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Acute Necrotizing Encephalopathy Related to Non-Influenza Viruses in Rare Adult Cases

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Abstract

Acute necrotizing encephalopathy (ANE) is a rare, rapidly progressive, and severe immune-mediated neurological disorder that frequently leads to severe neurological sequelae or mortality. Viral infection represents a common pathogenic factor, while cytokine storm constitutes the primary pathogenic mechanism. ANE is a distinct clinical entity characterized by specific clinical and imaging features. Immunomodulatory therapy and anti-cytokine interventions represent effective treatment strategies for ANE.

Keywords

Acute Necrotizing Encephalopathy, Viral Infection, Cytokine Storm, MRI

1. Introduction

Acute necrotizing encephalopathy (ANE) is a rare and severe form of acute encephalopathy, mainly marked by seizures or altered consciousness. ANE often follows a viral infection, most commonly influenza, and typically involves multiple symmetrical lesions in the thalamus, brainstem, and cerebellum. ANE mainly affects children under five [1], and is very rare in adults. This case report describes an instance of ANE that occurred without influenza infection.

2. Case

A 22-year-old male was admitted with a two-day fever and diarrhea, and impaired consciousness for half a day. The patient was comatose on arrival, unresponsive to stimuli, and uncooperative during examination. Both eyes showed vertical nys-

tagmus and anisocoria. The patient's medical history included hypertension, hypertensive heart disease, hypercholesterolemia, hyperuricemia, hypokalemia, renal insufficiency, and primary aldosteronism. On the day of admission, initial blood tests revealed elevated levels of white blood cells (WBC): 13.94×10^9/L; absolute neutrophil count: 8.50×10^9/L; lactate dehydrogenase (LDH): 277 U/L; C-reactive protein (CRP): 99.7 mg/L; and lactate (LAC): 10.77 mmol/L. On the second day of admission, PMC-MetaCAP high-throughput sequencing for pathogenic microorganisms was performed. Norovirus Genogroup II was detected in the patient's peripheral blood. Simultaneously, testing for common adult respiratory viruses and enteroviruses via nucleic acid detection returned negative results. The patient was diagnosed with a norovirus infection. On the third day of hospitalization, cerebrospinal fluid (CSF) analysis showed increased concentrations of chloride (Cl): 139 mmol/L; glucose (GLU): 7.39 mmol/L; and trace total protein (mTP): 968 mg/L, with a normal WBC count. During the first two days after admission, both WBC count and procalcitonin levels continued to rise before subsequently declining. CRP peaked on the first day and then gradually decreased thereafter. Imaging studies demonstrated the following findings: during the acute phase, CT showed symmetrical low-density areas in the bilateral thalamus with peripheral ring-shaped high-density shadows (**Figure 1(A)**), and the brainstem presented mixed high-density shadows with mottled changes, indicative of hemorrhage (**Figure 1(B)**). Corresponding MRI findings included mixed high signals in the brainstem on T2Flair (**Figure 1(C)**), symmetrical central low signals in the bilateral thalamus on T1WI, suggesting necrotic regions, and peripheral ring-shaped high signals, indicating subacute hemorrhage (**Figure 1(D)**). Additionally, T2Flair images displayed high signals with peripheral isointense or hypointense rings, suggestive of vasogenic edema (**Figure 1(E)**). Diffusion-weighted imaging (DWI) revealed target-like alterations (**Figure 1(F)**), while apparent diffusion coefficient (ADC) maps exhibited a characteristic three-color pattern, with central high signals indicating necrosis, intermediate low signals reflecting cytotoxic edema, and peripheral high signals representing vasogenic edema (**Figure 1(G)**). During the recovery phase, hemosiderin deposition was evident in the bilateral thalamus and brainstem on T2Flair (**Figure 1(H)**, **Figure 1(I)**). ANE was diagnosed through a comprehensive evaluation of cerebrospinal fluid analysis, clinical laboratory tests, and imaging examinations. Upon admission, the patient received anti-infective therapy—intravenous ceftriaxone 2 g q12h, omadacycline 0.1 g qd, and intravenous acyclovir 1 g q12h—as well as immunomodulatory therapy (hydrocortisone 100 mg q8h + immunoglobulin 42.5 g). On hospital day 25, the patient's inflammatory markers showed a downward trend: CRP 84.2 mg/L; white blood cell count 8.84×10^9/L; absolute neutrophil count 6.08×10^9/L; LAC 0.6 mmol/L; and procalcitonin (PCT) 0.2 ng/ml. A follow-up MRI of the head on March 2, 2025, demonstrated that perilesional edema around the abnormal signal foci in the bilateral thalamus and brainstem had subsided, and the lesion extent had decreased compared to previous findings (**Figure 1(H)**, **Figure 1(I)**). The patient's condition

was stable, and transfer to a lower-level hospital was arranged for continued antiviral and anti-infective therapy. A follow-up MRI of the head on May 24, 2025, showed that perilesional edema around the abnormal signal foci in the bilateral thalamus and brainstem had largely resolved, and the lesion extent had significantly diminished compared to prior imaging (Figure 2).

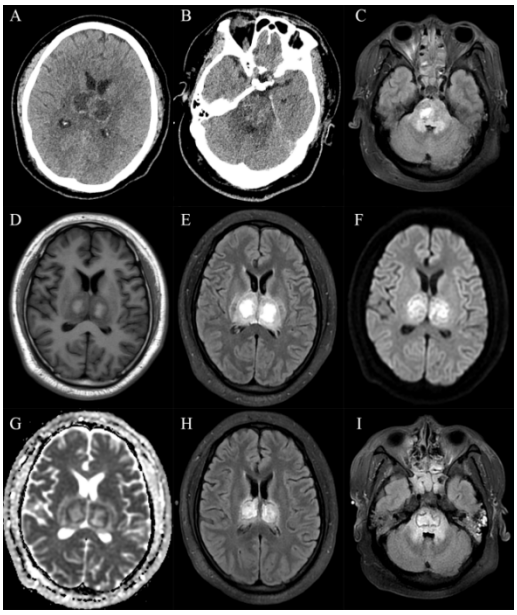

Figure 1. CT and MRI in Patient with typical radiological findings of ANE.

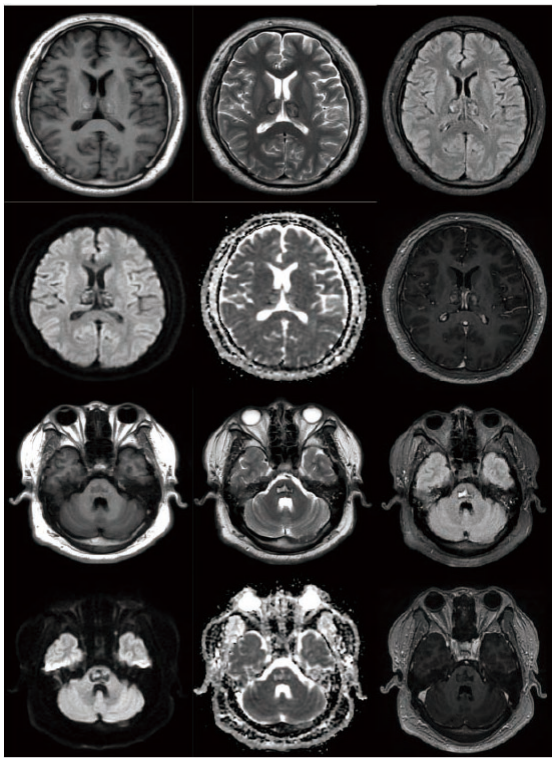

Figure 2. MRI findings in the thalamus and brainstem after two months of treatment.

3. Discussion

ANE is a rare and severe neurological disorder characterized by rapid progression, resulting in high rates of disability and mortality. It is predominantly observed in young children subsequent to viral febrile illnesses [2]. This case report describes an adult patient with ANE. Current research suggests that the clinical manifestations, laboratory findings, and imaging features of ANE in adults are largely comparable to those observed in pediatric cases [3]. Most cases of ANE are sporadic. Familial and recurrent ANE are caused by mutations in the RANBP2 gene [4]. ANE patients commonly exhibit signs of systemic inflammatory response syndrome (SIRS), including shock, multiple organ failure (MOF), and disseminated intravascular coagulation (DIC). The disease progression typically involves three phases: a prodromal phase, an acute encephalopathy phase, and a recovery phase [2] [5]. The pathogenic mechanism of ANE remains unclear, but viral infection is the major predisposing factor. Common viruses include influenza A virus, influenza B virus, and human herpesvirus type 6 [6] [7]. This case was attributed to norovirus infection, which differs from the commonly reported viral etiologies described in the literature. Furthermore, emerging evidence suggests that ANE associated with influenza viruses is more frequently accompanied by brainstem involvement compared to ANE secondary to non-influenza viral infections [8]. This case was induced by norovirus infection, which contrasts with the common viruses reported in the literature. Regarding imaging findings, the primary manifestations of ANE are multifocal and symmetrical brain lesions, predominantly affecting the thalamus, the tegmentum of the brainstem, periventricular white matter, and the cerebellum. Symmetrical lesions in the bilateral thalamus serve as a key diagnostic feature [4]. The imaging changes of ANE are a dynamic process, ranging from edema to hemorrhage, necrosis, and softening [9]. The dynamic changes and key features presented in the imaging of this case report are consistent with previous literature reports. Given that ANE is an immune-mediated condition triggered by viral infection, its CSF typically lacks inflammatory changes. This characteristic can be utilized to distinguish ANE from necrotizing encephalitis [10]. Although there are no established treatment guidelines, early initiation of immunotherapy and combination anti-cytokine therapy may lead to relatively favorable outcomes [11]. Seven cases of adult ANE have been documented in the literature [2] [11]-[15]. We reviewed and summarized the clinical and imaging features of these cases, as presented in **Table 1**. All seven patients exhibited bilateral thalamic lesions. Two patients received combined treatment with corticosteroids and intravenous immunoglobulin and achieved favorable outcomes. Early initiation of this therapeutic regimen was associated with improved prognosis. In contrast, the remaining six patients did not receive this combination therapy and unfortunately succumbed to the disease. In this case, the diagnosis of ANE was made at an early stage based on characteristic clinical presentations and imaging findings. A comprehensive treatment approach, including hormonal anti-inflammatory therapy and intravenous immunoglobulin administration, was implemented

to manage the cytokine storm phase. Once the patient's condition had stabilized, he/she was transferred to a lower-level healthcare facility for continued management. These findings are consistent with our case report. The presence of symmetrical bilateral thalamic lesions appears to be a characteristic neuroimaging feature of ANE, and combined corticosteroid and immunoglobulin therapy may offer a potentially effective treatment option. These findings are consistent with our case report.

Table 1. A literature review of clinical imaging findings in adult ANE.

Literature	Sex/age	Clinical manifestations	Laboratory examinations	Etiology	Bilateral thalamic lesion	Hormone combined with immunoglobulin	Prognosis
[11]	F/22	Epilepsy, coma	IL-2, IL-6, IL-8	COVID-19	Yes	Yes	Conscious, hemiplegia
[12]	F/70	Epilepsy, louding of consciousness	IL-6, CRP, LDH	COVID-19	Yes	None	Dead
[14]	F/54	Epilepsy, clouding of consciousness	CRP, IL-6	CPT2	Yes	None	Dead
[15]	F/46	Hyperpyrexia, exanthema	Elevated RBC count	AOSD	Yes	None	Dead
[2]	M/19	Coma	IL-6, CRP	Administer a whole-cell inactivated virus vaccine	Yes	None	Dead
[6]	F/66	Epilepsy, coma	CRP	HSV	Yes	None	Dead
[13]	M/20	Coma	ALT, AST	H1N1	Yes	None	Dead

4. Conclusion

ANE is a rare and severe central nervous system disorder characterized by rapid onset, poor prognosis, and a high rate of neurological disability. Although it predominantly affects children, it can also occur in adults, albeit rarely. By presenting this case of adult-onset ANE, we aim to highlight the importance of considering ANE as a potential diagnosis when managing patients with a recent history of prodromal infections—particularly viral illnesses—who present with high fever and altered mental status. Furthermore, this case underscores that gastrointestinal infections may also serve as a trigger for ANE. Prompt initiation of combined treatment with corticosteroids and intravenous immunoglobulin may be effective and could help prevent therapeutic delay.

CRediT Authorship Contribution Statement

Bangfeng Li: Conceptualization, writing and original draft. **Yongjun Peng:** Conceptualization, writing and review & editing.

Data Availability

Data will be made available on request.

Conflicts of Interest

The authors declare that they have no conflicts of interest related to this work.

References

[1] Cao, Z., Sun, Y. and Li, F. (2025) Advances in the Study of Acute Necrotizing Encephalopathy. *Infection and Drug Resistance*, **18**, 1713-1720. https://doi.org/10.2147/idr.s508092

[2] Pongpitakmetha, T., Hemachudha, P., Rattanawong, W., Thanapornsangsuth, P., Viswanathan, A. and Hemachudha, T. (2022) COVID-19 Related Acute Necrotizing Encephalopathy with Extremely High Interleukin-6 and RANBP2 Mutation in a Patient with Recently Immunized Inactivated Virus Vaccine and No Pulmonary Involvement. *BMC Infectious Diseases*, **22**, Article No. 640. https://doi.org/10.1186/s12879-022-07610-0

[3] Lin, Y., Lee, K., Ro, L., Lo, Y., Huang, C. and Chang, K. (2019) Clinical and Cytokine Profile of Adult Acute Necrotizing Encephalopathy. *Biomedical Journal*, **42**, 178-186. https://doi.org/10.1016/j.bj.2019.01.008

[4] Sakuma, H., Thomas, T., Debinski, C., Eyre, M., Han, V.X., Jones, H.F., *et al.* (2024) International Consensus Definitions for Infection-Triggered Encephalopathy Syndromes. *Developmental Medicine & Child Neurology*, **67**, 195-207. https://doi.org/10.1111/dmcn.16067

[5] Levine, J.M., Ahsan, N., Ho, E. and Santoro, J.D. (2020) Genetic Acute Necrotizing Encephalopathy Associated with RANBP2: Clinical and Therapeutic Implications in Pediatrics. *Multiple Sclerosis and Related Disorders*, **43**, Article ID: 102194. https://doi.org/10.1016/j.msard.2020.102194

[6] Wang, M., Liu, R., Zhang, L., Zhao, B., Jia, R., Zhao, Y., *et al.* (2022) Clinical Experience in the Diagnosis and Treatment of Adult Acute Necrotizing Encephalopathy. *Neuroimmunomodulation*, **29**, 468-475. https://doi.org/10.1159/000524955

[7] Shukla, P., Mandalla, A., Elrick, M.J. and Venkatesan, A. (2022) Clinical Manifestations and Pathogenesis of Acute Necrotizing Encephalopathy: The Interface between Systemic Infection and Neurologic Injury. *Frontiers in Neurology*, **12**, Article 628811. https://doi.org/10.3389/fneur.2021.628811

[8] Okumura, A., Abe, S., Kidokoro, H. and Mizuguchi, M. (2009) Acute Necrotizing Encephalopathy: A Comparison between Influenza and Non-Influenza Cases. *Microbiology and Immunology*, **53**, 277-280. https://doi.org/10.1111/j.1348-0421.2009.00124.x

[9] Qin, N., Wang, J., Peng, X. and Wang, L. (2023) Pathogenesis and Management of Acute Necrotizing Encephalopathy. *Expert Review of Neurotherapeutics*, **23**, 641-650. https://doi.org/10.1080/14737175.2023.2224503

[10] Vanjare, H.A., Selvi, B.T., Karuppusami, R., Manesh, A., Gunasekaran, K., Prabhakar, A.T., *et al.* (2020) Clinical and Radiologic Findings of Acute Necrotizing Encephalopathy in Young Adults. *American Journal of Neuroradiology*, **41**, 2250-2254. https://doi.org/10.3174/ajnr.a6803

[11] Chen, H., Lan, S., Tseng, Y., Chang, Y., Lu, Y. and Lan, M. (2024) Acute Necrotizing Encephalopathy in Adult Patients with Influenza: A Case Report and Review of the

Literature. *BMC Infectious Diseases*, **24**, Article No. 931. https://doi.org/10.1186/s12879-024-09844-6

[12] Ziemele, D., Ķauķe, G., Skrējāne, K., Jaunozoliņa, L. and Karelis, G. (2021) A Fatal Case of COVID-19-Associated Acute Necrotizing Encephalopathy. *European Journal of Neurology*, **28**, 3870-3872. https://doi.org/10.1111/ene.14966

[13] Arul, J.N., Madhavan, S., Krishnan, V. and Krishnamoorthy, V. (2020) Fatal H_1N_1-Related Acute Necrotising Encephalopathy in an Adult. *BMJ Case Reports*, **13**, e235264. https://doi.org/10.1136/bcr-2020-235264

[14] Kobayashi, Y., Kanazawa, H., Hoshino, A., Takamatsu, R., Watanabe, R., Hoshi, K., *et al.* (2019) Acute Necrotizing Encephalopathy and a Carnitine Palmitoyltransferase 2 Variant in an Adult. *Journal of Clinical Neuroscience*, **61**, 264-266. https://doi.org/10.1016/j.jocn.2018.11.045

[15] Yang, X., Wei, M., Chu, S. and Zhang, Y. (2022) Adult-Onset Still's Disease with Concurrent Acute Necrotizing Encephalopathy: A Case Report. *BMC Neurology*, **22**, Article No. 329. https://doi.org/10.1186/s12883-022-02844-6