Original Article

New-onset acute symptomatic seizure in a neurological intensive care unit

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Objective: New-onset acute symptomatic seizures can be the presenting feature of acute neurological diseases. The etiological spectrum of new-onset acute symptomatic seizures and outcome may be different in developing countries when compared to developed countries. **Aim:** To study the clinical profile of new-onset acute symptomatic seizures as the first presenting event in patients with acute neurological illness in a neurological intensive care unit (NICU) in a developing country. **Settings and Design:** Prospective study in a NICU in a tertiary care hospital. **Materials and Methods:** Consecutive patients with acute symptomatic new-onset seizure admitted to NICU in a tertiary care hospital over a period of 28 months. The etiology was determined by neuroimaging and appropriate investigations including cerebrospinal fluid examination. **Results:** Of the 3,151 admissions, 66 (2.1%) were related to new-onset acute symptomatic seizures as the first presentation. The mean age was 49.07 + 20.20 years. Tonic-clonic, generalized tonic-clonic or partial seizure with or without secondary generalization were the seizure type. At presentation 52 (79%) patients had single seizure, 10 (15%) patients had seizure clusters and four (6%) patients presented with status epilepticus (SE). The major etiological risk factors were central nervous system (CNS) infections (32%), metabolic disorders (32%) and cerebrovascular diseases (21%). In the NICU 10 (15%) patients had early seizure recurrence and three (4.5%) developed SE. Of these 13 patients, in nine (69%) patients the pathology was infection-related and the other commonality was involvement of cortical gray matter. Factors associated with seizure recurrence or SE were focal cerebral lesions involving cortical gray matter or diffuse cerebral pathology, meningoencephalitis. In 69% of these patients the pathology was infection-related. There were only two deaths, both in patients with SE and related to the underlying etiology. **Conclusion:** The risk of seizure recurrence and SE after the first acute symptomatic seizure is likely to be high in patients with acute focal cerebral lesions and diffuse CNS infections. The commonality in both the pathologies is cortical gray matter involvement.

Key words: Acute symptomatic, central nervous system infections, focal cerebral lesion, new-onset seizure, recurrence, status epilepticus

Seizures as the first presenting event can be the feature of acute medical or neurological disorders.[1] New-onset acute symptomatic seizures account for 40% of new-onset seizures.[2] Previous reports have addressed new-onset seizures in patients with nonneurological primary diagnosis admitted to medical and surgical intensive care units.[3-6] Very few studies have studied the frequency of seizures, mostly nonconvulsive seizures (NCSzs) and nonconvulsive status epilepticus (NCSE) in critically ill patients in neurological intensive care unit (NICU).[7-9] However, no study has attempted to determine the clinical profile of new-onset acute symptomatic seizures as the first presenting event in patients with acute neurological illness. Seizures complicating acute neurological disorders invariably add an additional layer of complexity to patient management. Neurological intensive care unit provides more easily collectable data in this group of patients.

Materials and Methods

Study setting and population

Consecutive patients with new-onset acute symptomatic seizure as the first presenting event in patients with acute neurological illness admitted to NICU in a tertiary care hospital over a period of 28 months (January 2003 to April 2005) were the subjects of the study. Patients were either referred by a practicing physician or came by self-referral. The data were collected prospectively in structured

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proforma. In our hospital all patients with acute seizures are attended by the neurology team and managed initially in the NICU. In our hospital all cases of traumatic brain injury are cared by the Neurosurgery team. We practice antiepileptic drug prophylaxis in patients with traumatic brain injury.

Definitions

Acute symptomatic seizure(s) was defined as seizure(s) caused or provoked by an acute medical or neurological insult.[1] Acute symptomatic seizures were further grouped into two broad categories: 1) acute symptomatic seizure(s) caused by acute neurological insult; and 2) acute symptomatic seizure(s) caused by acute metabolic disorder. Seizure type was classified using the classification proposed by the International League Against Epilepsy (ILAE).[10] Seizure cluster was defined as a repetitive series or a cluster of seizures that occur within a short time but that do not meet the criteria for a diagnosis of status.[11] Convulsive status epilepticus (SE) was defined as "(1) continuous convulsive seizure activity for more than 10 minutes or (2) two or more convulsive seizures, without full recovery of consciousness between seizures".[12] When the initial presenting feature was seizure cluster or SE, they were considered as a single seizure while considering recurrences.

Clinical data

Data collected included details of demography, modes of presentation, seizure semiology, etiological risk factors, management and outcome. All the patients had received brain imaging (CT/MRI), interictal EEG, routine laboratory investigations including metabolic profile, toxic screening, and other appropriate investigations like lumbar puncture were done in select patients to establish the underlying etiology. Diagnosis of neurocysticercosis was based on the criteria proposed by Delbrutto *et al*[13] and the diagnosis of tuberculoma was based on morphological features on contrast CT scan and or MRI.[14,15]

Treatment and outcome

The details of the antiepileptic drugs (AEDs) received, complications related to drug therapy were recorded. The outcome measures included immediate mortality and functional outcome at 30 days.

Results

Of the 3,151 admissions during the study period, 77 (2.4%) presented with new-onset seizures and 66 (2.1%) of them were related to acute, medical or neurological insult. In the remaining 11 patients, the cause of seizure was cryptogenic.

The mean age of patients with acute symptomatic seizures was 49.07+20.29 years (six months to 80 years). Twenty-four (36%) were aged 60 years and above, generalized tonic-clonic seizure was the seizure type in 36 (55%) patients and in the remaining 30 (45%) patients, the seizure type was partial with or without secondary generalization. Of the 30 patients with partial seizures, 28 (93%) had complex partial seizure and two (7%) had epilepsia partialis continua. At presentation 52 (79%) patients presented with single seizure, 10 (15%) patients had seizure clusters and four (6%) patients presented with SE. Postictal Todd's palsy was noted in four (6%) patients [Table 1].

The underlying etiological risk factors were central nervous system (CNS) infections in 21 (32%) patients, metabolic disorders in 21 (32%), cerebrovascular diseases (ischemic, venous and hemorrhagic) in 14 (21%) and others in 10 (15%). The distribution of the pathology in patients with CNS infections was meningoencephalitis in nine (43%) and parenchymal granuloma in 12 (57%) patients [(degenerative phase solitary cystic granuloma (SCG) in nine (75%) and tuberculoma in three (25%)] [Table 2].

The electroencephalography (EEG) was mostly interictal, done within 24h after the seizure had been aborted. It was abnormal in 37 (56%) patients, mostly nonspecific, either diffuse symmetric or focal theta or delta activity. None of the EEG showed spike or sharp wave activity and periodic discharges. There were no specific EEG features that could predict the recurrence seizures and SE.

Of the 66 patients with seizures, 10 (15%) patients had early seizure recurrence and three (4.5%) developed SE

Table 1: Etiology and presenting seizure type, seizure recurrence and status epilepticus

Etiological risk factor	Seizure frequency at presentation (%)			Seizure recurrence in NICU (%)	
	Single	SC	SE	Recurrence	*SE*
Hyponatremia (15)	15 (100)	-	-	-	
Stroke (14)	11 (79)	3 (21)	-	1 (7)	1 (7)
Granulomatous lesions					
Solitary cysticercus granuloma (9)	5 (56)	4 (44)	-	4 (44)	-
Tuberculoma (3)	2 (67)	1 (33)	-	-	
Meningoencephalitis (9)	6 (67)	-	3 (33)	4 (44)	1 (11)
Glycemic disorders (6)	4 (67)	2 (33)	-	-	
Others (10)	9 (90)	-	1 (10)	1 (10)	1 (10)

SC: Seizure cluster, SE: Status epilepticus, *All these patients presented with single seizure at admission

Table 2: Etiological risk factors

Etiological risk factor		Number of patients (%)
Central nervous system Infections		21 (32)
Meningoencephalitis	9	
Neurocysticercosis-SCG	9	
Tuberculoma	3	
Cererbrovascular diseases		14 (21)
Intracerebral hematoma	9	
Ischemic	3	
Cortical sino-venous thrombosis;	2	
Metabolic		21 (32)
Hypoglycemia	2	
Hyperglycemia	4	
Hyponatremia	15	
Others		10 (15)
Alcohol	6	
Hypoxic encephalopathy	2	
Tumor	1	
Acute disseminated encephalomyelitis	1	

SCG: Solitary cysticercus granuloma.

in the NICU. The pathology in 10 patients with seizure recurrence was focal cerebral lesions in six (60%) (ischemic stroke one, SCG four, glioma one) and meningoencephalitis in four (40%). The pathology in the three patients with SE was focal cerebral lesions in two (cerebral sino-venous thrombosis, CSVT) and meningoencephalitis in one patient. Of the 13 patients who had seizure recurrence or who developed SE, in nine (69%) the pathology was infection-related.

Of the 28 patients with focal lesions, eight presented with seizure clusters (28.6%), six (21.4%) had early seizure recurrence and two (7%) developed SE in the NICU. The location of focal cerebral lesions was either cortical or at the gray-white matter junction. Of the 11 patients with diffuse cerebral pathology (meningoencephalitis nine, hypoxic encephalopathy two), four (36%) presented with SE, one (9%) developed SE in the NICU and four (36%) had seizure recurrence [Table 3].

The pathology in the seven patients with SE included focal cerebral lesions in two [cerebral sino-venous thrombosis (CSVT) one, acute disseminated encephalomyelitis (ADM) one)] and diffuse cerebral pathology in five (meningoencephalitis four, hypoxic encephalopathy one).

Drug response

All patients received intravenous benzodiazepines (lorazepam or midazolam) at arrival. Patients with seizure cluster and those who had seizure recurrence in the NICU received phenytoin- or sodium valproate loading dose followed by oral maintenance dose. At the time of discharge only patients who had recurrent seizures, seizure cluster and SE were kept on AEDs, either phenytoin or sodium valproate. In patients with SCG and tuberculoma AEDs were withdrawn only when the follow-up CT demonstrated complete resolution of the lesion. In the other patients AEDs were withdrawn at three to six months intervals. None of the patients with acute symptomatic new-onset seizures due to metabolic disorders received AED prophylaxis. None had seizure recurrence during the follow-up.

Of the seven patients who presented with SE or developed SE in the NICU, in five patients SE responded to intravenous midazolam or lorazepam followed by phenytoin- or fosphenytoin-loading dose. Both the patients who were given third drug, intravenous midazolam infusion, died. The death was related to the underlying etiological risk factors, tuberculous meningitis and CSVT.

Discussion

Seizures may herald or complicate acute neurological and medical disorders. In our study 2.1% of admissions were related to new-onset seizures occurring with acute neurological disorders. As mentioned in the methodology, all acute seizures are admitted directly from the emergency department to NICU and triaged. A retrospective study from Mayo Clinic[4] reported new-onset seizures in 0.8% of patients admitted to medical and surgical ICUs. A review by Bleck *et al*[3] noted that 3.5% of patients with critical medical illness had new-onset seizures. Both these studies are incidence studies of new-onset seizures in patients with non-neurological primary diagnosis admitted to medical and surgical ICUs. Our study differs substantially from these two studies. We studied new-onset seizures as the first manifestation in patients with acute neurological primary diagnosis and not incidence cases in NICU. New-onset seizures in the elderly requiring hospitalization mostly occur with acute neurological insults.[16-18] In a retrospective study, acute symptomatic neurological insults accounted for 41% of etiologies.[17]

New-onset acute symptomatic seizures can occur as single events, brief clusters or status epilepticus.[3,4,19] Of

Table 3: The pathology and seizure recurrence

Pathology	Seizure recurrence	
Focal pathology - 28*	Seizure cluster at presentation - 9 (28.6%)	
	Seizure recurrence in NICU - 5 (21.4%)	16 (57%)
	Status epilepticus in NICU - 2 (7%)	
Diffuse cerebral pathology - 11	Status epilepticus at presentation - 4 (36%)	
	Status epilepticus in NICU - 1 (9%)	9 (81%)
	Seizure recurrence - 4 (36%)	

*The location of focal pathology was either cortical or gray-white matter junction, NICU - Neurological intensive care unit

the 66 patients, cluster of seizures was the presenting event in 10 (15%) patients. Eight patients had focal lesion on CT scan involving cortical gray matter or gray-white junction. Six of the lesions were granulomas. Seizure clusters have been reported more frequently in patients with SCG.[20]

There are scanty data regarding SE incidence in the ICU. In this series seven (11%) patients had SE. Four patients presented with SE and three (4.5%), incidence cases developed after admission to NICU. Bleck *et al*[3] prospectively evaluated 1850 patients admitted to a medical ICU, four patients were admitted with primary refractory SE. Of 217 patients with nonneurological admissions who developed neurological complications, 61 (28.1%) had seizures, six of these patients were in SE. Thus ten (0.5%) of medical ICU admissions were primary or secondary SE. In the Mayo Clinic series,[4] of the 55 patients with new-onset seizures among 27,273 patients admitted to the medical and surgical ICU, only four (7.3%) patients developed SE.

The etiological spectrum in the present study was distinctly different when compared to the data from developed countries.[21,22] In our study CNS infections accounted for 32% of the etiology. Similar were the observations in the other studies from developing countries.[19,23] Solitary cystic granuloma, degenerative phase of NCC accounted for 43% of the CNS infections. In developing countries endemic to NCC, cysts in the degenerative phase is the most common cause of new-onset acute symptomatic seizures.[24]

New-onset acute symptomatic seizures are different from unprovoked seizures in that they generally do not recur and usually do not need long-term AED therapy. However, this study suggests that the risk of seizure recurrence or SE after the first seizure is likely to be high in patients with acute focal cerebral lesions and diffuse CNS infections like meningoencephalitis and encephalitis. Of the patients who had seizure recurrence or developed SE, in 69% the pathology was infection-related and the other commonality was cortical gray matter involvement. Probably this group of patients, particularly patients with CNS infections, with high risk of seizure recurrence may need AED prophylaxis, at least for the period of resolution or stabilization of acute CNS insult. This concept is best illustrated by the seizure disorder associated with SCG. A growing body of clinical observation supports the concept that the seizure disorder associated with SCG requires AED treatment for the period of resolution of CT lesion.[25]

When considering the results of this study the limitations of the study must be recognized. This is a highly selected population and the findings may not be generalizable. In developing countries CNS infections like Japanese encephalitis, tuberculous meningitis, bacterial meningitis and NCC are endemic and are frequent risk factors for new-onset acute symptomatic seizures. There is a need to study a large population of patients with these pathologies for the risk of recurrence of seizures as it may have therapeutic implications, possible AED prophylaxis.

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