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Identification of Non-Polio Enterovirus in an Infant with Impaired Immunity in Sri Lanka

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Abstract

Enteroviruses are a group of small RNA viruses. With their ubiquitous nature, they cause a wide spectrum of diseases worldwide. The majority of infections can be seen in the pediatric age group. Enteroviruses usually cause mild infections but also cause severe infections including encephalitis, acute flaccid paralysis, myopericarditis, acute respiratory and gastrointestinal infection, and sepsis. Patients with impaired immunity often have severe enteroviral infections with a high case fatality rate. Clinicians should be aware of the wide spectrum of clinical diseases associated with Enteroviral infections. Also, accurate and prompt diagnostic methods are important for the treatment and prevention of enteroviral infections.

Keywords: Enterovirus; Pediatric age group; Impaired immunity; Live vaccination; The wide spectrum of diseases.

Introduction

Enteroviruses are a group of viruses that belong to the genus enteroviruses in the family Picornaviridea [1]. They are small non-enveloped RNA viruses and have a single-stranded positive-sense RNA genome [1]. Genus Enterovirus has many species, namely Enterovirus A, B, C, D, and Rhinovirus A, B, and C according to the international committee for the taxonomy of viruses. Each Enterovirus species has many types of viruses including Poliovirus, Coxsackie A, and B, Echovirus, and Enteroviruses [1]. Enteroviruses show worldwide distribution [2]. These viruses can be transmitted via both fecal-oral and respiratory routes [2]. The majority of enteroviral infections are asymptomatic [2]. Symptomatic non-polio enteroviral infection includes a spectrum of diseases including aseptic meningitis, encephalitis, myopericarditis, acute flaccid paralysis, dermatomyositis, pleurodynia, acute hemorrhagic conjunctivitis, acute respiratory tract infections, herpangina, and diarrhea [1]. Patients with impaired immunity often have severe enteroviral infections with a high case fatality rate [3]. The isolation of the virus in cell culture, molecular techniques (RT-PCR), or retrospective serologic methods are used to diagnose the enteroviral infection [2]. An effective antiviral drug to treat serious enterovirus infections and severe disseminated infections in immunocompromised children may be needed. However, Pleconaril is yet to be approved as a therapeutic agent [2]. Well-established vaccines are available for poliovirus infection. Vaccines for Non-polio enteroviruses are still in the development stage. Standard, contact, and droplet precautions should all be used as infection control and prevention strategies to prevent enteroviral infections [4].

Here, we report a case of non-polio enterovirus pathogen identified in a stool specimen of a 6-month-old infant with impaired immunity.

Case history

A 6-month-old previously unevaluated baby girl from the northwestern part of Sri Lanka was transferred to the major Children's hospital in Sri Lanka with a history of fever, cough, loose stools, and skin nodules around the left side of the neck and arm for two weeks duration. She was up to date on all her childhood immunizations with BCG, pentavalent vaccine, Bivalent Oral Polio Vaccine (bOPV), and Inactivated Polio Vaccine (IPV) and was awaiting the 6 month vaccine doses. In developmental assessment, she had severe failure to thrive, despite adequate breastfeeding and complementary feeding. The Child Health and Development Record (CHDR) showed normal weight following age-appropriate centiles up to 3 months of age, af-

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ter that height or weight parameters were not assessed. The baby had an uneventful antenatal history, birth history, and past medical history. She also had no significant surgical exposure. She was the 3rd child in a low-income family with two elder brothers who are schooling. The mother denied any infant deaths in the family.

The examination revealed pallor and signs of malnutrition including thin skin, hair, severely reduced age-appropriate weight and height parameters, and overall reduced activity. She had signs of inflammation over the Bacille Calmette-Guerin (BCG) vaccination site on her left arm and ipsilateral axillary lymph nodes compatible with BCG adenitis. Her abdominal examination revealed mild hepatomegaly. Other system examinations were unremarkable including the nervous system examination.

Basic investigations showed severe leucopenia with a leucocyte count of 30 cells/µl and severe neutropenia and leukopenia, also she had a low hemoglobin level of 6 g/dL and a low platelet count. Inflammatory markers showed a high C-reactive protein level. The blood picture showed signs of severe bacterial infection, features of iron deficiency anemia with possible hemoglobinopathy. She also had deranged liver and renal functions. She was subjected to SARS-CoV-2 Rapid Antigen Test (RAT) and it was found to be positive. Dengue virus-specific IgM/IgG antibody test was negative. The cerebrospinal fluid full report (CSF) was clear and colorless, and CSF protein and glucose levels were within the normal range. The septic screening, including blood, urine, and cerebrospinal fluid culture did not identify any bacterial pathogen. The Ultrasound Scan (USS) of the left axillary region showed enlarged lymph nodes with early liquefaction. USS-Neck showed an absence of thymus. USS-Abdomen showed enlarged liver with a small amount of free fluid in the abdomen. Her stool full report was negative for amoeba, parasitic eggs, and cysts. Further, a stool sample was subjected to enterovirus isolation, suspecting that she might be a chronic excretor as she had already received two doses of bivalent Oral Polio Vaccine (OPV). The retroviral screening was negative. GeneXpert MTB/RIF was done with cerebrospinal fluid, and it was negative for mycobacterium tuberculosis. However, she was clinically suspected to be having Primary Immunodeficiency Disease (PID). As she had received a blood transfusion three weeks prior to admission, further immunological tests to confirm the primary immunodeficiency were delayed. Meanwhile, she was going into a septic shock and was admitted to the intensive care unit for further management. Broad-spectrum antibiotics, antivirals, and antifungals were started empirically to cover possible opportunistic infections. Also, she was put on anti-tuberculosis drugs suspecting disseminated mycobacterial infection/atypical mycobacterial infection. Unfortunately, she ended her battle for survival, two days after being admitted to the intensive care unit. Her stool sample which was sent to the reference laboratory for enteroviruses in Sri Lanka isolated a Non-Polio Enterovirus (NPEV) pathogen, which was later confirmed by the Real-Time Reverse Transcription Polymerase Reaction (rRT-PCR) assay.

Discussion

This 6-month-old baby girl was suspected of having Primary Immunodeficiency (PID) and she was in the process of laboratory confirmation with flow cytometry and serum immunoglobulin assay. This child has received live-attenuated vaccines before the immune deficiency was suspected and identified. So, she may have contracted the live virus contained in the live vaccines or vaccine strains excreted by her close contacts, such as contacts who have received recent OPV vaccination. As a result, the clinical team wanted to screen the child for poliovirus excretion. For this purpose, the reference laboratory for enterovirus received a stool sample from this patient. Upon receiving the sample, it was started to process. The Processed Feces (PF) was inoculated into two different cell lines as RD (derived from a human rhabdomyosarcoma, highly susceptible to polioviruses) and L20B (a mouse cell line (L-cells), genetically modified to express the human poliovirus receptor, highly selective for polioviruses) in tube cultures. After ten days of incubation with daily observation for characteristic Cytopathic Effect (CPE), fortunately, this child was not found to be a chronic poliovirus excretor. But she was positive for non-polio enterovirus in stool culture. This isolate was further tested by rRT-PCR, which was developed by the World Health Organization (WHO) and the center for disease control and prevention (CDC). It confirmed the presence of NPEV Ribonucleic Acid (RNA) in the child's stool sample. This isolate could theoretically be either a Coxsackie virus, an Echovirus, or an Enterovirus. Due to logistical constraints, further, identification wasn't possible in this child.

Patients with Primary Immunodeficiency Disease (PID) are unusually vulnerable to enteroviral infections [5]. According to the literature, patients with Common Variable Immunodeficiency (CVID) and autosomal recessive agammaglobulinemia have a greater susceptibility to contracting severe enterovirus infections [6].

This patient might have had disseminated non-polio enteroviral infection, encephalitis, aseptic meningitis, or myopericarditis-like serious infection. The altered liver enzymes and liver function test also support the suspicion of EV-induced hepatitis. However, when it comes to aseptic meningitis or encephalitis the CSF full report was negative without supporting the suspicion of viral infection. It may be due to empirical antimicrobial therapy which was administered with the clinical suspicion of primary immunodeficiency. On the other hand, CSF was not tested for enteroviral infection, so the central nervous system infections associated with enteroviral infection cannot be ruled out. The 2D echocardiogram, which is used to exclude myopericarditis has not been performed on this child as her initial vitals, including blood pressure and pulse rate were normal.

Alternatively, NPEV excretion might be an incidental finding in this child, as with the impaired immune system she could have excreted the virus longer than the immunocompetent individuals. The primary infection or bystander pathogen state could have been differentiated if we had performed, the enterovirus-specific Real-Time Polymerase Chain Reaction (RT-PCR) in blood, CSF, or nasopharyngeal swabs. Then those results can be correlated with the duration of the illness either to confirm or exclude non-polio enteroviral infection. When the Non-Polio Enterovirus (NEPV) stool culture results became available, the patient had already passed away, making it impossible to do the tests stated above.

A high level of clinical suspicion is needed to diagnose the infections associated with non-polio enteroviral infections, especially in immunocompromised patients [6]. On the other hand, accurate diagnosis up to the species level with molecular diagnostic methods is also of utmost importance. The prolonged viral replication in this kind of immunocompromised patient tends to develop new viral mutations, which may sometimes result in a severe spectrum of diseases. For these patients, proper clinical management, follow-up, and surveillance are crucial to preventing the development of severe infections and the trans-

mission of virus variants that could pose local and global health repercussions. Also, the family history of immunodeficiency should be evaluated in all newborns before live vaccines are administered.

Declarations

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All authors read and approved the final manuscript.

References

1. Specter SC, Hodinka RL, Wiedbrauk DL, Young SA. Clinical virology manual. American Society for Microbiology Press, 2009.
2. Bennett JR, Dolin R, Blaser MJ. Mandell, douglas, and bennett's principles and practice of infectious diseases E-book. Elsevier Health Sciences, 2019.
3. Galama JMD. "Enteroviral infections in the immunocompromised host," Rev Res Med Microbiol. 1997; 8: 33-40.
4. "Enterovirus D68 (EV- D68) for Health Care Professionals | CDC," 2022.
5. Chronic enteroviral meningoencephalitis in agammaglobulinemic patients.
6. Dropulic LK, Cohen JI. Severe Viral Infections and Primary Immunodeficiencies Clin Infect Dis Off Publ Infect Dis Soc Am. 2011; 53: 897-909.