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Spread of Epidemic Keratoconjunctivitis Due to a Novel Serotype of Human Adenovirus in Japan▽

We have reported a novel human adenovirus (HAdV) that has caused a nationwide epidemic of keratoconjunctivitis (EKC) in Japan (11). This virus has been characterized serologically and genetically as a novel serotype, and we propose naming it HAdV-54. The GenBank accession number of the nucleotide sequence of HAdV-54 is AB333801.

Adenovirus EKC is typically caused by three serotypes of HAdV-D, namely, HAdV-8, -19, and -37, and one serotype of HAdV-E, namely, HAdV-4. These strains frequently cause nosocomial outbreaks (3–5, 18) and were originally isolated from patients with EKC in 1951, 1955, and 1976 (8, 9, 12). Although several variants, including a novel hexon-chimeric intermediate type (HAdV-22,37/H8), have also been described (1, 2, 6, 7, 10, 14, 17), no other new serotype has appeared. HAdV-54 was first isolated from an EKC patient in Kobe, western Japan, in 2000 and then caused an EKC epidemic in 2000 to 2007. During this epidemic, 343 HAdV isolates were obtained from patients with EKC in 16 nosocomial and 15 sporadic outbreaks. HAdV-54 caused 5 (31.3%) of the 16 nosocomial outbreaks and 5 (33.3%) of the 15 sporadic outbreaks. Four other serotypes accounted for 51.6% and HAdV-22,37/H8 was responsible for 16.1% of both types of infections.

HAdV-54 continued to cause EKC in 2008 (Fig. 1). It has been reported only in Japan, but it is not yet known whether HAdV-54 is limited to this country. Also, the origin and route of transmission of HAdV-54 are unknown. The phylogenetic analysis indicates that HAdV-54 had already appeared in 1995 as the causative agent of EKC. On the other hand, HAdV-54 did not originate from the specimens collected in Saudi Arabia, Austria, Nepal, Bangladesh, and Vietnam (13, 15, 16). It is also possible that this virus is circulating in humans with asymptomatic infections, although no asymptomatic infection was detectable in the present study. The virus might gain pathogenesis by some unknown mechanism. In cell culture, HAdV-54 grows slowly, and the Kobe strain was isolated after eight blind passages. Because this strain is close to HAdV-8 according to both neutralization assays and phylogenic analyses, it has been diagnosed occasionally as HAdV-8. In Japan, approximately 1,000 HAdV strains were isolated from patients with EKC in 2003 to 2007 (Infectious Agents Surveillance Report URL: http://idsc.nih.go.jp/iasr/29/338/tpc338.html). The major causative agents were HAdV-4, -19a, and -37, and several infections have also been caused by HAdV-8. As EKC infections due to HAdV-8 have apparently been rare since 2000, we undertook phylogenetic analyses to confirm the causative HAdV strains by using partial hexon sequences derived from all prototypes of HAdV serotypes, including the novel serotype HAdV-54. We found that HAdV-8 strains reported during 2003 to 2005 were actually HAdV-54. The novel serotype

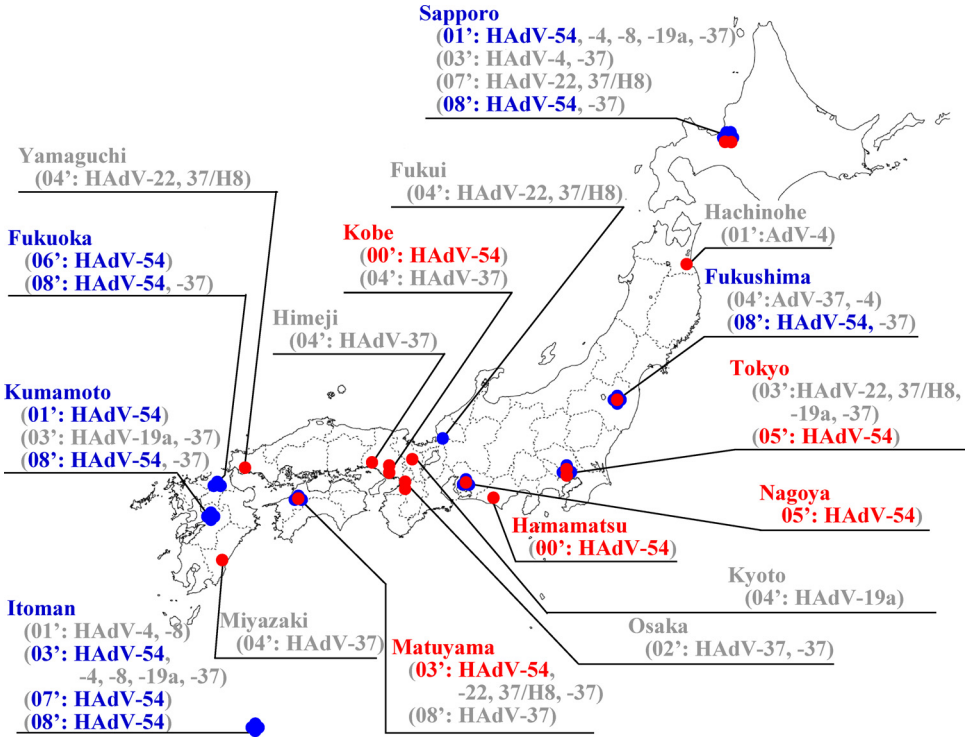

FIG. 1. Nosocomial and sporadic EKC infections analyzed in Japan during 2000 to 2008. A total of 343 HAdV isolates were obtained from patients with EKC in 16 nosocomial (red circles) and 15 sporadic (blue circles) outbreaks during 2000 to 2008. HAdV-54 was isolated from patients with nosocomial (red) and sporadic (blue) infections. (The map serving as the basis for this figure is reproduced from http://www.freemap.jp/).

HAdV-54 should therefore be monitored for worldwide as an emerging adenoviral infection.

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