Phylogenetically different strains of a variant of coxsackievirus A 24 were repeatedly introduced but discontinued circulating in Japan

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Summary. Variations in the nucleotide sequence of 3C proteinase of coxsackievirus A 24 variant (CA 24v) were analyzed to define the route of transmission and spread of the virus which was introduced to Japan on three separate occasions, 1985–86, 1988, and 1989. The nucleotide sequences of isolates from the same year's outbreak in Japan were identical or closely related, while the isolates from different outbreaks were less closely related to one another than to those from other countries in the same year. All Japanese isolates from Okinawa and other prefectures in 1985 and 1986 were closely related to the Taiwan strains in those same years, indicating common-source outbreaks. Two 1988 isolates from Chiba Prefecture, Japan, were closely related to those from Singapore in 1987, China in 1988 and Hong Kong in 1988. All seven Japanese isolates from Chiba Prefecture in 1989 comprised a group together with the Taiwan and Singapore strains in 1988. The results indicate that CA 24v was

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introduced into Japan on each occasion from the outside. Furthermore, in contrast to the explosive epidemics in Okinawa Prefecture in 1985 and 1986, the virus which was repeatedly introduced to other areas in Japan did not circulate endemically, and disappeared within a short time.

Introduction

A variant of coxsackievirus A24 (CA24v) causing acute haemorrhagic conjunctivitis (AHC) is a new antigenic variant isolated for the first time in 1970 in Singapore [29], one year earlier than enterovirus 70, another causative enterovirus of AHC [10]. Since other variants of coxsackievirus A24 are associated with general clinical manifestations of enterovirus infections such as respiratory illnesses and diarrhea, its high infectiousness to human conjunctiva is a newly acquired characteristic. With this pathogenicity, CA24v caused an expanded epidemic.

The virus spread in two steps; in spite of extremely explosive epidemics, CA24v was confined to Southeast Asia and the Indian subcontinent until 1985 when it suddenly appeared for the first time in non-contiguous areas, including Taiwan [12], Japan [15], Central America [2, 3], and Africa [1]. In Japan, CA24v appeared in 1985 in Okinawa Prefecture, the Southwest islands, in an unusually explosive fashion [15]. However, the epidemic was confined to the prefecture and did not spread to the rest of Japan. Serological evidence showed that prior to the outbreak, the neutralizing antibody against the virus was rarely found in the Japanese population, including inhabitants of Okinawa [16]. Thus, CA24v provides an important model for analyzing a mode of introduction and subsequent transmission of a virus in an immunologically virgin area.

Comparison of the nucleotide sequences of viruses provides reliable analysis for the phylogenetic relationship among them. We recently published the complete nucleotide sequence of the standard strain of CA24v, EH24/70 [25]. Furthermore, we have determined the nucleotide sequence encoding 3C proteinase (3Cpro) of 32 CA24v isolates collected over two decades from various Asian countries and Ghana, and analyzed them for mutual phylogenetic relationships [8]. The results revealed that CA24v appeared at one focal place in 1963, several years before the first isolation of CA24v, and that all the recent epidemic strains isolated in various areas from 1985 to 1989 derived from a common progenitor prevalent around 1981. In addition, it was noticed that four Japanese isolates from different outbreaks were less closely related to one another but more closely related to the isolates from other countries in the same year.

In this study, a total of 16 Japanese isolates were explored to identify the route of introduction and subsequent transmission in Japan. Our study involved all representative CA24v isolates collected through the network of the National Epidemiological Surveillance of Infectious Diseases in Japan. Therefore, we consider that the findings described here represent the total picture of CA24v transmission in this country.