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A swimming pool-associated outbreak of pharyngoconjunctival fever caused by human adenovirus type 4 in Beijing, China

Jie Li^{a,b}, Xiaoyan Lu^c, Yamin Sun^d, Changying Lin^{a,b}, Feng Li^d, Yang Yang^{a,b}, Zhichao Liang^{a,b}, Lei Jia^{a,b}, Lijuan Chen^{a,b}, Baoming Jiang^{c,**}, and Quanyi Wang^{a,b,*}

^aBeijing Center for Disease Prevention and Control, No. 16 Hepingli Middle Road, Beijing 100013, People's Republic of China

^bResearch Center for Preventive Medicine of Beijing, No. 16 Hepingli Middle Road, Beijing 100013, People's Republic of China

^cCenters for Disease Control and Prevention, 1600 Clifton Road NE, Atlanta, GA 30329, USA

^dBeijing Haidian District Center for Diseases Control and Prevention, Beijing, People's Republic of China

Abstract

Patients with swimming pool-acquired human adenovirus (HAdV) infections usually manifest characteristic clinical features that include fever, pharyngitis, and conjunctival inflammation, syndromically referred to as pharyngoconjunctival fever (PCF). HAdV types 3, 4, and 7 are most commonly associated with PCF. This article reports an outbreak of PCF that involved 55 students and staff at a university in Beijing, China. Fifty patients had used the same swimming pool 2 weeks before the onset of symptoms. HAdV type 4 was identified from patient eye and throat swabs and concentrated swimming pool water samples. Partial hexon gene sequences obtained from the water samples were 100% identical to the sequences obtained from the swab samples, which clustered with HAdV-4 within species E. Swimming pool water contaminated with HAdV-4 was the most likely source of infection, although one instance of likely person-to-person transmission was noted.

Keywords

Pharyngoconjunctival fever; Human adenovirus; Outbreak

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*Corresponding author at: Beijing Center for Disease Prevention and Control, No. 16 Hepingli Middle Road, Beijing 100013, People's Republic of China. **Corresponding author: bjcdcxm@126.com (Q. Wang).

Ethical approval

The study was approved by the Human Research Ethics Committee of Beijing Centers for Disease Prevention and Control.

Conflict of interest

No conflict of interest to declare.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Introduction

Human adenoviruses (HAdVs) belong to the *Mastadenovirus* genus, family *Adenoviridae*. They are further divided into seven species (A to G), and 86 types have been characterized to date (Human Adenovirus Working Group, 2018). HAdVs are highly stable and can survive for extended periods in water (Mena and Gerba, 2009). The transmission of HAdVs in swimming pools can occur through ingestion, inhalation, or by direct eye contact with contaminated water (van Heerden et al., 2005). Patients with swimming pool-acquired HAdV infections usually manifest characteristic clinical features that include fever, pharyngitis, and conjunctival inflammation, syndromically referred to as pharyngoconjunctival fever (PCF). HAdV types 3, 4, and 7 are most commonly associated with PCF (Artieda et al., 2009; Harley et al., 2001; Sinclair et al., 2009; Turner et al., 1987). This article describes an outbreak of PCF associated with a swimming pool contaminated with HAdV-4 that occurred among students and staff at a university in Beijing, China.

Case report

On May 30, 2013, Haidian District Centers for Disease Control and Prevention (HCDC) noticed three related cases of acute conjunctivitis reported by a hospital through the Beijing Infectious Disease Symptom Monitoring Information System. The patients had become ill 0–7 days after swimming at the same university swimming pool. In response, HCDC immediately initiated an epidemiological investigation. Questionnaires were designed and used by trained personnel to collect demographic and clinical information. Informed consent was obtained from all participants according to the study protocol. The protocol was reviewed and approved by the institutional review board of the participating university at which the pool is located.

A case-patient was defined as a person consulting the health center affiliated with the university or other nearby hospitals with symptoms of conjunctivitis and/or pharyngitis. A retrospective investigation found that the first case reported symptoms beginning on May 12, and 33 additional PCF cases were identified before May 30. HCDC implemented control measures on May 30, the date on which the first cases were detected by HCDC. Control measures included closing the pool, emptying the water, and thorough disinfection with sodium hypochlorite (500 mg/l), in addition to quarantining of the case-patients.

A total of 55 patients (49 students and six staff) were identified with symptom onset from May 12 to June 6 when the last case was detected (Supplementary material, File 1). Among the 55 cases, 44 (80%) were male and the median age was 23 years (range 20–77 years). All 55 cases were clinically diagnosed with PCF; 52 (95%) had conjunctivitis, 31 (56%) had pharyngitis, and 25 (45%) had fever. The combined clinical manifestations of the patients from whom samples were collected are described in Table 1. The 50 subjects (91%) who had used the university swimming pool within the past 14 days were considered primary cases. The other five subjects (9%) who met the case definition but had not used the swimming pool were defined as secondary cases. One of the five secondary cases had been in contact with two of the primary cases who lived in the same dormitory. The other four had had no contact with a primary case.

To identify the etiological agent, throat and eye swabs were obtained from 15 cases and a throat swab was collected from one case. The swabs were stored in minimum essential medium (MEM) and transferred immediately to Beijing Center for Disease Prevention and Control for laboratory testing. Total nucleic acid extraction was performed on eye and throat swab specimens and HAdVs were detected by conventional PCR (Elnifro et al., 2000). All eye swab specimens from 15 cases (100%) and nine throat swabs (56.2%) from 16 cases tested positive for HAdV (Table 1). HAdV-positive samples were typed as type 4 based on PCR and sequence analysis of the partial hexon gene (Lu and Erdman, 2006). Nucleotide sequences obtained from all eye and throat specimens were 100% identical, indicating that this outbreak was likely caused by the same source of infection.

The indoor swimming pool is located on the university campus. It is 50 × m 25 m in size and divided into a deep water zone with a depth of 2.2 m and a shallow water zone with a depth of 1.2 m. The water in these two zones is exchanged by a water circulation system. Only people with a deep water certificate are allowed to enter the deep water zone. A total of 6950 people (about 240 users per day) visited the swimming pool between May 2 and May 30, 2013. The pool has a detector installed in the water return pipe for real-time monitoring of residual chlorine. If the free chlorine in the water in the return pipe is lower than 0.3 mg/l, the equipment injects sodium hypochlorite into the intake pipe, which then flows into both the deep water zone and the shallow water zone through multiple returns. According to the record book, the equipment was functioning properly during the outbreak period.

To determine whether the pool was a possible source of the outbreak, 10 water samples of 5 l each (five from the deep water zone and five from the shallow water zone) were collected from points 30 cm deep at different locations of the swimming pool on May 30. Five water samples (three from the deep water zone and two from the shallow water zone) were tested for the aerobic bacterial count and coliform bacteria, in accordance with the national guidelines of China for the microbiological examination of swimming pool water (PRC Ministry of Health of the, 2000a,b). The results were all within the normal range.

The other five water samples (two from the deep water zone and three from the shallow water zone) were concentrated using the adsorption–elution method (Fong et al., 2010) and tested for HAdV (Elnifro et al., 2000), enterovirus (Li et al., 2013), norovirus (Trujillo et al., 2006), and rotavirus (Zhang et al., 2014). Two samples collected in the shallow water zone were positive for HAdV. Partial hexon gene sequences obtained from the water samples were 100% identical to the sequences obtained from the swab samples, which clustered with HAdV-4 within species E and showed 97.7% nucleotide sequence identity with HAdV-4 proto-type strain RI-67 (accession number **KX384949.1**; Supplementary material File 2).

A 549 cells were used to isolate HAdV from the concentrated sample. The A549 cells were cultured in MEM with 10% fetal bovine serum until 75% of the bottom of the flask was covered by a cell monolayer. The specimen was then inoculated onto the A549 cells using MEM with 2% fetal bovine serum. The cytopathic effect of the HAdV-infected A549 cells was observed every day. Virus isolation from the two concentrated water samples was not successful.

Discussion

This article describes a swimming pool-associated outbreak of PCF affecting students and staff at a university in Beijing, China. Laboratory investigations demonstrated that HAdV-4-contaminated swimming pool water was the most likely source of infection, although one instance of likely person-to-person transmission was noted. Since HAdV was detected only by PCR and not by viral culture, it was speculated that the HAdVs might have been damaged during the concentrating process.

Fifty-five cases of PCF were identified during the outbreak period. The number of cases was most likely under-reported since only persons who visited the health center or local hospitals were included in the case definition and persons with milder symptoms who did not seek medical care were not included. Therefore, the actual number of cases could have been much higher.

Water quality and disinfection play an important role in preventing water-borne disease outbreaks. As almost 240 people had used the swimming pool every day during the outbreak period and only people with a proper certificate had been allowed to swim in the deep zone, most people had stayed in the shallow water zone. This high occupant load in the pool at the same time might have affected water circulation and disinfection, and thus negatively influenced water quality, resulting in the HAdV-associated PCF outbreak (Fattal et al., 1991). This outbreak highlights the need to monitor the number of visitors simultaneously in the pool, as well as regular measurements of the residual chlorine concentrations at more than one location in the swimming pool. Overcrowding with too many swimmers in the water might have influenced the disinfection effect, and as a result, this could have created potentially unsafe conditions and given rise to the infections.

This study has two limitations. First, no process controls were included to assess the recovery efficiency and the presence of PCR inhibitors, thus it was not possible to predict the exact concentration of HAdV in the swimming pool. Second, the same sample was not tested for both indicators and pathogen, which made it impossible to compare the contamination indicators with the presence of viruses in the water.

In conclusion, this article describes a swimming pool-associated outbreak of PCF affecting students and staff at a university in Beijing, China. Laboratory investigations demonstrated that HAdV-4-contaminated swimming pool water was the most likely source of infection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Detection of human adenovirus in eye and throat swabs from 16 patients with pharyngoconjunctival fever.

Table 1

Case number	Human adenovirus		Interval between disease onset and sample collection (days)	Clinical presentations		
	Eye swab	Throat swab		Fever	Pharyngitis	Conjunctivitis
1	Pos	Neg	17	Y	Y	Y
2	Pos	Neg	19	Y	Y	Y
3	Pos	Neg	14	Y	N	Y
4	Pos	Neg	12	N	N	Y
5	NS	Neg	12	Y	Y	Y
6	Pos	Neg	7	Y	N	Y
7	Pos	Pos	6	Y	Y	Y
8	Pos	Pos	4	Y	N	Y
9	Pos	Pos	5	Y	N	Y
10	Pos	Pos	5	N	Y	Y
11	Pos	Pos	0	N	N	Y
12	Pos	Pos	6	Y	Y	Y
13	Pos	Pos	1	Y	Y	Y
14	Pos	Pos	7	Y	N	Y
15	Pos	Neg	1	N	N	Y
16	Pos	Pos	6	N	Y	Y

Pos, positive; Neg, negative; NS, no sample; Y, yes; N, no.