

Education-Family Physician Corner

Adenovirus Isolated from an Outbreak of Acute Hemorrhagic Conjunctivitis

Aysha Waheed Agab, MB BCh BAO* Muneera Abdulla Abu Najma, MD, Saudi Board of Ophthalmology**
Ghada Al Bin Ali, Saudi Board of Ophthalmology, FRCS***

There are no published data documenting possible previous acute hemorrhagic conjunctivitis (AHC) outbreaks in Bahrain. We report an outbreak of adenoviral-related AHC in two Bahraini siblings.

AHC is a rare form of conjunctivitis that is highly infectious. Diagnosis of AHC is mainly based on clinical presentation. Signs and symptoms usually occur after 24 to 48 hours of incubation. The infection is of short duration, self-limited and associated with good visual prognosis requiring only supportive care. Patient education regarding personal hygiene and close contact with infected individuals plays an important role in its management to prevent the spread of this highly contagious form of conjunctivitis.

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AHC is highly infectious. It is usually caused by enterovirus serotypes, mainly human enterovirus 70 (EV-70) and human coxsackievirus A24 variant (CV-A24v). Rarely, adenovirus serotypes have been involved¹. Transmission occurs through direct or indirect contact with eye secretions^{2,3}. This epidemic ocular infection is characterized by sudden onset of ocular pain, photophobia, eyelid edema, foreign body sensation, epiphora or excessive tearing and conjunctival hemorrhages^{4,5}. Outbreaks are often linked to close contact in community settings, such as schools, swimming pools and eye clinics^{2,3,6}. They usually last for one to two months and secondary attacks rates within households are more than 50%⁷.

Diagnosis of AHC is mainly based on clinical presentation, which occurs after 24 to 48 hours of incubation⁷. This infection is typically short in duration, self-limited and associated with good visual prognosis, requiring only supportive care⁸.

Adenoviruses are double-stranded DNA viruses that were first isolated in 1953¹. Human adenoviruses (HAdVs) are known to cause a broad range of infections; HAdV subgroups B and D are associated with ocular infections, such as AHC, epidemic keratoconjunctivitis (EKC) and pharyngoconjunctival fever (PCF)^{1,6}.

The first AHC outbreak occurred in Ghana in 1969; since then, 11 adenoviral-related outbreaks have been described. The main serotypes isolated were HAdV -2, HAdV -4, HAdV -7, HAdV -8, HAdV -11 and HAdV -19⁶.

The aim of this study is to report an uncommon presentation of conjunctivitis caused by HAdV in two Bahraini siblings.

THE CASE

Case 1

A seven-year-old male presented in December 2015 with a three-day history of eye redness associated with tearing, foreign body sensation, mild eye pain and a one-day history of left-sided upper eyelid edema and low-grade fever. There was no associated history of recent travel or sick contacts.

On examination, superior palpebral conjunctival follicles, mild bulbar conjunctival injection bilaterally and left-sided upper eyelid edema were noted. The rest of the examination was within normal limits. Two days later, the patient was reviewed and appeared to have developed periorbital ecchymosis with gross hemorrhages in the superior half of the bulbar conjunctiva bilaterally, see figure 1 (A to D).

The diagnosis of acute hemorrhagic conjunctivitis was suspected, and palliative treatment with lubricant eye drops and erythromycin ointment prophylactically were initiated. However, as there was no associated history of trauma and the patient had been admitted two months before with hematuria (later diagnosed as glomerulonephritis), the patient was referred to the pediatric clinic to rule out systemic causes of periorbital ecchymosis, but he did not attend.

* Junior Resident
** Chief Resident
*** Consultant Ophthalmologist
Anterior Segment and Uveitis Specialist
Acting Head of Eye and Laser Center
Department of Ophthalmology
Eye and Laser Center
Bahrain Defence Force Hospital
The Kingdom of Bahrain
E-mail: a.w.agab@gmail.com



Figure 1 (A)



Figure 1 (B)



Figure 1 (C)



Figure 1 (D)

Figure 1 (A to D): Clinical Appearance on Day Five

The following day, the patient was admitted with a high-grade fever, sore throat, anorexia, vomiting and abdominal pain; he was admitted to rule out neuroblastoma. All investigations performed including US abdomen, CT brain and orbit, urine vanillylmandelic acid (VMA) and homovanillic acid (HVA) were negative. He was discharged and followed in the ophthalmology clinic.

Case 2

A five-year-old female presented one-week after the initial presentation of her sibling (Case 1) with a three-day history of left-eye pain, redness, tearing and foreign body sensation. This was associated with a history of fever and mild abdominal pain.

On examination, left-eye superior and inferior tarsal conjunctival follicles were noted with upper and lower eyelid edema, as well as bilateral superficial punctate keratitis. The rest of the examination was within normal limits. Two days later, the patient developed minimal upper eyelid ecchymosis with gross hemorrhage in the superior half of the bulbar conjunctiva of the left eye, see figure 2 (A and B).



Figure 2 (A)



Figure 2 (B)

Figure 2 (A and B): Clinical Appearance on Day Two

The diagnosis of acute hemorrhagic conjunctivitis was confirmed, and the patient was started on palliative treatment. Conjunctival swabs from both patients were collected; the inferior tarsal conjunctiva and fornix were swabbed with a Dacron swab soaked with 2 mL of Eagle's viral transport medium. These specimens were tested for human adenovirus and enterovirus by RT-PCR. Both samples were positive for human adenovirus but negative for enterovirus. Serotyping was not performed as it was not available.

The symptoms resolved almost completely within three weeks in both patients.

DISCUSSION

AHC is commonly caused by EV-70 and CV-A24v; both belong to the family Picornaviridae and have been implicated in epidemics since the 1970s^{9,10}. Human adenovirus was identified as the cause of the outbreak in these two cases; this virus is less frequently associated with AHC. The source of this virus is unknown. Furthermore, without an epidemiological study, it is difficult to know whether more cases have been documented in Bahrain.

Documented cases of AHC worldwide were mainly caused by HAdV -2, -7, -8 and -11, and were commonly associated with co-infection with other agents. This co-infection may strengthen their transmission capability, resulting in severe ocular symptoms and signs⁶. However, no co-infection was documented in our two cases, and we lacked the resources to identify the HAdV serotype.

Zhang et al performed a virology and epidemiology analysis of global adenovirus-associated conjunctivitis outbreaks that occurred during the years 1953 to 2013. They reported that AHC outbreaks were the largest compared to EKC and PCF outbreaks, indicating the highly contagious nature of the adenovirus⁶.

The parents of our patients were educated regarding the contagious nature of the disease to prevent the spread of the infection and emphasized the importance of general hygiene measures, such as handwashing. They were advised to keep the children at home as not to spread the infection at school. In addition, they were informed about the self-limiting, benign course of the disease, since no curative treatment modality exists, as well as the essentially good visual prognosis¹¹.

Currently, no specific chemotherapeutic agent or broad-spectrum adenoviral vaccine against ocular infections exists. Prevention is achieved with strict infection-control practices. The adenoviral vaccine that has been administered to US military personnel since 1971 elicits immunity only to serotypes 4 and 7^{6,12}.

CONCLUSION

AHC is commonly caused by EV-70 and CV-A24v; however, the two cases presented were caused by HAdV, which is less frequently associated with AHC. Essentially, this re-emergent infectious disease, although benign with good visual prognosis, should be controlled.

To limit the spread of infection, it is important to maintain infectious control practices and educate the infected individual to avoid sharing towels, glasses or any other item in contact with the eyes. In addition, these individuals should stay at home and avoid going to work or school when symptomatic in order to prevent spreading the infection.

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REFERENCES

1. Ayoub EA, Shafik CF, Gaynor AM, et al. A Molecular Investigative Approach to an Outbreak of Acute Hemorrhagic Conjunctivitis in Egypt, October 2010. *Virology Journal* 2013;10:96.
2. Chansaenroj J, Vongpunsawad S, Puenpa J, et al. Epidemic Outbreak of Acute Haemorrhagic Conjunctivitis Caused by Coxsackievirus A24 in Thailand, 2014. *Epidemiol Infect* 2015; 143(14):3087-93.
3. Langford MP, Anders EA, Burch MA. Acute Hemorrhagic Conjunctivitis: Anti-Coxsackievirus A24 Variant Secretory Immunoglobulin A in Acute and Convalescent Tear. *Clin Ophthalmol* 2015; 9:1665-73.
4. Wu B, Qi X, Xu K, et al. Genetic Characteristics of the Coxsackievirus A24 Variant Causing Outbreaks of Acute Hemorrhagic Conjunctivitis in Jiangsu, China, 2010. *PLoS One* 2014; 9(1):e86883.
5. Ayoub EA, Shafik CF, Gaynor AM, et al. A Molecular Investigative Approach to an Outbreak of Acute Hemorrhagic Conjunctivitis in Egypt, October 2010. *Virology* 2013; 10:96.
6. Zhang L, Zhao N, Sha J, et al. Virology and Epidemiology Analyses of Global Adenovirus-Associated Conjunctivitis Outbreaks, 1953-2013. *Epidemiol Infect* 2016; 144(8):1661-72.
7. Centers for Disease Control and Prevention (CDC). Acute Hemorrhagic Conjunctivitis--St. Croix, U.S. Virgin Islands, September-October 1998. *MMWR Morb Mortal Wkly Rep* 1998; 47(42):899-901.
8. Sklar VEF, Patriarca PA, Onorato IM, et al. Clinical Findings and Results of Treatment in an Outbreak of Acute Hemorrhagic Conjunctivitis in Southern Florida. *American Journal of Ophthalmology* 1983; 95(1): 45-54.
9. Lim KH, Yin-Murphy M. An Epidemic of Conjunctivitis in Singapore in 1970. *Singapore Med J* 1971; 12(5):247-9.
10. Ishiko H, Takeda N, Miyamura K, et al. (1992) Phylogenetic Analysis of a Coxsackievirus A24 Variant: The Most Recent Worldwide Pandemic Was Caused by Progenies of a Virus Prevalent around 1981. *Virology* 1992; 187(2):748-59.
11. Plechaty G. Acute Hemorrhagic Conjunctivitis. <http://emedicine.medscape.com/article/1203216-overview> Accessed on 03 February 2016.
12. Croyle MA, Patel A, Tran KN, et al. Nasal Delivery of an Adenovirus-Based Vaccine Bypasses Pre-Existing Immunity to the Vaccine Carrier and Improves the Immune Response in Mice. *PLoS ONE* 2008; 3(10): e3548.