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Identification of Viral Causes in Cerebrospinal Fluid of Patients Under Investigation for Central Nervous System Infections During the COVID-19 Epidemic: A Cross-Sectional Study

Nasrin Aliabadi [1], Nahid Heydari Marandi [1], Gholamreza Pouladfar [2], Seyedeh Sedigheh Hamzavi [2], Marzieh Hosseini [1], Rosemina Bahrololoom [1], Marzieh Jamalidoust [1], Mazyar Ziyaeyan [1,*]

[1] Department of Clinical Virology, Clinical Microbiology Research Center, Namazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Clinical Microbiology Research Center, Namazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

[*] ***Corresponding Author:*** Department of Clinical Virology, Clinical Microbiology Research Center, Namazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. Email: ziyaeyan@gmail.com

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Abstract

Background: Although viral etiology of central nervous system (CNS) infections such as meningitis and encephalitis are investigated widely worldwide, it remains to be declared under the COVID-19 pandemic.

Objectives: The focus of this study was to examine the etiology of viral CNS infections in patients hospitalized in a single referral hospital during the outbreak in Iran.

Methods: We retrospectively collected the cerebrospinal fluid (CSF) samples and reviewed the medical records of patients hospitalized with suspected viral CNS infection in Shiraz, a large city in southern Iran, from April 2021 to May 2022. One hundred sixty-six CSF samples were tested primarily for detection of HSV-1 and -2 and retrospectively analyzed by primers polymerase chain reaction (PCR) targeted to coronavirus 2 (SARS-CoV-2), human herpesviruses1 to 6 (HHV-1 to 6), polyomaviruses JC, and enteroviruses (EV).

Results: Of the total CSF samples analyzed by PCR, 22 (13.3%) were positive for only one viral pathogen, and just one (0.6%) sample was detected with multiple viruses (HSV-1 and CMV). The SARS-CoV-2 (6 cases) was the second most common viral etiology just after Herpes simplex virus-1 (HSV-1) 6.6% (11 cases). Other detected viruses were CMV for 1.8% (3 cases), VZV for 1.2% (2 cases), and JC for 0.6% (1 case) of the cases.

Conclusions: This study highlights the prevalence of viral pathogens in CSF samples from patients with suspected meningitis at Namazi Teaching Hospital. Notably, HSV-1 was the most common virus detected, followed by SARS-CoV-2. These findings underscore the importance of viral testing in the diagnosis and management of meningitis.

Keywords: Central Nervous System, Cerebrospinal Fluid, Cytomegalovirus Infections, Epstein-Barr Virus Infections, Herpes Simplex Infections, SARS-CoV-2, Varicella-Zoster Virus Infections

1. Background

Viruses are the leading cause of central nervous system (CNS) infections, surpassing bacteria, parasites, and fungal agents (1). Among these, enteroviruses (EV), arboviruses, and human herpes viruses are the most common causes of viral CNS infections (2). Throughout the coronavirus 2 (SARS-CoV-2) pandemic, numerous case reports have outlined the neurological symptoms associated with the disease (3). Despite its respiratory and cardiovascular tropisms, SARS-CoV-2 is recognized as potentially neurotropic. Common neurological symptoms include loss of smell and taste, headache, muscle pain, dizziness, cognitive impairment, and disturbances of consciousness (4). Studies indicate that neurological symptoms occur in more than 35% of COVID-19 patients, with some experiencing neurological manifestations as their initial symptoms. Extensive

as the PCR test for SARS-CoV-2 has near-perfect specificity.

Various factors may account for the low viral detection rate among patients suspected of CNS infections. Firstly, CSF analysis is indicated in patients presenting with a wide range of clinical manifestations caused by infectious and inflammatory diseases. A broad spectrum of infectious and inflammatory conditions may mimic CNS viral infection [Whitley et al., 1989; Adler-Shohet et al., 2003]. Additionally, the test was designed to detect nucleic acid from a limited range of viruses and other microbes potentially associated with encephalitis or meningitis. Another factor influencing the detection of viral nucleic acid is the time elapsed between the onset of neurological symptoms and CSF sampling.

The limitations of our study, conducted during the COVID-19 pandemic, significantly hindered our ability to collect a larger sample size. Furthermore, our single-center approach restricted access to CSF samples, potentially affecting the generalizability of our findings. Despite these limitations, we believe our results provide valuable insights into the viral causes of CNS infections during this period.

5.1. Conclusions

This study, conducted at Nemazi Teaching Hospital, analyzed CSF samples from patients suspected of having meningitis to identify viral pathogens. The results revealed that Herpes simplex virus-1 (HSV-1) was the most prevalent virus detected, followed by SARS-CoV-2. These findings highlight the importance of conducting viral tests in suspected meningitis cases, as accurate identification of causative agents is essential for effective diagnosis and treatment. Gaining a better understanding of the viral landscape can significantly enhance patient management and improve outcomes in meningitis cases.

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Footnotes

Authors' Contribution: Nasrin Aliabadi contributed to study concept, data search, data extraction and analysis, and drafting of the manuscript; Gholamreza Pouladfar contributed to study concept, supervision, revision of the manuscript and drafting of the manuscript; Nahid Heydari Marandi, Seyedeh Sedigheh Hamzavi, Marzieh Hosseini, and Marzieh Jamalidoust cooperated in data extraction and analysis, critical revision of the manuscript; Rosemina Bahrololoom contributed to data extraction and drafting of the manuscript; Mazyar Ziyaeyan were involved in the study concept, supervision, revision of the manuscript, guarantor of the article. All authors read and approved the final manuscript before submission.

Conflict of Interests Statement: The authors declare that they have no financial or non-financial conflict of interest.

Data Availability: The datasets used in the study are not publicly available due to protecting the participants' anonymity but are available on reasonable request.

Ethical Approval: The study design and protocols were approved by the Department of Medical Ethics and Philosophy of Health, Shiraz University of Medical Sciences, Iran under IR.SUMS.REC.1401.468, approved on 24 Nov 2022.

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