Title

Identification of Viruses in Cases of Pediatric Acute Encephalitis and Encephalopathy Using Next-Generation Sequencing

Key Points

- We evaluated the utility of next-generation sequencing for detecting viruses in clinical samples of encephalitis/encephalopathy patients.
- Among 18 pediatric patients with acute encephalitis/encephalopathy of unknown etiology, viral sequences were detected in 4 patients.
- Next-generation sequencing is useful for detection of causative viruses in patients with pediatric encephalitis/encephalopathy.

Summary

Associate Prof. Yoshinori Ito, Dr. Jun-ichi Kawada in Department of Pediatrics, Nagoya University Graduate School of Medicine (Dean: Masahide Takahashi, M.D., Ph.D.), and Dr. Yusuke Okuno in Center for Advanced Medicine and Clinical Research, Nagoya University Hospital, and their colleagues evaluated the utility of next-generation sequencing for detecting viruses in clinical samples of encephalitis/encephalopathy patients.

Acute encephalitis/encephalopathy is a severe neurological syndrome occasionally associated with viral infection. In many cases, the viral pathogen responsible for the disease is not identified and, therefore, comprehensive virus detection assays are desirable. We evaluated the of next-generation sequencing (NGS) for detecting viruses in clinical samples of encephalitis/encephalopathy patients. To assess NGS as a means of detecting viral sequences, samples from 18 pediatric patients with acute encephalitis/encephalopathy of unknown etiology were used for analysis. Results showed that large numbers of coxsackievirus A9 and mumps viral sequences were present in the cerebrospinal fluid of 2 and 1 patients, respectively. In addition, sequences of Pepper mild mottle virus were detected in the serum of one patient. These data indicate that NGS is useful for detection of causative viruses in patients with pediatric encephalitis/encephalopathy.

Research Background

Acute encephalitis/encephalopathy is a severe neurological syndrome occasionally associated with viral infection. To identify specific viral pathogens in cases of encephalitis/encephalopathy, PCR and viral antigen detection kits have been used. However, in many cases of acute encephalitis/encephalopathy, the pathogen is not identified because detection assays have not been established or are not commonly available for many viruses.

Next-generation sequencing (NGS) offers the prospect of relatively unbiased testing for

all previously catalogued and sequenced viruses in a single test. In this study, we examined cerebrospinal fluid (CSF) and serum samples taken from pediatric patients with acute encephalitis/encephalopathy using NGS.

Research Results

To investigate the NGS-based approach of detecting virus-derived sequences in clinical samples, CSF and serum taken from patients with a confirmed diagnosis of viral infection were examined. We extracted nucleic acid, and generated DNA and RNA sequencing libraries. NGS was performed using MiSeq or HiSeq 2500 instruments to obtain more than 5,000,000 sequence reads per sample. We confirmed that both DNA and RNA virus sequences could be detected by NGS with high sensitivity.

Next, we investigated the ability of NGS to detect viral sequences in 18 pediatric patients with acute encephalitis/encephalopathy of unknown etiology. Results showed that large numbers of coxsackievirus A9 and mumps viral sequences were present in the cerebrospinal fluid of 2 and 1 patients, respectively. In addition, sequences of Pepper mild mottle virus were detected in the serum of one patient. These data indicate that NGS is useful for detection of causative viruses in patients with pediatric encephalitis/encephalopathy.

Research Summary and Future Perspective

Our study demonstrates that the NGS-based approach for detection of virus-derived sequences may be a useful and reliable method for identifying the responsible viral pathogen in cases of encephalitis/encephalopathy. The NGS-based approach has great potential as an unbiased and highly sensitive method for analysis of pathogens present in clinical samples, and will likely contribute in the clinical and public health settings.

Publication

Japanese ver.

http://www.med.nagoya-u.ac.jp/medical/dbps_data/_material_/nu_medical/_res/topix/2016/next_20160921jp.pdf