

Unveiling the Undiscovered: Etiology of Acute Encephalitis Syndrome in North India

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Introduction

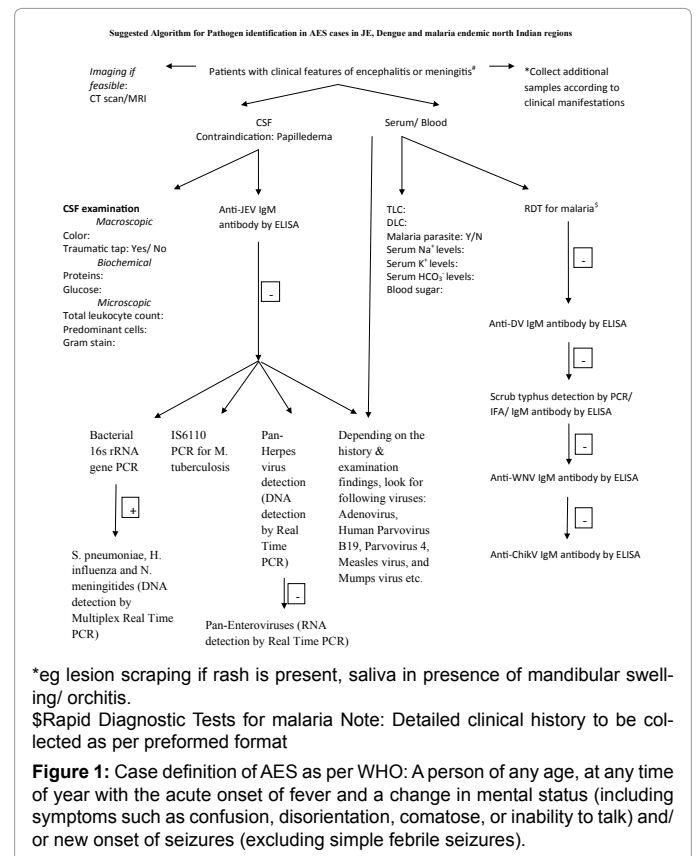
Acute Encephalitis Syndrome (AES) poses a great public health problem in India, occurring both in epidemics and sporadically. The magnitude of the problem has been estimated to be around 50,000 cases and 10,000 deaths annually [1]. Traditionally Japanese encephalitis (JE) has been considered to be the most important cause of AES in our country. The overemphasis on JE is so much so that AES surveillance is paralleled to JE surveillance for all practical purposes. In 2014, the total numbers of AES cases and deaths reported from India were 10,853 and 1717 respectively and the corresponding values for JE were 1657 (~15%) and 293 (~17%) respectively [2]. This implies that other undiscovered or neglected etiology of AES, which accounts for about 85%, also exists and should also be looked for.

AES in India, especially Northern India, as per definition of WHO [3] encompasses several other illnesses; it has malaria, enteric encephalopathy, tubercular meningitis, dengue with neurological manifestations, scrub typhus, bacterial meningitis, etc. It surely is a mixed pot.

Scientific literature discusses about several other infectious agents; only few of them are treatable. Bacterial meningoencephalitis, most commonly caused by *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B, is amenable to specific antibiotic treatment and can be prevented by the available vaccines. Tuberculosis also requires specific treatment. Scrub typhus caused by *Orientia tsutsugamushi* causes encephalitis that is difficult to diagnose, but can be treated easily. Enteric encephalopathy is not rare and needs different management. Malaria is endemic and cerebral malaria is common. However, sufficient data is not available from India on these easily treatable causes of AES [4].

Today, world is more concerned about the untreatable and not known causes. When AES cases from Uttar Pradesh, India, were investigated for the etiological diagnosis, viral etiology could be determined for approximately 58% cases, which included Japanese encephalitis virus 16%, Dengue virus 11%, Herpes simplex virus, Mumps virus and measles virus 9% each, and Varicella Zoster virus 4%. Total 42% cases were AES cases with unknown etiology, which still need to be determined [5]. Dengue encephalitis and neurological manifestations are commonly seen [6]. Viruses that have been implicated in outbreaks of AES, but have not been studied countrywide include Chandipura virus, West Nile virus, Nipah virus, Kyasanur Forest Disease Virus, Enteroviruses and Adenoviruses [7]. Case reports are available on human Parvovirus B19V as a potential cause of encephalitis and encephalopathy in immunocompetent cases. Human Parvovirus 4 can be an emerging cause of encephalitis in patients with acute encephalitis syndrome. We detected human parvovirus 4, from CSF of two patients presenting as acute encephalitis syndrome in northern India, though causative association is yet to be proved [8]. Consideration should be given to detection of these non-JE AES etiologies, as it will directly impact the formulation of health policies of AES in India. This includes identifying targets for immunization, chart preventive strategies and implement appropriate control measures, especially in outbreak situations and formulating other public health interventions.

In a resource limited country like India, testing all the AES samples for all the possible pathogens is a remote possible. Moreover, the volume of cerebrospinal fluid available for laboratory testing is often small. Therefore, an algorithmic approach for the diagnosis of encephalitis is advocated which may serve many purposes, including patient management, research, and facilitating public health disease surveillance. An algorithm should be designed for each region, based on the local prevalence of the disease organisms and this will help to diagnose most cases of AES, using minimum resources within a reasonable period of time. An attempt was made to design an algorithm for Uttar Pradesh (Figure 1), a region endemic for both JEV and DV, which can be used as an example.



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