5)	0 (0.0)
	≥70	41 (17.5)	2 (4.9)
Sex			
	Male	124 (53.0)	12 (9.7)
	Female	110 (47.0)	7 (6.4)

Data presented as number and percentage. The denominator of total was 234 and the denominator of cases was each corresponding numbers.

Table 2. Clinical Symptoms of cases of hepatitis A outbreak in long term care hospital

Symptoms	Case
Jaundice	9 (47.4)
Lethargy	8 (42.1)
Nausea	6 (31.6)
Vomiting	5 (26.3)
Fever	5 (26.3)
Abdominal pain	5 (26.3)
Chill	4 (21.1)
Asymptomatic	6 (31.6)

The total cases were 19 and the symptoms included the multiple responses.
Data presented as number and percentage.

The prevalence of anti-HAV IgG was 11.5% for people in their 20s, 28.6% for people in their 30s, 91.7% for people in their 50s, and 100% for people in their 60s and older. The incidence of patients in their 20s and 30s (57.9%) is relatively high compared to that of other age groups (Fig. 3). The cases occurred from December 25, 2017 to January 16, 2018, and there was no secondary outbreak. The end of the epidemic was declared on March 12, 2018 after twice the average incubation period of hepatitis A (56 days). [3] The time of exposure was estimated as November 28, 2017 considering the average incubation period of HAV.

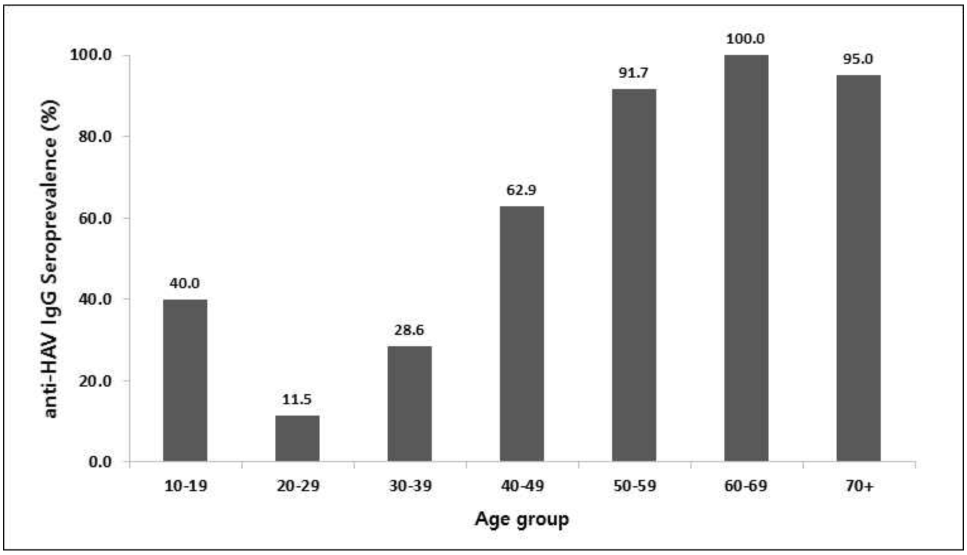
2. Environmental factor investigation results

Among four collected food samples, HAV was detected in radish kimchi (Korean Sukbakgi), which is uncooked. HAV was also detected in groundwater samples used for cooking and domestic water, in the effluent of a septic tank, and in reservoir A, which is located near the hospital (Fig. 4a). However, HAV was not detected in individual groundwater samples or a small water supply system about 900 meters from H hospital (Fig. 4b). This groundwater supply was no longer used, and bottled water was acquired for drinking until the stability of the water source was secured. In reservoir A, measures were taken to restrict resident water usage by prohibiting fishing and use of drinking water from the reservoir.

Phylogenetic analysis showed HAV 1A type in each sample of groundwater, food, and reservoir water, with each sample nucleotide sequence exhibiting 100% match. The similarity of domestic and foreign isolates of HAV 1A from GenBank was 99.5 – 99.9%, and the nucleotide sequence of this strain was lower than that of the existing sequence (Fig. 5).

Construction of a waterway was completed near the groundwater source from October 2015 to January 2016. To ascertain contamination from damage during construction, endoscopic inspection of the sewage pipe was performed to confirm leakage from a collapsed pipe.

Figure 3. Seroprevalence of Hepatitis A anti-IgG by age group.



The sewer pipe was immediately replaced after detecting the leak. Although H hospital applied two methods, chlorination and UV irradiation, to eradicate the virus, HAV was continually detected in the groundwater. A new groundwater well was drilled, from which HAV was not detected. On June 28, 2018, H hospital resumed the use of groundwater from the new well and closed the previous well.

Figure 4. Location of outbreak hospital and groundwater pipe.
A: Septic tank, sewer pipe, reservoir A, and groundwater wells 1 and 2 are in close proximity.
B: Sewer pipe continued to a village about 900 m away.

A B

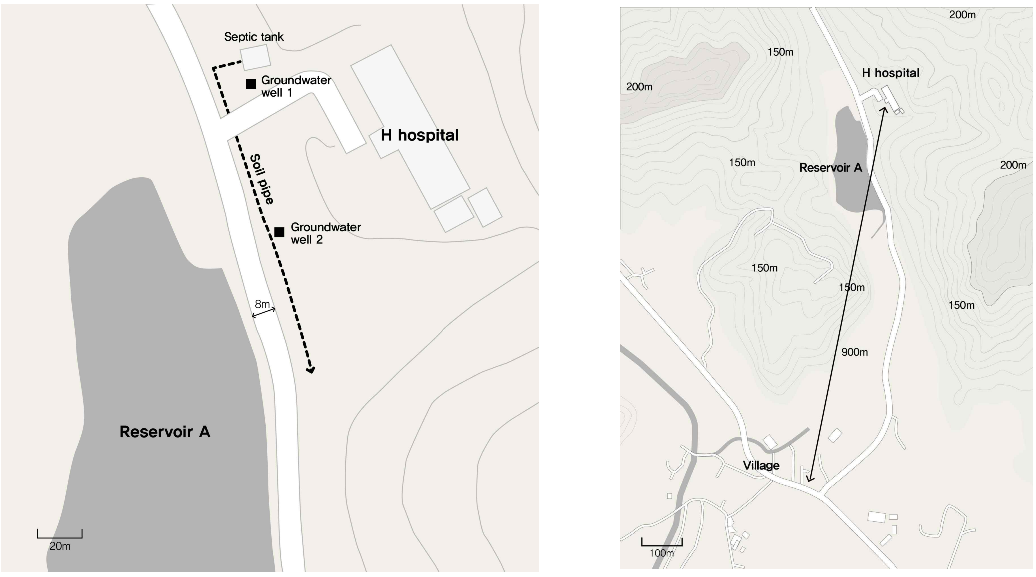
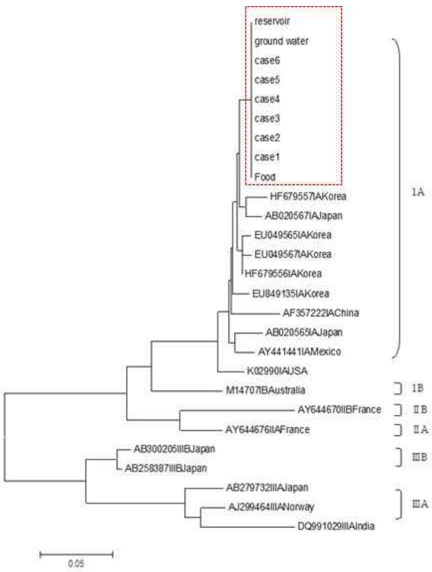


Figure 5. Phylogenetic tree of Hepatitis A virus from patients and environmental samples. The samples in the doted square box are the samples obtained in this study.



DISCUSSION

HAV has a minimum incubation period of 15 days and a maximum incubation period of 50 days, a relatively longer incubation period than other food- and water-borne pathogens. Due to this long incubation, even a few cases of HAV infection are recognized as an epidemic. Most cases of hepatitis A infection are caused by contaminated food. This outbreak is an interesting example of groundwater pollution, which is rare in Korea. In this epidemic, HAV was detected in the groundwater used in a psychiatric medical institution. Phylogenetic analysis was consistent in human and environmental samples. However, it is difficult to estimate the precise exposure time, the infectious agent, and the incubation period. It is challenging to understand the underlying cause of pollution and the relationship between pollutants due to characteristics of the groundwater formed by inflow of various sumps.

The epidemic ended when there were no additional patients or secondary outbreaks, but viruses were continuously detected in the groundwater source. In the natural environment, considerable time is necessary for natural purification of a contaminated aquifer. HAV can survive for longer than 12 weeks in groundwater at 5 ℃, and it is stable at room temperature and low pH [11, 12]. There was no disinfection system in H hospital, and automatic chlorine injection was installed as a first remedial action. However, the effectiveness of chlorine disinfection is influenced by residence time and concentration of chlorine [16] and the pH stability of HAV [12], additional water treatment was needed. Based on the related literature and expert advice, an ultraviolet (UV) water purification system was additionally installed [17]. Because chlorine and UV purification systems, such as chlorine input and UV filter replacement, require continual management, and HAV was still detected in the water from the original wells, a new well was created by bore drilling.

It is also difficult to estimate the correlation between groundwater and reservoir contamination due to the characteristics of groundwater. The reservoir around the hospital could be contaminated by water from the valley, and the contaminated reservoir water may then be introduced into the groundwater. This results in contaminated drinking water or food or even situations in which contaminated feces from patients with HAV are not completely removed from the reservoir, thus polluting the groundwater. However, it is not possible to confirm the precise relationship between pollutants.

Domestic law for groundwater management were defined by Drinking Water Management Act and Enforcement Decree of the Groundwater Act. But, there were no standards for controlling Hepatitis A virus such as what kinds of disinfection methods and the minimum distance between septic tank and well.

There are some limitations in this study. First, the face-to-face interview for psychiatric patients was restricted, and case investigation for some patients was carried out only through medical records and medical staff. Second, immunoglobulin injection was recommended within two weeks after exposure to HAV. However, the exposure period was estimated to be have been longer than two weeks on January 3. A total of 48 subjects that were negative for both anti-HAV IgM and IgG were vaccinated against HAV instead of receiving immunoglobulin. Third, we did not culture the HAV from the groundwater, so we could not confirm the virulence. Fourth, we did not know the test methods for specific IgM and IgG to HAV because the samples transferred to the commercial diagnostic institutes.

HAV outbreak due to groundwater in Korea recently is not detected or very rare. The authors investigated the outbreak of HAV in a long term care psychiatric hospital by HAV contaminated groundwater, and described the result of human and environmental samples and post management. It was detected more than 6 months HAV in the groundwater and we could not find the standard methods for handling groundwater for HAV elimination. The outbreak continued for 23 days and the groundwater contamination lasted for 6 months. Since groundwater quality test does not include for viruses, there is a possibility of HAV outbreaks when groundwater is contaminated with HAV. Furthermore, the managing of groundwater is associated with several government departments like Ministry of Agriculture, Food and Rural affairs, Land, Transport and Maritime Affairs, and Food and Drug Safety. It could make the management of virus contamination of groundwater difficult, which can also make it more vulnerable of people who use groundwater as drinking water. Therefore, a comprehensive approach is required from relevant government ministries in the future.

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