IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Encephalitis: an overview

Ashwin Mahajan, Sakshi Somase, Vishal Supekar

Encephalitis is an inflammation of the brain parenchyma, presents as diffuse and/or focal neuropsychological dysfunction. There is difference between encephalitis and meningitis, though on clinical evaluation both can be present with signs and symptoms of meningeal inflammation, such as photophobia, headache, or stiff neck. It is also different from cerebritis. Cerebritis describes the stage preceding pus formation and implies a highly destructive bacterial infection of brain tissue, whereas acute encephalitis is most commonly a viral infection with parenchymal damage varying from mild to profound.

Although bacterial, fungal, and autoimmune disorders can produce encephalitis, predominant cases are viral in origin.

Japanese Encephalitis:

Japanese encephalitis is an infectious disease of central nervous system found worldwide. It is a vector-born disease with an annual estimation of 50,000 cases and 15,000 deaths worldwide. Half of the survivors suffer from severe neuropsychiatric sequels. Japanese encephalitis is caused by Japanese encephalitis virus and transmitted by Culex mosquitoes. It has been described as “plague of Orient”.

- History:

Encephalitis were described in Japan from 1870. Term Type “A” encephalitis was used to distinguish between Type A encephalitis (i.e. sleeping sickness). In 1933 the infiltrating agent was transmitted in monkeys to cause encephalitis. In 1935 the prototype Nakayama strain of JE was isolated.

- Epidemiology:

Japanese encephalitis virus belongs to genus Flavivirus, family Flaviviridae. Genetic material of virus has single –stranded, positive-sense RNA of nearly 11 kb in length.

Humans are dead end hosts for JEV. JE is mostly occurred in children and young adults. Immunologically naïve adults are more susceptible to disease. Susceptibility is demonstrated by incidences of JE in US troops commissioned in Japan, Korea, Viatnam during conflicts. During summer months huge epidemics occur.

Japanese encephalitis is transmitted by mosquitoes, and infect people across eastern and southern Asia, Pacific rim and northern Australia. Around 67,900 cases occurred annually in 24 countries. JE have range of 20%-30% fatality rate, with 30%-50% neurological or psychiatric sequels observed in survivors.

The disease mainly observed in northern areas - Bhutan, Bangladesh, People’s Republic of China, Taiwan, Japan, South Korea, Nepal, northern Vietnam, India, Thailand, Pakistan and Russia – with typical seasonal characteristics.

In southern areas- Australia, Burma, Brunei Darussalam, Cambodia, Indonesia, Laos, Malaysia, Papua New Guinea (PNG), Philippines, Singapore, southern Vietnam, southern Thailand, southern India, Sri Lanka, and Timor-Leste – occur sporadically throughout year.

- Geogrphical Distribution of JE:

Australia:

The disease was first recognised in 1995. Cx.annulirostris was the major vector.

Bangladesh:

First reported in 1977. All JE cases were from rural areas. 90% cases occurred during May-October.

Myanmar:

JE existed in Burma since 1968 but first reported in 1975. All cases reported in July-October. 93% of patients were under 20 year age. Main vector was found to be Cx. tritaeniorhynchus

Camobodia:

Japanese encephalitis virus was first isolated in 1965. Survilance reports shows that 90% of patients were under 12 years of age, and disease occurred whole year without prominent seasonal peak.

People's Republic of China:

In 1940 JE was first reported in People's Republic of China. From 1951 the JE case reporting system has been mandated. Disease occurred from June to October. Peak period is July and August. Majority of patients are below age of 15 years. Virus was isolated from Cx. tritaeniorhynchus .

India:

In 1950s serological survey recognised Japanese encephalitis. In 1973 first outbreak of JE was reported In West Bengal. Uttar Pradesh is the main epidemic area in the northern states of India. JE cases occurred throughout year in the region with peak in the rainy season. The main mosquito vectors are Cx. vishnui, Cx. tritaeniorhynchus , Cx. seudovishnui and Anapheles subpictus.

Enzootic Cycle:

Japanese encephalitis virus is transmitted between birds and mammals by culex mosquitoes – Cx. tritaeniorhynchus , which breeds in a stagnant water bodies and rice paddy fields. Birds may also responsible for spread of JEV. Pigs are often kept close to humans and they have prolonged and high viraemias. Due to this reason pigs are most important natural host for transmission to humans. Disease is not occurs in the natural host although the virus is present in the body.

Virology:

JEV is prototype virus of JE in genus Flavivirus. JE serogroup include West Nile virus, St. Luis encephalitis virus and Murray Valley encephalitis virus. JE virus has small lipoprotein (around 50nm) surrounding a nucleocaspid comprising of core protein and single stranded RNA (11 kb). Length of genomic RNA of virus is 10,968 nucleotides. The RNA consisting of 95-nucleotides 5'NCR, a10299-nucleotide ORF and 574-nucleotide 3'NCR. 3-N terminal structural proteins are essential for the formation of infectious virions. The 7 C- terminal non-structural proteins are involved in multiple steps of viral life cycle (RNA replication).

Replication Cycle:

First step of virus replication include attachment of virion to host cell with the help of viral E protein which binds to unknown cellular receptors on cell surface.

In second step fusion of viral membrane with the host's endosomal membrane triggered due to conformational changes in E glycoprotein due to low pH in endosomes.

In third step the genetic material of virus is released into cytoplasm and translated.

Fourth step includes replication of genetic material and particle assembly of virus.

In fifth step virions are formed.

Then matured virions are released into extracellular environment by exocytosis.

Clinical Features:

JE has an incubation period of approx. 5 to 15 days from initial exposure to virus. Patients with JE shows symptoms like illness. coryza, diarrhoea, reduced level of consciousness and some abnormal behaviour in some patients.

85% of children and 10% of adults have been reported for convulsions followed by rapid recovery of consciousness.

Recent studies shows that patients with JEV presented polio-like acute flaccid paralysis in one or more limbs, despites normal level of consciousness. 30% of such patients subsequently developed encephalitis with deduced level of consciousness.

Early stage of disease starts with flu-like symptoms, fever, headache, and vomiting. JE patients often show a parkinsonian syndrome.

Diagnosis:

Japanese encephalitis is diagnosed serologically. The hemaglutination inhibition test was used past years n 1980s IgM and IgG capture enzyme linked immunosorbant assays (ELISAs) were developed. Recently IgM ELISA has been modified to nitrocellulose membrane based format in which change of colour (result) is detectable with necked eyes.

JEV RNA is detected in human CSF sample by using RT-PCT, in the infected patients. A lumbar puncture (LP) should be performed on all patients suspected of having a viral encephalitis. Urine or serum toxicology screening may be indicated in selected patients presenting with a toxic delirium or confusional state.

Pathogenesis:

JEV develops clinical features of infection. The mechanism by which JEV enters through BBB is unknown. Staining of human post-mortem material indicates haematogenous route of entry. Microscopic studies of mice report that virus replicates in rough ER and golgi body

Histopathology -

Histopathological studies shows haemorrhages in gray matter. The white matter usually appear normal. Discoloured gray matter of spinal cord in some patients observed. Tremor and dystonias occur due to heavy damage of midbrain, thalamus and basal ganglia. Infiltration of T cells into parenchyma, perivascular cuffing, and phagocytosis of infected cells causes invasion of neurons in JE. Monoclonal antibodies (CD8+ and CD8-) are localised at perivascular cuff. Both CD8+ and CD8- are found in CSF In acute encephalitis infection.

Immunology -

In human plasma and CSF endogenous interferon-α has been detected in the case of encephalitis. Rapid and potent IgM response occur in serum and CSF within one day of infection if disease is caused by primary infection.

Cellular immunity prevent disease before it invade CNS. Very little information is present about cell mediated immunity.

Treatment:

There is no antiviral treatment for patients with JE. Treatment is supportive to relieve symptoms and stabilize the patient. But because the specific virus may not be identified immediately or at all recommended treatment is antiviral drugs with supportive care.palliative theory is recommended in Japanese encephalitis.

Antiviral Drugs used for JE:

Acyclovir

Ganciclovir

Foscarnet

Supportive care includes-

IV fluids for rehydration,

Breathing assistance,

Anticonvulsant drugs - phenytoin ,

Anti-inflammatory drugs, etc.

Follow-up therapy:

Follow-up therapy is necessary in case of complications.

Physical Therapy - It is necessary to improve strength, flexibility, balance, motor coordination and mobility of patient.

Occupational therapy - To develop every day activity.

Occupational therapy

Psychotherapy

Prevention Of Disease:

Vaccination is the only option to develop sustainable immunity against Japanese encephalitis virus. live attenuated vaccines,& inactivated vaccines are used to prevent. Crude inactivated antigerms prepared from nakayama strain infected chicken embryos were earliest vaccines used in humans. During 2nd world war ,mouse brain derived crude vaccines was used to prevent disese in US army personnel.OCT-541 strain was earliest live attenuated vaccines used in human.

In eary decades,MBDI was only vaccine safe for human. Upto 2005 production

Was stopped.& last stock was expired in 2011. Due to adverse events & cases of acute disseminated encephalomyelitis in vaccinated subject use of MBDI was stopped

References :-

1. Diagnosis and treatment of viral encephalitis :- A Choudhuri , P G E Kennedy, postgrad Med J 2002;78 : 575 – 583 .

2. The challenges of Communicable diseases in the WHO South East Asia Region :- Jai P Narain[a] and R Bhatia[a] Bull World Health Organ 2010 ; 88 : 162 | doi : 10.2471/BLT.09.065169

3. A clinical approach to diagnosis of autoimmune encephalitis :- Francesc Graus Maarten J Titulcler , et.al Lancet Neurol 2016 ; 15: 391 – 404 published February 19, 2016 http;||dx.doi.org/10.1016/51474-4422(15)00401-9. Page no – 349

4. Enteroviruses in patients with acute encephalitis, Uttar Pradesh :- Gajanan N. Sapkal , Vijay P. Bondrte.et.al. Emerging Infectious diseases. www.cdc.gov/eid-vol 15 No 2 february 2009.

5. Infectious Encephalitis in France 2007 :- Alexandra Mailles[1] and Jean-Paul stahl[2] , 1838 CID 2009 : 49 (15 Decembar)

6. Japanese Encephalitis , Neurological Aspects of Tropical disease published :- Tom Solomon, Nguyen minh Dung et.al March 10,2015 ,2000; 68:405-415

7. Encephalitis in children :- Clara Thompson[1] , Rachel Kneen[2] , et.al, Arch Dis child 2012 ; 97 150-161 . doi:10.1136/archdischild – 2011 – 300100

8. Emerging & re-emerging infections in India :- T. Dikid[*], S.K.Jain[*] et.al. Indian J. Med Res 138, July 2013. PP 19-31

9. Autoimmune Encephalitis Epidemiology & a comparison to Infectious Encephalitis :- Divyanshu Dubey, MD,[1] Sean J.pittock , MD,[1,2] et.al, American Neurological Association © 2018 , DOI : 10.1002/ana.25131, page no 166.

10. Nervous System involvement after infection with COVID-19 & other Coronaviruses . Brain Behav Immun. :- Wu, Y.,et al .,2020 https:||doi.org/10.1016/j.bbi.2020.03.031.

11. Viral Encephalitis :- Richard J.Whitley , M.D., New England . Medical progress publication July 26,1990.