Acute Necrotizing Encephalopathy: an emerging atypical and rare encephalopathy

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Introduction:

Acute Necrotizing Encephalopathy (ANE) is a rare condition with an unknown origin that develops after an abrupt febrile viral illness and is characterised by acute fulminant severe encephalopathy and multifocal symmetrical brain destruction. [1] The first instance was reported in 1995 by the Japanese academic Mizuguchi. [2] Acute necrotizing encephalopathy, which develops as an atypical encephalopathy observed almost exclusively in previously healthy young children or new-borns in East Asian countries, such as Japan and Taiwan, was once thought to be a childhood disease. [3] Although the peak age for infection is between six and 18 months, it has also been seen in adults and teenagers.[4] However, isolated incidences of it have been documented globally. [5,6] The most prevalent associated pathogens are influenza viruses A and B, new influenza A virus (H1N1), parainfluenza virus, herpes simplex virus, varicella-zoster virus, human herpesvirus 6 (HHV-6), coxsackie virus, rotavirus, measles virus, rubella virus, mycoplasma pneumoniae, and others. [7-9] The blood-brain barrier breaks down as a result of this uncommon complication of influenza and other viral infections, which has also been linked to intracranial cytokine storm, but there is no direct viral invasion or parainfectious demyelination. [10] This illness is present all year round, however it is most prevalent in the influenza season.A third year MBBS student from Kanpur, India, who had

been suffering from a viral fever for the previous few days, was recently diagnosed with ANE. [11] After receiving the medication, she was brought to the emergency room where, after her temperature dropped, she complained of an excruciating headache and after a few hours, she lost consciousness. She had to be taken to a critical care unit right away, where her health worsened, and she entered a coma. She tested negative for the most frequent causes of fever in our country—dengue, chikungunya, malaria, and typhoid—and samples for a few other viral illnesses, like Japanese encephalitis, have also been submitted. According to accounts, a CT scan revealed that her brain was completely destroyed.

Pathogenesis:

Early in the pathogenesis process, viral infection is crucial. Along with the extrinsic influences, genetic changes and personal sensitivity may also play a role. Despite having a microbe as its most frequent cause, inflammatory encephalitis is not how ANE manifests. [12] ANEC development was influenced by proinflammatory cytokines such IL-6, IL-1, and tumour necrosis receptor-1. Cytokine storm is a popular theory that describes the aetiology of ANEC. It results from an overly aggressive immunological reaction to viral infections.[12] The systemic inflammatory response syndrome (SIRS), which presents as abrupt renal failure, hepatic dysfunction, disseminated intravascular coagulation, and shock, is brought on by the accumulation of proinflammatory cytokines from an overactive immune response. Additionally, without any vessel breakage, this disease will result in brain damage via increased vessel wall permeability. [13] The blood-brain barrier is damaged by focal vascular injury, plasma exudation, brain oedema, dot haemorrhage, and necrosis of neuronal and glial cells are the main pathological alterations seen in ANE. The thalamus, brainstem tegmentum, deep white matter of the brain, and cerebellum all exhibit symmetrical encephalomalacia in conjunction with partial brain breakdown.[14] The genotypes of human leukocyte antigen may possibly play a role in the occurrence of ANE (HLA). The pathophysiology of ANE may be influenced by mutations in the RNABP2, SCN1A, and CPT2 genes.[4]

Clinical Features:

The most frequent clinical manifestations include fever, abrupt changes in consciousness, febrile seizures, movement disorder, frontal lobe encephalopathy, and multiorgan failure. Typical brain imaging findings include bilateral thalamic lesions with supra- and infra-tentorial lesions of varying sizes, among other things. [2] Guillain-Barre syndrome, transverse myelitis, acute disseminated encephalomyelitisand myositis are examples of subacute symptoms. Parkinsonism and encephalitis lethargica are late symptoms. [15] This disease has a very bad prognosis and extremely high fatality rates that are close to 30%.

Sequalae:

With the exception of the cardiovascular system, involvement of numerous different organs has been documented as a sequelae of acute necrotizing encephalopathy, however a case report subsequently published highlights specific findings upon postmortem investigation. Histological analysis of the heart revealed subendocardial collagenous fibrosis extending into the deep myocardium, as well as areas of fibrosis in the endocardium and myocardium were evident on macroscopic examination. The coronary arteries and pericardium were healthy.[16]

Prevention:

Acute necrotizing encephalopathy does not have a specific preventive strategy, but as it is thought to be a result of viral infection, vaccinations for viral infections like influenza may be helpful. Since the condition is so severe, early detection and prompt treatment are extremely necessary.

Conclusion:
Acute necrotizing encephalitis is a rare disease with non specific symptoms comprising of rapidly progressing fever, severe headache, convulsions and coma for which the patient may require ventilatory support. It leads to multiple organ failure. Causes may be post infectious or genetic predisposition. Diagnosis may be done by CT or MRI. There are no specific preventive strategies but early diagnosis and prompt treatment may be helpful although the prognosis is very poor with mortality rates of around 30%.

Conflict of Interest: None
Financial support and sponsorship: Nil

References:
1. https://rarediseases.info.nih.gov/diseases/13233/acute-necrotizing-encephalopathy[last assessed on 29/09/2022]
2. Mizuguchi M, Abe J, Mikkaichi K, Noma S, Yoshida K, et al. (1995) Acute necrotising encephalopathy of childhood: A new syndrome presenting with multifocal, symmetric brain lesions. J NeurolNeurosurg Psychiatry 58: 555-561.
3. Mizuguchi M. Acute necrotizing encephalopathy of childhood: a novel form of acute encephalopathy prevalent in Japan and Taiwan. Brain Dev. 1997 Mar;19(2):81-92. Review.
4. Yuan P, Zhong M (2018) Acute Necrotizing Encephalopathy in Children: A Case Report and Literature Review. Int J Pediatr Res 4:045. doi.org/10.23937/2469-5769/1510045
5. Wang HS, Huang SC. Acute necrotizing encephalopathy of childhood. Chang Gung Med J 2001 Jan;24(1):1-10.
6. Campistol J, Gassió R, Pineda M, Fernandez-Alvarez E. Acute necrotizing encephalopathy of childhood (infantile bilateral thalamic necrosis): two non-Japanese cases. Dev Med Child Neurol 1998 Nov;40(11):771-4.
7. Martin A, Reade EP (2010) Acute necrotizing encephalopathy progressing to brain death in a pediatric patient with novel influenza A (H1N1) infection. Clin Infect Dis 50: e50-e52.
8. Anand G, Visagan R, Chandratre S, Segal S, Nemeth AH, et al. (2015) H1N1 triggered recurrent acute necrotizing encephalopathy in a family with a T653I mutation in the RANBP2 gene. Pediatr Infect Dis J 34: 318-320.
9. Tabarki B, Thabet F, Al SS, Al AN, Chehab M, et al. (2013) Acute necrotizing encephalopathy associated with enterovirus infection. Brain Dev 35: 454-457.
10. Rossi A. Imaging of acute disseminated encephalomyelitis. Neuroimaging Clinics 2008;18(1):149–161. DOI: 10.1016/j.nic.2007.12.007.
11. http://timesofindia.indiatimes.com/articleshow/94521990.cms?utm_source=contentofinterest&utm_medium=text&utm_campaign=cppst [Last assessed on 29/09/2022]
12. Wu X, Wu W, Pan W, Wu L, Liu K, Zhang HL. Acute necrotizing encephalopathy: an underrecognizedclinicoradiologic disorder. Mediators Inflamm. 2015;2015:1-10.
13. Handryastuti et al. Difficulties in Diagnosis Acute Necrotizing Encephalopathy of Childhood: A Case Report. Child Neurology Open Volume 9: 1-5. DOI: 10.1177/2329048X221095699
14. Ishii N, Mochizuki H, Moriguchi-Goto S, Shintaku M, Asada Y, et al. (2015) An autopsy case of elderly-onset acute necrotizing encephalopathy secondary to influenza. J NeurolSci 354: 129-130.
15. Yoganathan S, Sudhakar SV, James EJ, et al. BMJ Case Rep 2016 Published online doi:10.1136/bcr-2015- 213429
16. Wanigasinghe J, Jayathunge T, Ratnayake PD. Acute necrotizing encephalitis associated with cardiovascular manifestations. Neurol India 2017;65:867-8