The Egyptian Journal of Hospital Medicine (October 2022) Vol. 89 (2), Page 8054- 8057

Acute Disseminated Encephalomyelitis in ICU Patients with Acute Disturbance of Consciousness

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ABSTRACT

Background: Acute Disseminated Encephalomyelitis (ADEM) is an acute demyelinating syndrome of the CNS. Due to the non-specific diagnostic tools and presence of many demyelinating conditions that overlap with ADEM, there might be over estimation of cases of ADEM.

Objective: The aim of the present study is the early detection and estimating the prevalence of ADEM in patients admitted to pediatric intensive care unit (ICU) with acute disturbance of consciousness.

Patients and methods: A cross-sectional study was conducted on 66 children (36 males and 30 females) admitted to Pediatrics ICU at Zagazig University Hospitals fit to the inclusion criteria during the period between March 2021 and February 2022. Complete history was taken from all parents. Physical examination was done for each case and including mental status, cranial nerves, motor and sensory examination, coordination, reflexes, and gait. All patients also underwent magnetic resonance imaging, cerebrospinal fluid analysis, C-reactive protein, complete blood count, electrolytes (Na - K) and fundus examination.

Results: According to MRI findings, lesions were typically asymmetrical (68.2%). The commonest distribution of lesion was cortical GM in 45.5% of cases followed by Juxtacortical WM in 31.8%. The commonest pattern was that of patchy (33.3%), followed by confluent/ larger areas seen in 24.2% of cases. Diffusion restriction and brain edema was presented in 31.8% and 33.3% respectively.

Conclusion: Understanding the prevalence can help raise awareness of these illnesses in children because ADEM can be a difficult diagnosis. This is significant since there are signs that the incidence among children under the age of 12 may be rising.

Keywords: ADEM, Consciousness, Children, Neurology, Cross-sectional study, Zagazig University.

INTRODUCTION

Acute Disseminated Encephalomyelitis (ADEM) is an acute demyelinating syndrome of the CNS, usually preceded by infection and less common by vaccination. It might manifest with a variety of distinct symptoms, but the defining feature is multifocal neurological impairments linked to encephalopathy [(1)]. ADEM is primarily diagnosed through clinical and radiological means; no specific laboratory tests or pathognomonic imaging findings are required [(2)]. Maintaining a high clinical suspicion index and consistently including the illness in differential diagnoses to rule out other etiologies, particularly infections, are necessary. Due to the non-specific diagnostic tools and presence of many demyelinating conditions that overlap with ADEM, there might be over estimation of cases of ADEM [(3)].

The aim of the present study is the early detection and estimating the prevalence of ADEM in patients admitted to pediatric intensive care unit (ICU) with acute disturbance of consciousness.

PATIENTS AND METHODS

A cross-sectional study was conducted on 66 children (36 males and 30 females) admitted to Pediatric ICU at Zagazig University Hospitals fit to the inclusion criteria during the period between M arch 2021 and February 2022.

All patients admitted with acute disturbance of consciousness aged from 2 to 12 years were included in the study.

Complete history was taken from all parents. Physical examination was done for each case and including mental status, cranial nerves, motor and sensory examination, coordination, reflexes and gait. All patients also underwent magnetic resonance imaging, cerebrospinal fluid analysis, C-reactive protein, complete blood count, electrolytes (Na - K) and fundus examination.

Ethics approval and consent to participate:

Both the Institutional Review Board [IRB] and the local committee of ethics approved the protocol of this research in the Faculty of Medicine of Zagazig University. All guardians were asked for their written informed permission prior to their actual involvement in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Microsoft Excel software was used to code, enter, and analyze historical data, basic clinical examinations, laboratory investigations, and outcome measurements. Statistical Package for Social Sciences (SPSS version 20.0) software was then used to import the data and conduct the analysis. When the quantitative data were parametric, they were displayed as means, standard deviations, and ranges; when they were non-parametric, they were displayed as medians and interquartile ranges

Received: 19/7/2022
Accepted: 21/9/2022

(IQR). Qualitative variables were also shown as percentages and numbers. When the predicted count in a particular cell was less than 5, the groups were compared using the Chi-square test and/or Fisher exact test. Independent t-tests were used to compare two groups' quantitative data with parametric distribution, while Mann-Whitney tests were used with non-parametric distribution. P value $\leq$0.05 was considered significant.

RESULTS

The study reported that pyramidal signs were observed in 59% of patients, followed by cranial neuropathy (33.4%), then lateralization (27.2%) **(Table 1).**

Table 1: Neurologic examination findings among the studied groups.

Variable	Patients (N= 66)	%
Pyramidal	39	59%
Cranial	22	33.4%
Extra pyramidal	8	12.2%
Lateralization	18	27.2%
Visual Affection	10	15.1%
Meningism	14	21%
Cerebellar Affection	5	12.2%

Table 2 demonstrates the biochemical findings among the studied groups. according to MRI findings.

Table 2: Biochemical findings among the studied groups.

Variable	Patients (N= 66) Mean ± SD
Hemoglobin	10.5 ± 1.4
WBCs	12.3 ± 2.3
Platelets	282.6 ± 33.4
CRP	39.1 ± 6.5
Glucose	66.8 ± 12.5
Protein	77.8 ± 10.3
Cells	39.2 ± 5.1
Na+	138.2 ± 5.3
K+	4.2 ± 0.47

Table 3 clears that lesions were typically asymmetrical (68.2%). The commonest distribution of lesion was cortical GM in 45.5% of cases followed by Juxtacortical WM in 31.8%. The commonest pattern was that of patchy (33.3%), followed by confluent/ larger areas seen in 24.2% of cases. Diffusion restriction and brain edema was presented in 31.8% and 33.3% respectively.

Table 3: MRI findings among the studied groups.

Variable	Patients (N= 66)	%
Symmetry		
Symmetrical	21	31.8%
Asymmetrical	45	68.2%
Distribution of lesion		
Cortical GM	30	45.5%
Juxtacortical WM	21	31.8%
Deep WM	6	9.1%
PVWM	14	21.2%
Cerebellum	8	12.1%
Basal Ganglia	13	19.7%
Thalami	13	19.7%
Brain Stem	11	16.7%
Size of lesions		
Patchy\Small	22	33.3%
Confluent\Large	16	24.2%
Extensive	5	7.6%
Large Tumor like	3	4.5%
Diffusion Restriction	21	31.8%
Brain edema	22	33.3%

All cases were initially presented with DCL and paresthesia, followed by seizure, irritability and ataxia, and psychiatric and headache **(Table 4).**

Table 4: Initial disease presentations among the studied groups

Variable	Patients (N= 66)	%
DCL	66	100%
Seizure	34	51.2%
Irritability	13	19.2%
Paraesthesia	66	100%
Psychiatric	8	12.2%
Ataxia	13	19.2%
Headache	8	12.2%

Table 5 showed different diagnosis of cases.

Table 5: Diagnosis of the studied patients.

Diagnosis		N	%
Demyelinating disease (N=24)	ADEM	12	18.2%
	Auto Immune Encephalitis	6	9.1%
	Post infectious encephalitis	4	6.1%
	Leukoencephalopathy	2	3%
Metabolic Encephalopathy (N= 6)	Hepatic encephalopathy	2	3%
	Mitochondrial encephalopathy	2	3%
	Wernicke's encephalopathy	2	3%
Vascular (N= 10)	Hypoxic ischemic Encephalopathy	4	6.1%
	Intra cranial Hemorrhage	3	4.5%
	Infarction	2	3%
	Stroke	1	1.6%
CNS Infection (N= 10)	Encephalitis/ meningitis	4	6.1%
	Cerebritis	4	6.1%
	Cerebellitis	2	3%
Hypertensive encephalopathy (N= 4)		4	6.1%
PRES (N=4)		4	6.1%
Toxicity (N= 3)	Drug overdose	3	4.5%
Brain Atrophy (N= 3)	Hydrocephalic changes	2	3%
Died Undiagnosed (N= 3)		3	4.5%
Total		66	100%

About 53.3% of patients received IVIG and 27.2% received steroids while 19.5% did not receive any immunomodulator **(Table 6).**

Table 6: Treatment with immunomodulator among the studied groups.

Variable	Patients (n=66)	%
Steroids	18	27.2%
IVIG	35	53.3%
None	13	19.5%

Table 7 shows that 72.7% of patients was treated, 9.1% their outcome was stationary while 18.2% died.

Table 7: Outcome among the studied groups.

Variable	Patients (N= 66)	%
Treated	48	72.7%
Untreated (stationary)	6	9.1%
Died	12	18.2%

DISCUSSION

Acute disseminated encephalomyelitis (ADEM) is a rare but treatable immune-mediated disease that mostly affects children. It is an inflammatory demyelinating illness that primarily affects subcortical white matter and is distinguished by encephalopathy and polyfocal neurologic symptoms that typically accompany a viral infection or a vaccine [(4)].

There is a noticeable increase in number of cases of ADEM recently exceeding the documented numbers. So, we carried out this study with the objectives to monitor the change in the frequency of cases of ADEM in Patients admitted with Acute Disturbance of Consciousness in Pediatric Intensive Care Unit of Zagazig University Hospitals. In our study, we found 51.2% of patients had Seizures, 60.6% had Fever and 21% had Meningismus, while only 12.2% of patients Reported Headache against 44% in Koelman's series and 58% in the series by Dale [(5,6)]. This may be due difference in Conscious level on admission as all of our cases had disturbed conscious level on admission and lacked the requisite sensorium to report headache.

In Our Study, Neurologic symptoms, and signs pyramidal signs (59%), Ataxia (19.2%), cranial nerve palsies (33.4%), visual Affection (15.1%), spinal cord involvement (24%) and paresthesia (2%). This goes in agreement with Anlar, Tenembaum and colleagues [(7,8)]. Extrapyramidal signs were another neurological signs reported by **Tenembaum *et al.*** [(9)] represented (12%). In our study we found extrapyramidal signs in (12.2%) of cases.

Neuroimaging findings using MRI reported a focal or multifocal areas of increased signal intensity on T2-weighted and fast fluid-attenuated inversion-recovery images, in the cortical grey mater (45.4%), juxta-cortical white matter (31.8%), Deep white mater (9.1%), Periventricular white mater (21.2%) with total white matter affection in (62.1%), thalami (19.7%), basal, ganglia (19.7%), brainstem (16.7%), cerebellum (12.1%), and spinal cord (16.7%). **Alper *et al.*** [(10)] found distribution of lesions as Following: cortical grey mater (43%), Juxta-cortical white matter (21%), deep white mater (68%), and Periventricular white mater (18%) with total white matter affection in (62.1%), brainstem (41%) and cerebellum (50%).

In our study, MRI Lesions were Bilateral in 46 patient (70%) and Asymmetrical in 45 patient (68%). Restricted Diffusion was found in (31.8%) of cases. This goes in agreement with **Bulut *et al.*** **[(11)].**

Blood test results in our study revealed leukocytosis (>10,000/mm3) 39 patient (58.5%) (Mean 12,300/ µl, range 2.9–27.4/µl) and elevation of C-reactive protein concentration (<6mg/dl) of 28 patients (42.5%) (Mean 38.9 mg/l, range 1– 300 mg/l). The first CSF examination showed pleocytosis in 17 patients (25%) (Mean 39.2/ µl, range 0–1000/ µl) and protein elevation (>40 mg/dl) in 16 patients (24.4%) (Mean 77 mg/dl, range 0–800 mg/dl. According to **Dale *et al.*** [(6)]

and **Mikaeloff *et al.*** [12], cerebrospinal fluid(CSF) analysis in ADEM shows evidence of inflammation (either pleocytosis or high protein) in 70–75% of patients The CSF shows mild pleocytosis in 40–81% of patients with ADEM (0–137 with a mean of 41). Elevated CSF protein occurs in 36–60% of the patients (range 45–120 mg/dl with a mean of 74 mg/dl). In **Murthy *et al.*** [13] the peripheral white blood cell (WBC) count may be elevated in 39–64% of the patients. While **Dale *et al.*** [6] found C reactive protein was elevated in about a third of the patients.

CONCLUSION

Our work demonstrates how different illnesses can initially mimic ADEM. Due to potential therapy and prognosis, it is crucial to take these illnesses into account when making an ADEM differential diagnosis. Knowing the prevalence can raise awareness of these conditions in children. ADEM can be a difficult diagnosis. This is significant since there are signs that the incidence among children under the age of 12 may be rising.

Acknowledgement: The authors are grateful for the patients without whom this study would not have been done.

Funding: None.

Conflicts of interest: The authors affirm that they have no conflicts of interest.

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