Reversion to the Neurovilurent Genome Sequence of Polio Vaccine Virus Isolated from Community-Acquired Meningitis

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Abstract: Neurologic complication associated with the use of live attenuated oral poliomyelitis vaccine is uncommon, but vaccine-associated paralytic poliomyelitis in recipients or contacts sometimes has been reported. We report here a community-acquired aseptic meningitis case and the genetic investigation of the isolated poliovirus type 2. The results of the genetic analysis indicate that the mechanism of this meningitis could have resulted from the reversion of the virus during replication in the other vaccine recipients, suggesting a quest for revising the current vaccination program.

Keywords: Poliovirus, vaccine, meningitis, genetic reversion, neurovirulence.

INTRODUCTION

Neurologic complication associated with the use of live attenuated oral poliomyelitis vaccine is uncommon, but vaccine-associated paralytic poliomyelitis (VAPP) in recipients or contacts sometimes has been reported every year [1]. We report here a community-acquired aseptic meningitis case and the genetic investigation of the isolated poliovirus type 2 [2].

CASE REPORT

A healthy 9-year-old boy developed high fever, severe headache and nausea. Next day, he was admitted to our hospital with a provisional diagnosis of aseptic meningitis. His temperature was 37.9 °C and neck stiffness and Kerning’s sign were positive. The leukocyte count was 12,700/mm3 and CRP was negative. Cerebrospinal fluid (CSF) analysis revealed leukocyte count of 114/mm3 (90% lymphocytes and 10% monocytes), protein value 48 mg/dl, glucose level of 57 mg/dl; and a negative Gram stain. Bacterial culture of CSF was done with Hep-2, primary rhesus monkey kidney, and W-1-38 cell. Neutralization with type-specific antisera revealed that the isolate was type 2 poliovirus. Viral RNA was extracted from 250 microliters of sample. After RNA extraction, complementary DNA was synthesized from the resuspended RNA using Moloney murine leukemia virus reverse transcriptase. The complementary DNA product was amplified using PCR and the products were gel-isolated, purified, and sequenced on an automated DNA sequencer using a fluorescent dideoxychain terminator (3-5). We compared the obtained partial sequence of the 5' non-coding region (nt84-544) of the isolated poliovirus with the published sequence of Sabin 2 strain [2]. It revealed a substitution from adenine to guanine at position 481 that is related to the virulence of type 2 poliovirus [3-5].

DISCUSSION

Our patient had meningitis caused by vaccine-associated strain of type 2 poliovirus, although he had been immunized previously with oral polio vaccine. However, he was not a direct recipient of polio vaccine or immunocompromised host when he had this illness, and he had no discernible contact with the polio vaccine recipients. The virulence-associated nucleotide change of the isolated virus was revealed by our genetic analysis of the isolate. This indicates that the mechanism of this meningitis could have resulted from the reversion of the virus during replication in the other vaccine recipients [6-9]. Ozawa et al. [10] reported acute disseminated encephalomyelitis (ADEM) associated with polio vaccine due to neurovilurent mutations of the virus. The several nucleotide changes observed in this strain and our strain could be the candidates for the research of the genetic basis of the poliovirus virulence.

The oral live polio vaccines (OPV) have been widely used in many countries including Japan and USA, but in Western European countries, inactivated polio vaccine (IPV) has been used instead of OPV or combined with the following OPV. The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention in the USA also has a recommendation regarding the advantages of
IPV, because IPV may cause only 2 days of fever with no neurologic complications (1). Nevertheless, the OPV has certain advantages as follows: 1) OPV is more easily administered than IPV, 2) OPV confers humoral and serum immunity by infecting the gastrointestinal epithelial cells, and 3) children immunized with OPV can spread infection to non-immunized persons and provide herd immunity [1, 11]. However, the third advantage itself can cause the serious disadvantages, as observed in the reported cases and our patient, due to the easiness of the reversion of the genome sequences of the vaccine virus [11]. The vaccination program should be discussed considering these issues to establish a better immunization strategy regarding polio vaccines.

REFERENCES


