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Review Article On Overview Of Viral Meningitis

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ABSTRACT

Abstract:

The central nervous system is severely harmed by meningitis. The meninges, which are the membranes that encircle the brain and spinal cord, are inflamed. Bacterial, viral, or fungal infections can result in meningitis. This neurological condition can be brought on by a variety of viruses, including influenza, herpes, and enteroviruses. The majority of viral meningitis cases, however, have been linked to enteroviruses globally. It can be challenging to make an early diagnosis of viral meningitis because, with few exceptions, the clinical manifestations and symptoms are the same across the different causative agents. More research is required to better understand the pathogenesis of viral meningitis so that patients can receive better healthcare.

Keywords: Meningitis, enteroviruses, herpesviruses, influenza viruses

INTRODUCTION

Introduction:

The three protective membrane layers known as the meninges, which cover the brain and spinal cord, are prone to inflammation in the case of meningitis [1]. Dura mater, arachnoid mater, and pia mater are the meninges' three outermost layers, respectively. The subarachnoid space, which contains cerebrospinal fluid (CSF), divides the two inner layers—the arachnoid and pia mater—and is also referred to as the leptomeninges [2]. Beginning in the 1950s, when it was thought that aseptic meningitis might serve as a model for chronic nervous system diseases, aseptic meningitis, also known as slow viral disease, attracted attention [3]. Meningitis is most frequently brought on by bacteria. Meningitis can also be caused by non-infectious substances like drugs, viruses, and fungi [2]. Through hematogenous dissemination, infections can enter the CSF in two ways: 1) by infecting immune cells, which then transport the pathogen to the brain system, or 2) by passing through blood capillaries and entering the CSF as free pathogens [4]. For inflammation of the meninges brought on by pathogens other than pus-producing bacteria, the term aseptic meningitis is used [5]. Young children5ys are often affected with viral meningitis, which is the most prevalent kind of aseptic meningitis [1]. Approximately 75,000 new instances of viral meningitis are reported each year in the United States due to enteroviruses (EVs), which are the most frequent cause of the condition [6]. The most frequent causes of viral meningitis, as well as its pathophysiology, are discussed below in general terms. The disease's diagnosis, clinical symptoms, and epidemiological aspects are also covered.

Epidemiology:

The two seasons where viral meningitis is most prevalent are summer and autumn [7]. According to a research done in England between 2011 and 2014, there were 2.73 occurrences of viral meningitis for every 100,000 people, with non-polio enteroviruses being the main culprit in most of these cases [8]. The frequency of viral meningitis brought on by EV and human parechovirus (HPeV) is twice as common as bacterial meningitis, according to a different research conducted in the UK [9]. Additionally, a Danish research that was conducted revealed similar results, with non-polio enteroviruses being the most typical cause. They also demonstrated that aseptic meningitis incidence declines with age (58.7 per 100,000 after delivery, 38.7 per 100,000 in 6-month-old infants, and 15.6 per 100,000 in 5-year-old kids) [10]. A research from China also revealed that EV-71-caused viral meningitis accounted for about 55.2% of neurological problems [11]. When aseptic meningitis broke out in South Africa, coxsackievirus A9 was found to be the culprit responsible, and children under the age of 10 made up 87.3% of the victims [12]. E-30 (36.4%), coxsackievirus-B (19.6%), and EV-71 (13.1%) were the most frequently identified viruses in a study of patients in Austria from 2001 to 2004 that indicated that 56% of them had viral meningitis [13]. In a case study involving a 24-year-old Japanese man who had aseptic meningitis brought on by SARS-CoV-2, the most current virus to be identified as causing meningitis was revealed. This was shown by doing an RT-PCR test on a patient's CSF sample. In this case report, SARS-CoV-2's propensity for neuroinvasion and its ability to result in CNS sequelae like meningitis are also discussed. [14].

Clinical manifestations and diagnosis:

The symptoms of meningitis are often the same, despite the fact that the cause might change. In fact, meningitis's signs and symptoms might be mistaken for those of other illnesses including encephalitis or brain abcesses [15]. As a result, viral meningitis may go undetected. Compromised immunity, advanced age, travel history, and HIV infection are some of the risk factors that have been shown to make people more vulnerable to getting viral meningitis [7]. For more than a century, the presence of the most well-known bedside tests used by doctors to determine whether a patient should undergo a lumbar puncture—Brudzinski's sign, Kering's sign, or nuchal rigidity—was considered a reliable indicator of meningitis. It is known as the Brudzinski sign when a person's knees and hips bend while the neck is flexed [16] due to significant neck stiffness.

When the patient's knee is bent to a 90-degree angle and the doctor carefully straightens the leg, there should be no resistance or discomfort [17]. Despite their widespread usage, investigations have demonstrated that the diagnostic efficacy of these physical examinations in meningitis patients and normal cases is not substantially different [16]. Meningitis is first identified by a physical examination and assessment of the patient's medical history for any of the aforementioned symptoms. The physical examination approach known as jolt accentuation of headache, which was recently established and is less well-known, is used to evaluate meningeal irritation.

A lumbar puncture and CSF sample are required to conduct the etiological agent tests. The operation is carried out when the patient is lying or sitting down, and the CSF is aspirated by inserting a hollow needle into the subarachnoid space between vertebrae L3, L4, or L5 [18]. After that, the CSF is examined to measure the amounts of protein and glucose as well as the red blood cell and leukocyte counts. The different kinds of meningitis may usually be distinguished using the cell counts. For instance, bacterial meningitis is often characterised by a high WBC count (500 cells/l) and a high percentage of neutrophils (> 80%). Additionally, the CSF glucose level in bacterial meningitis usually doesn't rise above (300 mg/dL), but a low glucose CSF/blood ratio (0.4) and a high protein level (1 g/l) are signs of the condition [2].

Additionally, with 100% specificity, viral and bacterial meningitis may be distinguished from each other by lactic acid content (4.2 mmol/l) [19]. The primary diagnostic techniques for diagnosing bacterial infections are gramme staining and bacterial culture [2], and viral meningitis is suggested when both tests for CSF culture and Gramme staining are negative. A high percentage of lymphocytes (>80%) make up the WBC count in viral meningitis, which generally ranges between 80 and 100 cells/l (pleocytosis) . Protein and glucose levels often stay within normal range [20]. For the diagnosis of viral meningitis, pleocytosis is typically regarded as a crucial factor. Pleocytosis is frequently not seen in EV meningitis cases involving babies (38%) or children (39%), or when a lumbar puncture is carried out at an early stage of the disease, according to a number of studies [21,22].

The immune system immaturity of young infants may provide an explanation for this, albeit the cause is unknown [23]. Neutrophil pleocytosis is often symptomatic of bacterial meningitis rather than viral meningitis. However, it has been discovered that 25% of individuals with CNS disorders brought on by viral agents also exhibit neutrophilic pleocytosis [24]. Additionally, a research found that 47% of study participants with enteroviral meningitis exhibited neutrophilic pleocytosis [25].

The polymerase chain reaction (PCR), which locates and measures viral DNA or RNA in the patient's CSF, is the gold standard method for diagnosing viral meningitis [26]. A study of EV-positive meningitis cases in paediatric patients found that real-time PCR (RT-PCR) testing of CSF samples produced 100% sensitivity, as opposed to viral culture's 38% sensitivity. Similar results were seen in a study of meningitis patients with HPeV positivity, where 100% sensitivity was obtained with RT-PCR but not with viral culture [27]. A 9-day-old baby with fever and agitation was recently the subject of a case report who was brought into the emergency room. The patient tested positive for EV (particularly, E-25), and viral meningitis was identified as the cause by means of molecular analysis (RT-PCR and sequencing) [28]. However, because acquiring CSF can be challenging, other specimens may be utilised in its place, such as blood, throat or nasal swabs, or stool samples, particularly in situations when EV infections are suspected [29].

However, serological tests can be used to diagnose infections with the mumps virus, herpesvirus, arboviruses, and the human immunodeficiency virus (HIV), even if the findings may be negative in the early stages of the illness. Therefore, a second sample should be acquired and analysed once more for viral agents two weeks later [5]. The efficacy of next-generation sequencing (NGS) as a diagnostic tool for meningitis patients is still unclear, and additional research is needed [30]. NGS has recently been employed in a number of studies to detect a wide range of infections, including viruses.

Pathogenesis:

When the causal agent enters the host by respiratory secretions or by the fecal-oral route to produce primary infection in the respiratory or gastrointestinal (GI) tract, viral meningitis pathogenesis starts. Meningitis or other neurological issues may result from the CNS's secondary infection that follows this. Infection of the lymphoid tissue, induction of inflammation and blood-brain barrier (BBB) collapse, infection of peripheral sensory neurological pathways, and infection of the choroid plexus epithelium are some of the several methods via which the CNS can get infected with viruses [31,32,33,34]. Increased amounts of chemoattractants, neutrophils, CD8 T cells, and monocytes are seen after the viral agent has entered the CNS, which shows that an immunological response has been induced [31]. INF- and IL-6 levels in CSF were shown to be raised in a research utilising a murine viral meningitis model in which mice were infected with the LCMV (lymphocytic choriomeningitis virus) [50]. In a different research, individuals with aseptic meningitis had higher levels of IL-1, a cytokine that promotes inflammation [36]. Aseptic meningitis therefore triggers a strong inflammatory immune response that is crucial to the pathophysiology of the illness. But due to a lack of data, research into the pathophysiology of aseptic meningitis is challenging. Additionally, it is made more difficult by the fact that the majority of viral meningitis cases go unreported, and fatal cases show as severe encephalitic syndrome rather than meningitis. [17].

Management:

Although patients with viral meningitis typically do not require hospitalisation, medication should be offered, including antipyretics, antiemetics, and analgesics that may be taken at home. However, some individuals, such as those who experience seizures, need to be under medical monitoring [5]. Although corticosteroids are frequently used in cases of suspected bacterial meningitis to lessen the inflammatory impact that the illness causes, there is little proof of their effectiveness against viral meningitis, and additional research is still required [37]. Pleconaril is an antiviral medication that works as an inhibitor of enterovirus replication by concentrating on the viral capsid structure [38]. It is approved for use as intranasal therapy for the common cold, but because it reaches many times greater concentrations in the CNS, it may also be used to treat other conditions that affect the brain, such as meningitis [39]. The duration of symptoms, particularly headaches, are shortened by pleconaril, according to a number of studies [6, 39].

There was no discernible difference between the treatment and placebo groups, however, according to other research [40]. Due to the medicine's ability to activate the CYP3A enzyme and produce a drug interaction, particularly with oral contraceptives, the FDA did not approve its oral use [41]. According to a UK study, individuals with viral meningitis spent an average of 4 days in the hospital and those receiving antiviral medication spent an average of 9 days there. They came to the conclusion that lengthier hospital stays and long-term morbidity were related to delays in lumbar puncture procedures and needless therapies [8]. Aseptic meningitis does not have a defined course of therapy; instead, supportive drugs are typically used to reduce symptoms including fever and headache. In the majority of cases, complete recovery takes 5 to 14 days [5].

Regarding HSV treatment, one research found that immunocompromised individuals with HSV-induced meningitis should begin antiviral therapy right once and that any delay in administering the medication might lead to the emergence of negative side effects [42]. Acyclovir's effectiveness in treating HSV-2-induced meningitis was also studied, and treated patients had improved results. One patient, however, experienced concentration issues as a meningitis symptom that persisted for around three months [43]. Psoromic acid, a bioactive chemical produced from lichens, has recently been shown to impede the replication of both HSV-1 and HSV-2 by inhibiting proteases and DNA polymerases, making it a potential treatment for meningitis brought on by HSV [44]. The capacity of valacyclovir to reduce viral replication and prevent meningitis recurrence was also examined in clinical studies. The use of valacyclovir (twice daily) as a therapy, however, was not suggested for the prevention of recurrent meningitis [45, 46]. For certain viruses, including EV-71 [47], vaccinations have been created.

A virus-like particle (VLP) vaccination against EV-D68 has recently been created [48]. A 3CD protease and P1 precursor-expressing recombinant baculovirus makes up the VLP. High vaccination effectiveness was demonstrated in clinical studies [48].

Conclusion:

One of the most prevalent clinical disorders affecting people of all ages is viral meningitis. In adults, it frequently remains unnoticed or develops into a self-limited illness. Infants and young children, however, are susceptible to serious consequences that can result in high fever, mental impairment, and in extreme circumstances, even death. Aseptic meningitis has been linked to several viral pathogens, including enterovirus, parechovirus, and herpesviruses. Knowing the most frequent causes of aseptic meningitis would thus aid in better understanding the condition and serve as the foundation for developing preventative and control programmes. Many nations, particularly the MENA area, lack molecular epidemiology research on viral meningitis. The aetiology and pathogeneses of this sickness should thus be better understood in order to create novel treatment strategies that will aid in improving outcome. Ortner B, Huang CW, Schmid D, Mutz I, Wewalka G, Allerberger F, Yang JY, Huemer HP. Epidemiology of enterovirus types causing neurological disease in Austria 1999–2007: detection of clusters of echovirus 30 and enterovirus 71 and analysis of prevalent genotypes. Journal of medical virology.

ETHICAL STATEMENT

Ethical statement:

This study has no cruelty to humans or animals. Since, it is a review article, we did not took a subjects in this study.

CONFLICT OF INTEREST

Conflict of interest:

The above study describes the early diagnosis of viral meningitis because, with few exceptions, the clinical manifestations and symptoms are the same across the different causative agents.

References:

1. Wolinsky JS, Klassen T, Baringer JR. Persistence of neuroadapted mumps virus in brains of newborn hamsters after intraperitoneal inoculation (1976).
2. Walker HK, Hall WD, Hurst JW. Clinical methods: the history, physical, and laboratory examinations (1990).
3. Ramilo O. Detection of interleukin 1β but not tumor necrosis factor—α in cerebrospinal fluid of children with aseptic meningitis (1990).
4. Bergström T, Alestig K. Treatment of primary and recurrent herpes simplex virus type 2 induced meningitis with acyclovir (1990).
5. Frei K. Production of B cell stimulatory factor-2 and interferon gamma in the central nervous system during viral meningitis and encephalitis. Evaluation in a murine model infection and in patients (1998).
6. Pevear DC. Activity of pleconaril against enteroviruses (1999).
7. Romero JR. Pleconaril: a novel antipicornaviral drug (2001).
8. Momméja-Marin H. Herpes simplex virus type 2 as a cause of severe meningitis in immunocompromised adults (2003).
9. Abzug MJ. Double blind placebo-controlled trial of pleconaril in infants with enterovirus meningitis (2003).
10. Seehusen DA, Reeves M, Fomin D. Cerebrospinal fluid analysis (2003).
11. Kumar R. Aseptic meningitis: diagnosis and management. The Indian Journal of Pediatrics. 2005 Jan..
12. Kupila L. Diagnosis of enteroviral meningitis by use of polymerase chain reaction of cerebrospinal fluid, stool, and serum specimens (2005).
13. Desmond RA, Accortt NA, Talley L, Villano SA, Soong SJ, Whitley RJ. Enteroviral meningitis: natural history and outcome of pleconaril therapy. Antimicrobial agents and chemotherapy. 2006 Jul.
14. Hviid A, Melbye M. The epidemiology of viral meningitis hospitalization in childhood. Epidemiology. 2007 Nov 1.
15. Logan SA, MacMahon E. Viral meningitis. 2008 Jan 3
16. Irani DN. Aseptic meningitis and viral myelitis (2008).
17. Wong KT. The distribution of inflammation and virus in human enterovirus 71 encephalomyelitis suggests possible viral spread by neural pathways (2008).
18. Kim JV. Myelomonocytic cell recruitment causes fatal CNS vascular injury during acute viral meningitis (2009).
19. Paintsil E, Cheng Y-C. Antiviral agents. In: Schaechter M (ed) Encyclopedia of microbiology (2009).
20. Hoffman O, Weber JR. Pathophysiology and treatment of bacterial meningitis. Therapeutic advances in neurological disorders. 2009 Nov
21. Ortner B. Epidemiology of enterovirus types causing neurological disease in Austria 1999–2007: detection of clusters of echovirus 30 and enterovirus 71 and analysis of prevalent genotypes (2009).
22. Visintin C. Management of bacterial meningitis and meningococcal septicaemia in children and young people (2010).
23. Seiden JA. Lack of cerebrospinal fluid pleocytosis in young infants with enterovirus infections of the central nervous system (2010).
24. Méchaï F. Caractéristiques clinicobiologiques des méningites à Enterovirus de l'adulte : étude de 59 cas. La Revue de Médecine Interne (2010).
25. Mehndiratta M. Appraisal of Kernig's and Brudzinski's sign in meningitis. Ann Indian Acad Neurol (2012).
26. Crom SC. Characteristics of pediatric patients with enterovirus meningitis and no cerebral fluid pleocytosis (2012).
27. Munster VJ. Rapid Nipah virus entry into the central nervous system of hamsters via the olfactory route (2012).
28. Aurelius E. Long-term valacyclovir suppressive treatment after herpes simplex virus type 2 meningitis: a double-blind, randomized controlled trial (2012).
29. Verstrepen WA. Rapid detection of enterovirus RNA in cerebrospinal fluid specimens with a novel single-tube real-time reverse transcription-PCR assay (2013).
30. De Crom S. Prospective comparison of the detection rates of human enterovirus and parechovirus RT-qPCR and viral culture in different pediatric specimens (2013).
31. Booss J, Tselis AC. Chapter 1—a history of viral infections of the central nervous system: foundations, milestones, and patterns (2014). https://doi.org/10.1016/B978-0-444-53488-0.00001-8

32. Hu Y, Jiang L, Peng HL. Clinical analysis of 134 children with nervous system damage caused by enterovirus 71 infection. The Pediatric infectious disease journal. 2015 Jul 1.
33. Esposito S. Enterovirus D68 infection (2015).
34. Kato K. Recurrent neonatal herpes simplex virus infection with central nervous system disease after completion of a 6-month course of suppressive therapy: case report (2015).
35. Jaijakul S. The clinical significance of neutrophilic pleocytosis in cerebrospinal fluid in patients with viral central nervous system infections (2017).
36. Bookstaver PB. Management of viral central nervous system infections: a primer for clinicians (2017).
37. Yi E-J. Enterovirus 71 infection and vaccines (2017).
38. Messacar K. Enterovirus D68 and acute flaccid myelitis-evaluating the evidence for causality (2018).
39. McGill F, Griffiths MJ, Bonnett LJ, Geretti AM, Michael BD, Beeching NJ, McKee D, Scarlett P, Hart IJ, Mutton KJ, Jung A. Incidence, aetiology, and sequelae of viral meningitis in UK adults: a multicentre prospective observational cohort study. The Lancet Infectious Diseases. 2018 Sep 1.
40. Buch K. Cerebrospinal fluid lactate as a marker to differentiate between community-acquired acute bacterial meningitis and aseptic meningitis/encephalitis in adults: a Danish prospective observational cohort study (2018).
41. Dai W. A virus-like particle vaccine confers protection against enterovirus D68 lethal challenge in mice (2018).
42. Hassan STS. Psoromic acid, a lichen-derived molecule, inhibits the replication of HSV-1 and HSV-2, and inactivates HSV-1 DNA polymerase: shedding light on antiherpetic properties (2019).
43. Kadambari S, Braccio S, Ribeiro S, Allen DJ, Pebody R, Brown D, Cunney R, Sharland M, Ladhani S. Enterovirus and parechovirus meningitis in infants younger than 90 days old in the UK and Republic of Ireland: a British Paediatric Surveillance Unit study. Archives of Disease in Childhood. 2019 Jun 1.
44. Hassan STS. Psoromic acid, a lichen-derived molecule, inhibits the replication of HSV-1 and HSV-2, and inactivates HSV-1 DNA polymerase: shedding light on antiherpetic properties (2019).
45. Hersi K, Gonzalez FJ, Kondamudi NP. Meningitis. 2020 Nov 21. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459360
46. Moriguchi T. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2 (2020).
47. Poplin V, Boulware DR, Bahr NC. Methods for rapid diagnosis of meningitis etiology in adults (2020).
48. Hudson JA. Outcomes beyond hospital discharge in infants and children with viral meningitis: a systematic review (2020).
49. https://media.springernature.com/2020.

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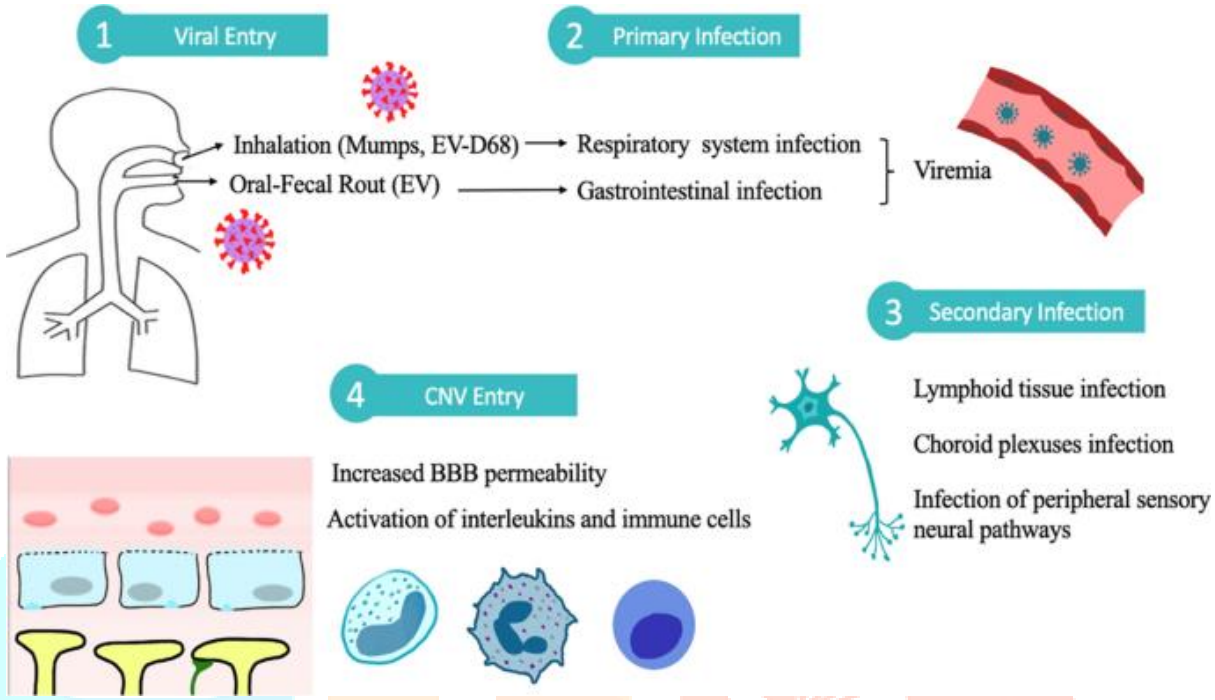

Fig: 1 (49).