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A Case of Urethritis Caused by Human Adenovirus Type 56

Satoshi Hiroi^{1*}, Keiichi Furubayashi², Takuya Kawahata¹, Saeko Morikawa¹, and Tetsuo Kase¹

¹*Division of Virology, Department of Infectious Diseases, Osaka Prefectural Institute of Public Health, Osaka 537-0025; and*
²*Sonezaki Furubayashi Clinic, Osaka 530-0057, Japan*

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Human adenoviruses (HAdVs) belong to the genus *Mastadenovirus* of the family *Adenoviridae*, and are grouped into seven species (HAdV-A through HAdV-G) (1,2). HAdVs are known to cause a variety of illnesses such as respiratory infections, gastroenteritis, and keratoconjunctivitis. HAdV-D is a major causative agent of keratoconjunctivitis, and isolation of HAdV-8, HAdV-19, HAdV-37, HAdV-53, HAdV-54, and HAdV-56 strains has been reported in Japan (3–5). HAdV-56 was recently identified as a new HAdV (5–7). Moreover, there have been reports of the isolation of HAdVs from male and female genital tracts and of cases of male urethritis caused by HAdV-D (8–14). We assumed that patients with urethritis contracted HAdV infection through sexual intercourse (11–13). However, there are not many reports on HAdV-associated urethritis. In this report, we describe a case of urethritis and conjunctivitis caused by a new type of HAdV in Osaka, Japan.

The patient was a man in his 30s with non-gonococcal non-chlamydial urethritis. In December 2011, he experienced urethral discomfort for a week after sexual intercourse, and in the week that followed, he visited a sexually transmitted disease (STD) clinic with the complaint of miction pain. On his visit, the patient also exhibited conjunctivitis in the left eye, which began a day prior to his visit; his urethral secretion, urine sample, and conjunctival swab were obtained for analysis. The patient's urethral secretion contained leukocytes, and the urine sediments and the conjunctival swab were positive for adenovirus when tested using an immunochromatography kit (TFB, Tokyo, Japan). The patient recovered without any treatment 8 days after clinical diagnosis.

The virus was isolated from the samples by inoculating 200 μ L of the samples onto A549 cell cultures. The HAdV isolates from the conjunctival swab samples and urine samples were named 20110150/Osaka/2011 and 20110151/Osaka/2011, respectively. DNA was extracted from the isolated strains (15) and the fiber and partial hexon genes were amplified using polymerase chain reaction (PCR), which was performed as previously reported (15–18). The penton base and the entire hexon

genes were amplified using PCR with primers that were designed on the basis of HAdV-56 sequences. The PCR products were sequenced by the Applied Biosystems 3130 genetic analyzer (Applied Biosystems, Foster City, Calif., USA). The sequences obtained in this study were submitted to the DNA Data Bank of Japan (DDBJ) and were assigned accession numbers AB690366 to AB690371. Sequence similarities were calculated using GENETYX Ver. 7 (Software Development, Tokyo, Japan), and the results showed that the penton base, hexon, and fiber genes of 20110150/Osaka/2011 and 20110151/Osaka/2011 were completely identical to the genes of HAdV-56 previously isolated in Japan (accession no. AB562588). These results indicated that both urethritis and conjunctivitis, as observed in this case, were caused by HAdV-56. To our knowledge, this is the first report of urethritis caused by HAdV-56.

HAdV-56 is a new type of HAdV that was identified by genetic analysis and isolated from pulmonary biopsy specimens and conjunctival swabs (5–7). Although HAdV-56 was detected in keratoconjunctivitis patients in several parts of Japan (4,5), the virus was never isolated from patients in our region of surveillance. Thus, this is the first case of HAdV-56 conjunctivitis reported in Osaka. In our case, the onset of conjunctivitis was subsequent to urethritis, suggesting that HAdV-56 initially caused the genital infection, and genitococular autoinoculation occurred in the patient. However, we could not ascertain the route of infection from the female to the male patient in this case. Since HAdVs cause pharyngitis, genital ulcers, and cervicitis (11), either oral sex or vaginal intercourse would be a possible route for HAdV transmission, and further investigation of additional cases is required to ascertain this assumption.

Although HAdVs are not usually recognized as a causative agent of genital infections, cases of HAdV-D-associated urethritis, particularly those caused by HAdV-37, have been reported in the United States and Australia (11,12,14). In recent years, HAdV-37 associated-urethritis cases have also been reported in Japan (19,20). In addition, we reported that HAdV-56 is an oculogenital pathogen similar to HAdV-8 and HAdV-37 (11,12,19,20); therefore, HAdV-37 may be a major pathogen causing HAdV urethritis, and our results indicate the possibility of an increase in HAdV-56-associated genital infection rates in the future.

In the present report, we presented a case of HAdV-56 urethritis and conjunctivitis and proposed that HAdV-56 is possibly a sexually transmitted pathogen. Investigation of HAdV is recommended for patients

*Corresponding author: Mailing address: Division of Virology, Department of Infectious Diseases, Osaka Prefectural Institute of Public Health, 1-3-69 Nakamichi, Higasinari-ku, Osaka 537-0025, Japan. Tel: +81-6-6972-1321, Fax: +81-6-6972-2393, E-mail: hiroi@iph.pref.osaka.jp

with idiopathic urethritis. In Japan, the accurate number of patients with genital HAdV infection is unknown, and we propose that an HAdV surveillance system should be undertaken for patients with STD.

Conflict of interest None to declare.

REFERENCES

1. Wold, W.S.M. and Horwitz, M.S. (2007): Adenoviruses. p. 2395–2436. In D.M. Knipe and P.M. Howley, (ed.), *Fields Virology*. 5th ed. vol. 2. Lippincott Williams & Wilkins, Philadelphia, Pa.
2. Liu, E.B., Ferreyra, L., Fischer, S.L., et al. (2011): Genetic analysis of a novel human adenovirus with a serologically unique hexon and a recombinant fiber gene. *PLoS One*, 6, e24491.
3. Ishiko, H. and Aoki, K. (2009): Spread of epidemic keratoconjunctivitis due to a novel serotype of human adenovirus in Japan. *J. Clin. Microbiol.*, 47, 2678–2679.
4. Nakamura, M., Hirano, E., Kowada, K., et al. (2011): Surveillance of adenovirus D in patients with epidemic keratoconjunctivitis from Fukui prefecture, Japan, 1995–2010. *J. Med. Virol.*, 84, 81–86.
5. Kaneko, H., Aoki, K., Ohno, S., et al. (2011): Complete genome analysis of a novel intertypic recombinant human adenovirus causing epidemic keratoconjunctivitis in Japan. *J. Clin. Microbiol.*, 49, 484–490.
6. Henquell, C., Boeuf, B., Mirand, A., et al. (2009): Fatal adenovirus infection in a neonate and transmission to health-care workers. *J. Clin. Virol.*, 45, 345–348.
7. Robinson, C.M., Singh, G., Henquell, C., et al. (2011): Computational analysis and identification of an emergent human adenovirus pathogen implicated in a respiratory fatality. *Virology*, 409, 141–147.
8. de Jong, J.C., Wigand, R., Wadell, G., et al. (1981): Adenovirus 37: identification and characterization of a medically important new adenovirus type of subgroup D. *J. Med. Virol.*, 7, 105–118.
9. Harnett, G.B. and Newnham, W.A. (1981): Isolation of adenovirus type 19 from the male and female genital tracts. *Br. J. Vener. Dis.*, 57, 55–57.
10. Phillips, P.A., Harnett, G.B. and Gollow, M.M. (1982): Adenovirus type 19 and a closely related new serotype in genital infection. *Br. J. Vener. Dis.*, 58, 131–132.
11. Swenson, P.D., Lowens, M.S., Celum, C.L., et al. (1995): Adenovirus types 2, 8, and 37 associated with genital infections in patients attending a sexually transmitted disease clinic. *J. Clin. Microbiol.*, 33, 2728–2731.
12. Bradshaw, C.S., Denham, I.M. and Fairley, C.K. (2002): Characteristics of adenovirus associated urethritis. *Sex. Transm. Infect.*, 78, 445–447.
13. Bradshaw, C.S., Tabrizi, S.N., Read, T.R., et al. (2006): Etiologies of nongonococcal urethritis: bacteria, viruses, and the association with orogenital exposure. *J. Infect. Dis.*, 193, 336–345.
14. Tabrizi, S.N., Ling, A.E., Bradshaw, C.S., et al. (2007): Human adenoviruses types associated with non-gonococcal urethritis. *Sex. Health*, 4, 41–44.
15. Hiroi, S., Koike, N., Nishimura, T., et al. (2011): Genetic analysis of human adenovirus type 54 detected in Osaka, Japan. *Jpn. J. Infect. Dis.*, 64, 535–537.
16. Xu, W., McDonough, M.C. and Erdman, D.D. (2000): Species-specific identification of human adenoviruses by a multiplex PCR assay. *J. Clin. Microbiol.*, 38, 4114–4120.
17. Madisch, I., Harste, G., Pommer, H., et al. (2005): Phylogenetic analysis of the main neutralization and hemagglutination determinants of all human adenovirus prototypes as a basis for molecular classification and taxonomy. *J. Virol.*, 79, 15265–15276.
18. Miura-Ochiai, R., Shimada, Y., Konno, T., et al. (2007): Quantitative detection and rapid identification of human adenoviruses. *J. Clin. Microbiol.*, 45, 958–967.
19. Mochizuki, K., Katada, T., Ohkusu, K., et al. (2010): Three cases of acute conjunctivitis caused by human adenovirus in medical workers. *J. Jpn. Assoc. Infect. Dis.*, 84, 469–473 (in Japanese).
20. Furubayashi, K. (2011): Adenoviral urethritis: a report of four cases. *Jpn. J. Sex. Transm. Dis.*, 22, 116–117 (in Japanese).