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Prevalence, Causes and Management of Encephalitis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Encephalitis is a major cause of morbidity, mortality, and permanent neurological disability in both adults and children. The term "encephalitis" literally means inflammation of part or all of the "brain" or the brain parenchyma. Encephalitis affects people of all ages; however, the incidence is higher

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in the pediatric population. Although both genders are affected, most studies showed slight dominance in men. There are two main types with different causes: primary or infectious encephalitis can develop when a fungus, virus, or bacteria infects the brain and accounts for approximately 70% of confirmed cases of encephalitis, and secondary or post-infectious encephalitis when the immune system is active and reacts. to a previous infection and mistakenly attacks the brain. The clinical manifestations depend on whether the brain parenchyma or the meninges are predominantly involved and cause an encephalitic or meningitis syndrome. Diagnostic tests should include a lumbar puncture, an MRI of the brain, and an EEG for suspected encephalitis. In encephalitis, a broad differential diagnosis, both infectious and non-infectious, should be considered. These alternatives include malignancy, autoimmune or paraneoplastic diseases (eg, anti-NMDA receptor encephalitis), brain abscess, drug-induced tuberculosis or delirium, neurosyphilis, or bacterial, fungal, protozoal, or helminthic encephalitis. Antiviral medications, such as intravenous acyclovir, are often given at the initial diagnosis of encephalitis before the cause is known. Acyclovir is the best treatment for herpes simplex encephalitis. If medication can be started soon after symptoms appear, the chance of a full recovery is much higher.

Keywords: Disability; encephalitis; inflammation; management; neurologic; brain parenchyma.

1. INTRODUCTION

Encephalitis is a major cause of morbidity, mortality, and permanent neurological disability in both adults and children. The term "encephalitis" literally means inflammation of part or all of the "brain" or the brain parenchyma [1].

Causes are diverse and include viral and non-viral infections of the brain, as well as autoimmune processes. In the West, autoimmune encephalitis is more common than any other infectious cause today, but infectious causes are even more common in Asia [2]. In 2006, the World Health Organization coined the term "acute encephalitis syndrome," which simply means acute fever with seizures or impaired consciousness, or both [2]. In 2013, the International Encephalitis Consortium established criteria for the diagnosis of encephalitis based on clinical and laboratory characteristics.

Diffuse noninflammatory dysfunction of the brain is known as "encephalopathy" and common causes are metabolic, toxic, or ischemic disorders. The term encephalopathy is also used to refer to behavioural changes due to any cause. Encephalopathy can also be acute or chronic [3].

Encephalitis and meningitis are overlapping syndromes. Pathologically, both viral and nonviral invasions of the brain cause some level of meningeal and parenchymal inflammation. Therefore, many doctors prefer the term "meningoencephalitis". Clinically there is a spectrum of manifestations, but in general two different patterns are observed. When the disease is associated with marked sensory changes, the clinical syndrome is called "encephalitis"; When the mening irritation is prominent, it is known as "meningitis". The term "aseptic meningitis" is used for self-limited meningitic presentation and little or no sensory change [4].

1.1 Objectives

The study aims to summarize the updated evidence regards, epidemiology, etiology, pathophysiology, clinical manifestations, diagnosis, and management of encephalitis.

2. EPIDEMIOLOGY

The incidence varies between studies, but is generally between 3.5 and 7.4 per 100,000 patient-years. Encephalitis affects people of all ages; however, the incidence is higher in children and adolescents. Although both genders are affected, most studies showed slight dominance in men [5].

Various factors such as age, geographic location, season, climate, and immune status of the host influence the epidemiology of encephalitis. Arboviruses, or arthropod-borne viruses, have their life cycle in insect vectors and vertebrates and occasionally infect humans who are "dead-end hosts." The different arboviral encephalitis have their own specific geographic distribution depending on the activity of their insect vectors. Arboviral encephalitis prevalent in the US includes, for example, western equine, eastern

equine, California, and St. Louis encephalitis. Venezuelan encephalitis occurs in South America and JE in Asia [6]. These encephalitis usually occur during epidemics or outbreaks. Occasionally, when a new pathogen is introduced into a vulnerable population, an explosive outbreak occurs. HSVE is the most common sporadic infectious encephalitis in western countries. It tends to occur worldwide with little seasonal or age- and gender-specific preference. West Nile encephalitis virus was introduced to the United States in the 1990s and is endemic there. Mumps, measles and rabies encephalitis has been largely eradicated in many developed countries thanks to effective vaccination programs [7].

2.1 Etiology

There are two main types with different causes: Primary or infectious encephalitis can develop when a fungus, virus, or bacteria attack the brain.

Secondary or postinfectious encephalitis is when the immune system reacts to a previous infection and mistakenly attacks the brain [8].

Infectious encephalitis can be etiologically viral, bacterial, fungal, protozoal, or helminthic. The etiology of many cases of encephalitis remains unknown despite extensive investigation. Viruses are the most commonly identified cause, accounting for about 70% of confirmed cases of encephalitis. In the United States, the most common causes of viral encephalitis are herpes simplex virus (HSV), and the two most common human herpes viruses identified in encephalitis are HSV1 and VZV. The HSV-PCR test can lead to false negative results, especially in children and in the early course of the disease [9]. If the suspicion of herpes simplex encephalitis persists despite a negative test in the first LP, a second CSF examination should be repeated within 3 to 7 days. West Nile virus and enterovirus. Some of the other viral pathogens are chickenpox virus, EpsteinBarr virus (EBV), cytomegalovirus (CMV), human herpes virus types 6 and 7, measles virus, mumps virus, rubella virus, St. Louis virus, eastern equine virus, western equine virus. and dengue virus Rabies virus [10].

Autoimmune encephalitis occurs more frequently in immunocompetent patients than in immunosuppressed patients (22% versus 3%). Most patients with antibody-associated encephalitis have seizures. Additionally, recent studies show that some forms of autoimmune encephalitis can be caused by herpes simplex encephalitis or a previous viral infection [11].

2.2 Path Physiology

Although they are not well understood for some etiologies, a variety of mechanisms contribute to encephalitis. Encephalitis can be infectious and caused by the pathogen that enters the brain directly, most commonly gray matter [12]. Viruses enter the host at a site outside the CNS and replicate. Most then reach the spinal cord and brain via the hematogenous route. HSV, rabies, and the herpes zoster virus are major exceptions. They migrate from nerve endings to the CNS in a retrograde manner. Once in the brain, the virus and the host's inflammatory response disrupt the function of nerve cells. [13].

Viruses invade the host at a site outside the CNS and replicate. Most then reach the spinal cord and brain hematogenously. HSV, rabies, and herpes zoster virus are important exceptions to this. They travel to the CNS from nerve endings in a retrograde manner. Once in the brain, the virus and the host's inflammatory response disrupt neural cell function. On gross examination, there is usually cerebral edema, vascular congestion, and hemorrhage. Infiltration with leukocytes or microglial cells is also a common feature. With EEE and JE, the extent of necrosis can be significant [13].

2.3 Clinical Manifestations

The clinical manifestations depend on whether the brain parenchyma or the meninges are predominantly involved and cause an encephalitic or meningitic syndrome. However, the same active ingredient can produce a predominantly meningitic image in one patient and an encephalitic image in another patient. The severity of manifestations varies widely from mild febrile illness with headache to severe illness with seizures, coma, neurologic deficits, and death [14]. The onset usually begins abruptly with fever and deteriorating mental status. You may experience irritability, agitation, screaming spells, confusion, delirium, drowsiness, drowsiness, or coma. Older children may complain of headaches. Typical symptoms are an initial stage of fever, headache, and vomiting lasting less than a week, followed by seizures, coma, and neurological disorders with or without signs of meningeal irritation. Severe cases can be accompanied by a life-threatening increase in brain tension, decerebration, or flaccid coma. In

general, this stage lasts 7 to 10 days, followed by a gradual recovery, with or without sequelae [15].

2.4 Diagnosis

Diagnostic tests should include a lumbar puncture, an MRI of the brain, and an EEG for all suspected encephalitis [16]. Diagnosis may require one or more test of the following:

- Brain imaging (MRI or CT) which may divulge any swelling of the brain.
- Spinal tap (lumbar puncture) as changes in spinal fluid may signpost infection and inflammation in the brain.
- Electroencephalogram (EEG).
- Other lab tests. Samples of blood, urine or excretions from the back of the throat can be tested for viruses or other infectious agents.
- Brain biopsy which is usually done only if symptoms are worsening and treatments are having no effect.

After clarifying the contraindications, a lumbar puncture with measurement of the opening pressure should be performed to obtain cerebrospinal fluid for total and differential cell counts, diagnostic tests, proteins and glucose. The CSF in viral encephalitis generally has essentially normal glucose, elevated protein, and mild to moderate mononuclear pleocytosis (predominantly lymphocytic, but may be neutrophilic early in the course). The normal white blood cell count of babies is higher than that of adults. A 95th percentile cutoff of no more than 19 leukocytes / µL in infants younger than 1 month or no more than 9 leukocytes / µL in infants 1 to 2 months of age defines pleocytosis. On the other hand, infectious encephalitis, especially with EV (~ 50%) or human parechovirus (HPeV), is more likely without pleocytosis. If symptoms persist or worsen, repeat lumbar puncture should be considered [17].

2.5 Investigations for Etiology

Large numbers of viruses are known to cause encephalitis, but virologic diagnosis is complex, expensive, and time-consuming. The responsible virus can only be detected in the brain itself and is not found or is temporarily found in blood or liquor. For these reasons, it is not surprising that, even in advanced centers, an etiological diagnosis is not made in more than half of the cases [18]. Different centers could develop their own research algorithms according to local etiological scenarios. The timing of sampling is important, as PCR will be positive at the onset of the disease, while IgM may take 4 to 7 days to appear. In Japanese JE encephalitis, the CSF IgM capture enzyme-linked immunosorbent assay (ELISA) is the gold standard for diagnosis. PCR for JE genome / DNA in CSF or serum, if positive, confirms the diagnosis. JE-PCR positivity varies greatly in different studies (9 to 77.8%) and early samples have a higher positivity rate. Serum IgM and NS1 antigens are used to diagnose dengue encephalitis / encephalopathy. The Rickettsial IgM Serum ELISA is used to diagnose typhoid scrub meningoencephalitis [19]. Multiplex PCR panels are being developed for a variety of drugs for the etiological diagnosis of encephalitis. Detection of autoantibodies in CSF or serum confirms the diagnosis of EIA.

Contrast and non-contrast magnetic resonance imaging of the brain using diffusion sequences, T2-weighted, and fluid attenuated inversion recovery (FLAIR) is the method of choice for evaluating changes consistent with brain parenchymal inflammation. For some pathogens, a specific MRI image can be seen [20]. Herpes simplex encephalitis classically affects the temporal and frontal lobes. Focal edema is seen on the medial aspect of the temporal lobes, the orbital surfaces of the frontal lobes, the cortex of the islets, and the cingulate gyrus. JE causes T2 hyperintensities in the thalamus, basal ganglia, and brainstem. Changes in the temporal lobe are also observed in a small proportion of JE. Imaging findings in patients with EIA can be normal or highly variable. Recognition of characteristic findings within limbic structures can alert clinicians to the possible diagnosis [21].

Brain CT may show specific abnormalities (reduced attenuation in one or both temporal lobes or areas of hyperintensity) suggesting HSV in up to 80% of patients at presentation [22]. EEG should be used to look for evidence of encephalopathy, localization signs, or subclinical seizure activity. Characteristic patterns such as periodically localized epileptiform discharges are seen in approximately one third of patients with HSVE. An extreme delta brush pattern can be seen in patients with EIA [23].

2.6 Differential Diagnosis

In encephalitis, a broad differential diagnosis, both infectious and non-infectious, should be

considered. These alternatives include malignancy, autoimmune or paraneoplastic diseases (eg, anti-NMDA receptor encephalitis), brain abscess, drug-induced tuberculosis or delirium, neurosyphilis, or bacterial, fungal, protozoal, or helminthic encephalitis [24].

2.7 Management

Intravenous acyclovir is a life-saving treatment for HSV encephalitis and has reduced mortality from more than 70% to around 10-20%. It is relatively safe, although there is little risk of kidney dysfunction due to crystal nephropathy. Kidney function should be monitored; The dose should be reduced in patients with known renal impairment [25].

Ideally, patients with suspected brain infection should have an LP followed immediately by empirical treatment. However, if LP is delayed for more than 6 hours, empirical acyclovir may be required before LP. Patients with HSV encephalitis are likely to remain CRP positive in CSF for at least the first few days after starting treatment, so LP should be performed as soon as possible in patients who have started acyclovir [26]. This contributes to the diagnosis and therefore determines the duration of treatment. UK guidelines recommend that acyclovir be taken for at least 2 weeks, after which the LP should be repeated. If HSV-PCR remains positive, acyclovir should be continued with LP repeat every week until PCR is negative. If the patient is perfectly healthy, some would suggest that a repeat LP is not required [27].

The treatment of autoimmune encephalitis with immunotherapy is not standardized and is based on evidence from retrospective studies. Most neurologists use intravenous or oral corticosteroids for initial therapy. Intravenous immune globulin or plasma exchange are also used frequently, especially in patients who do not improve [28]. Patients should be closely screened for underlying malignancies, as a proportion of cases are paraneoplastic. Available evidence suggests that early treatment improves outcomes and that if initial therapy is ineffective, second-line therapy with stronger agents is beneficial [29].

Of the patients with encephalitis, 50% to 60% have acute-phase seizures, which can be clinically subtle, and their control is a key aspect of treatment. Seizures are best treated with intravenous anticonvulsants, such as phenytoin or valproate, which do not depress the sensorium. Once the patient has stabilized and the cramps are under control, tube feeding can begin. Care should be taken to avoid aspiration and protocol should be followed for the treatment of a comatose patient. The patient should be placed on their side or semi-dry [30].

If there are signs of increased intracranial pressure, an infusion of mannitol (0.25 to 1.0 mg / kg every 4 to 6 hours) or intravenous furosemide may be necessary. Hypertonic saline (3%) at a dose of 0.1 to 1 ml / kg per hour to maintain serum sodium between 145 and 155 mEq / L is another option. Hyperventilation, to keep the blood pressure of carbon dioxide (CO 2) between 25-30 mm Hg, can also be used to combat increased intracranial pressure. If facilities are available, brain tension monitoring makes sense. If brain tension rises rapidly with clinical deterioration that does not respond to drug treatment, surgical decompression can be life-saving [31].

Caring for patients with encephalitis is a challenge for nurses. Patients often have physical, neuropsychological and communication difficulties that make it difficult to interact with their environment and loved ones.
Most patients with encephalitis continue to have some degree of neuropsychological impairment (22) and the prevalence of attention, behavioral, and emotional disorders in survivors remains high up to 3 years after diagnosis. Access to neuropsychological services can be invaluable for memory problems and other psychological changes in encephalitis [32].

3. CONCLUSION

Encephalitis is a major cause of morbidity, mortality, and permanent neurological disability in both adults and children. It means inflammation of part or all of the "brain" or brain parenchyma. There are two main types with different causes: primary or infectious encephalitis, which accounts for approximately 70% of confirmed cases of encephalitis, and secondary or post-infectious encephalitis. The clinical manifestations depend on whether the brain parenchyma or the meninges are predominantly affected. Diagnostic tests should include a lumbar puncture, an MRI of the brain, and an EEG for all suspected encephalitis. In encephalitis, a broad differential diagnosis, both

infectious and non-infectious, should be considered. Antiviral medications, such as intravenous acyclovir, are often given when encephalitis is first diagnosed before the cause is known. Acyclovir is the best treatment for herpes simplex encephalitis. If medication can be started soon after symptoms appear, the chance of a full recovery is much higher.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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