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Convulsive status epilepticus due to different evolutionary stages of neurocysticercosis - solitary cyticercus granuloma, low cyst load, and single calcific lesion in an endemic country: Clinical profile

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ABSTRACT

Purpose: The aims of the study were: (a) to evaluate the clinical profile of convulsive status epilepticus (CSE) due to different evolutionary stages of neurocysticercosis (NCC), solitary cysticercus granuloma, low cyst load and single calcific lesion in an endemic country; (b) to evaluate the response of CSE to antiepileptic drugs; and (c) to evaluate long-term outcomes

Methods: A retrospective review of case records of patients with CSE due to different evaluative stages of NCC seen over a period of 18 years.

Results: During 18 years period, 41 (24 males, mean age 25.3 years, range 8–65 years) patients with CSE due to different evolutionary stages of NCC were admitted to our Neurological Intensive Care Unit. There were 7 patients with 3–5 degenerative cyst load, 20 with solitary cysticercus granuloma (SCG), and 14 with single calcific (cNCC) lesion. Of the 41 patients, CSE was the initial presenting feature in 38 (93%) patients. The mean duration of CSE was 5.85 h (range 0.5–48 h). The mean duration of CSE due to single cNCC was significantly shorter when compared to the duration of CSE due to degenerative stages of NCC (1.96 + 1.39 h vs. 7.87±13.18; $p < 0.026$). Of the 41 patients, 39 (95%) responded to first-line treatment (intravenous (IV) benzodiazepine followed by IV phenytoin/ fosphenytoin or valproate), two patients required continuous IV midazolam. Both the patients developed aspiration pneumonia. There were no deaths, and all the 41 patients had Glasgow Outcome Score of 5 at 90-day follow-up and were back to their previous occupation.

Conclusions: This study suggests that CSE due to different evolutionary stages of NCC, SCG, low lesional load, and single calcific lesion is rare even in countries endemic to NCC and is associated with an excellent outcome.

1. Introduction

Seizures and epilepsy are the most common manifestations of all the evolutionary stages of neurocysticercosis (NCC) (78.8%, 95% CI: 65.1%–89.7%) [1]. Seizure presentation can be as an isolated seizure, seizure cluster, or convulsive status epilepticus (CSE) [2,3]. CSE is a rare presentation of all the evolutionary stages of NCC [2–5]. Extremely rarely,CSE due to NCC may evolve into super refractory SE [6]. However because of its rarity, CSE due to different evolutionary stages of NCC has not been well characterized. The purpose of this study was: (1) to characterize the clinical profile of CSE due to different evolutionary stages of NCC, solitary cysticercus granuloma (SCG), low cyst load, and single calcific stage of NCC (cNCC); and (2) to evaluate the response of CSE to antiepileptic drug (AED) treatment; and (3) to evaluate long-term outcomes.

2. Methods and material

This was a retrospective review of case records of patients with the diagnosis of CSE due to different evolutionary stages of NCC: low cyst load; SCG, and single cNCC, admitted to our Neurological Intensive Care Unit (NICU) between January, 1994 and December, 2012 (18 years). The diagnosis of NCC was based on the clinical and radiological criteria proposed by Del Brutto et al. [7]. All the patients had either contrast computed tomography (CCT) and/or contrast magnetic resonance imaging (MRI). None of the patients had serological testing for antibodies. The data collected included: demographic data, seizure type, type of SE, duration of SE before admission, neurological features, CT and/or MRI findings, drug therapy and response, complications, and 90-day morbidity and mortality.

First-line drug therapy included intravenous (IV) benzodiazepine

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(lorazepam or midazolam) followed by IV loading dose of phenytoin/fosphenytoin or valproate. Patients who failed to respond to first line therapy, received continuous intravenous (cIV) infusion of midazolam. None of the patients had continuous EEG monitoring. Recovery from altered mental status with no further breakthrough seizures was considered as therapeutic response.

Patients with SCG and multiple cysts in the degenerative phase received four weeks of cysticidal drug (albendazole: 15 mg/kg/day in two divided doses for 30 days) treatment. They also received a short course of steroid therapy (1 mg/kg in a tapering dose over 4 weeks) [8]. Patients with SCG and multiple cysts in degenerative phase were put on AEDs for the period of resolution of the lesion in the follow-up contrast CT. Patients with single cNCC were put on AEDs prophylaxis [8].

Patients were followed at monthly interval. During the follow-up period the data collected included, seizure recurrence, AED adherence, drug adverse events, and functional outcome. Glasgow Outcome (Score GOS) was used to determine 90-day mortality and functional outcome: (1) dead; (2) persistent vegetative state and patient exhibits no obvious cortical function; (3) severe disability and patient depends on others for daily support; (4) moderate disability and patient is independent as far as daily life is concerned; (5) good recovery and resumption of normal activities [9].

3. Operational definitions

Convulsive SE in adult and older children was referred to > 5 min of (a) continuous seizure or (b) two or more discrete seizures between which there is incomplete recovery of consciousness [10].

CSE due to degenerative phase of NCC including SCG was categorized under acute symptomatic aetiology and CSE due to cNCC was categorized under structural aetiology [11].

4. Results

During the18 years period, 41 [24 males and 17 females; mean age 25.3 years; range 8–65 years] patients with CSE due to different evolutionary stages of NCC were admitted into our NICU. This cohort included 15 patients with CSE which formed part of our earlier publication [5]. The mean duration of SE was 5.85 h (range 0.5–48 h). In 32 (78%) patients the CSE was focal onset convulsive seizures with generalization and in 9 (22%) it was generalized convulsive status from the onset (Table 1). In 38 (93%) patients CSE was the presenting feature and 3 patients with SCG, developed CSE while on AEDs.

The distribution of different evolutionary stages of NCC in the 41 patients was as follows: 7 (17%) with low degenerative cyst (3–5 cysts) load; 20 (49%) with SCG; and 14 (34%) with single cNCC. There were no significant differences in the gender distribution, mean age and age range amongst the three groups (Table 1). However, the mean duration of SE was significantly shorter in patients with CSE due to single cNCC when compared to patients with degenerative phase of NCC (1.96 ± 1.39 h vs. 7.87 ± 13.18 h; $p < 0.026$).

Table 1
Demographic data, status duration, and seizure type.

Variables	Total (n = 14)	Multiple cyst (n = 7; 3-5)	SCG	Calcific NCC (n = 20)
Mean age (yr)	25.3	25.6	26.2	23.9
(range)	8–65	10–45	8–55	6–65
M:F	24:17	5:2	12:8	7:7
SE mean duration (h)	5.85	6.35	8.4	1.96*
(range)	(0.5–48)	(1–24)	(0.5–48)	(0.5–5)
Seizure type (focal onset vs GTCS at onset)	32:9	6:1	17:3	9:5

* p = 0.027.

Table 2
NCC- SE: Outcomes.

	Total (n = 41)	Multiple cyst (n = 7; 3–5)	SCG (n = 20)	Calcific NCC (n = 14)
First line drugs (%)	39 (95%)		18 (90)	14 (100)
Second line drugs	-	-	2 (100)	-
Complications	-	-	2*	-
Outcome	G5 = 41	G5 = 7	G5 = 20	G5 = 14

* Aspiration pneumonia (both required second-line drugs).

Of the 41 patients with CSE, 39 (95%) patients responded to first-line drug therapy (benzodiazepine + IV loading phenytoin/fosphenytoin or valproate) and the remaining 2 patients (both due to SCG) required cIV midazolam to terminate the SE (Table 2). They required mechanical ventilation for the period of seizure remission. Both the patients developed aspiration pneumonia, which was successfully treated.

There were no deaths and all the 41 patients had GOS 5 outcome at 90-day follow-up. All the 27 patients with lesions in the degenerative phase including SCG who received 30-days of cysticidal drug (albendazolam), short course of oral steroids, and AEDs (mostly monotherapy, carbamazepine) made good recovery with GOS score of 5. These patients received AEDs (mostly monotherapy, carbamazepine) for the period of resolution of the lesion in the fallow-up contrast CT [8]. None of the patients had seizure recurrence during 2 years follow-up period after AED withdrawal. All of them improved to their premorbid state and back to work. All the 14 patients with single cNCC were off AEDs after 5 years of seizure free period. They were back to their previous occupation.

5. Discussion

This study suggests that CSE due to different evolutionary stages of NCC: SCG, low degenerative cyst load and single cNCC, is rare. We had seen 41 patients over a period of 18 years with a mean of 2.28 patients per year. The clinical characteristics of CSE due to different evolutionary stages of NCC were: often convulsive, of shorter duration, response to AEDs excellent, and associated with excellent outcome. The duration of CSE due to single cNCC was significantly shorter when compared to the duration of CSE due to degenerative phase of NCC including SCG. In this series there was no case with extensive parenchymal cysticercosis.

Convulsive SE due to different evolutionary stages of NCC is rare in the hospital-based studies, even in countries endemic to NCC in spite high prevalence of epilepsy due to NCC in these countries. In the rural community-based prevalence study in Uttarakhand a province in north India, of the 141 persons with active epilepsy, 49 (34.7%) persons had epilepsy due to different evolutionary stages of NCC [12]. In the prevalence study in Vellore district in south India, of the 194 persons with active epilepsy, 55 (34%) persons had epilepsy due to different evolutionary stages of NCC. Extrapolating these results to the country as a whole, it leads to an estimated disease burden of 1 million patients in India with active epilepsy attributable to NCC [13]. In spite of the high burden of the disease, the reported frequency of CSE due to NCC in the hospital-based series is rare. In a prospective university hospital-based study of 85 patients with CSE in south India, different evolutionary stages of NCC accounted for 17.6% of the aetiology.[5] Even among the patients with CSE due to infections of central nervous system it accounted for 3 (8%) patients in a university hospital-based study of 37 patients in north India [14].

SCG is the common form of NCC reported from India and it accounts for ˜20% of cases of NCC in other endemic countries [8]. In the Uttarakhand prevalence study, of the 141 persons with active epilepsy, SCG was the cause in 33 (23%) persons [12]. The reported incidence of CSE in patients with SCG varied between 0.07% and 13% in different

hospital-based series.[3] In the hospital-based study of 526 patients with acute symptomatic seizures in south India, different evolutionary stages of NCC was the cause in 312 (59.3%) patients. SCG was the lesion in 262 (49.8%) patients. Of the 262 patients with SCG, only 4 (1.5%) patients presented with CSE [2].

The systematic review and meta-analysis of the relationship between epilepsy and neurocysticercosis in Latin America found that the median NCC proportion among people with epilepsy was 32.3% (95% CI 26.0–39.0). The association between NCC and epilepsy was significant ($p < 0.001$) with a common odds ratio of 2.8 (95% CĪ 1.9–4.0) [15]. However, the reported frequency of CSE due to the different evolutionary stages of NCC in the hospital-based studies was rare Latin American countries. In the study from Ecuador, of the 203 patients with various evolutionary stages of NCC, only 5 (2.46%) patients presented with CSE [4]. NCC accounted for 3.2% of etiology for CSE in a study in Honduras, where NCC is a common cause of symptomatic epilepsy [16]. In the rural Honduras epidemiologic study, the Salama study, of the 90 persons with active epilepsy who consented to diagnostic studies, 56 (62.2%) had symptomatic epilepsy, it was primarily due to NCC, 33 (36.6%) [17].

The exact prevalence of single cNCC as a cause of CSE is unknown. In our study of 85 patients with CSE, single cNCC accounted for the etiology in 5 (5.9%) patients [5]. In the rural prevalence study in Uttarakhand, north India, of the 141 with active epilepsy, 14 (9.9%) had cNCC lesions [12]. In our study the mean duration of SE was significantly shorter in patients with CSE due to single cNCC when compared to patients with degenerative phase of NCC.

Recently Kariuki et al studied the prevalence and risk factors of CSE among 1196 people with active convulsive epilepsy (ACE), identified in multisite survey in Africa (Agincourt, South Africa; Iganga-Mayuge Uganda; and Kilifi, Kenya) endemic to NCC [18]. They performed serological assessment for the presence of antibodies to parasitic infections including Taeniasis and human immunodeficiency virus (HIV) and determined adherence to AEDs. Risk factors for CSE in ACE were neurologic impairment, acute encephalopathy, previous hospitalization, and presence of antibody titers to falciparum malaria and HIV. However, presence of antibody titer to Taeniasis did not show any increased risk for CSE in ACE, [pooled univariate and adjusted analysis: people without CS (%) 1/48 (2) vs. people without CSE (%) 1/36 (3); adjusted OR 1.55 (95% CI 0.09–28.12; p = 0765] [18].

The mean duration of CSE was shorter in all the three groups. It was significantly shorter in patients with single cNCC lesion when compared to patients with degenerative phase of NCC. Response to AED therapy was excellent, of the 41 with CSE due to different evolutionary stages of NCC, 39 (95%) patients responded to first line treatment. The response to second line drugs was excellent in the remaining two patients and only 2 (4.8%) patients developed complications which were successfully treated.

We used GOS as outcome scale. Other studies have also shown the usefulness of this scale in assessing outcome in CSE [5,19,20]. At 90-days all the patients with SCG and low lesional load had excellent outcome (GCS 5) and back to their previous occupation. The seizure disorder due to SCG and low cyst load, is self-limiting and resolves with the resolution of the CT lesion [8,21–23] and is pharmaco-responsive [8]. Similar were the observations in our patients. All the 14 patients with CSE due to single cNCC were seizure free and were off AEDs after five years of seizure freedom. They are back to work. In our earlier study, 71.5% (95% CI 7–85.4) of patients achieved 3-year remission and 66% (95% CI 32.4–88.2) achieved 5-year remission [24].

Parenchymal brain cysticercus cysts in the degenerative phase are the most epileptogenic [25]. Products from acute cysts injected into animal brains are significantly more epileptogenic than are products from chronic granulomas [25]. Degenerative phase is characterized by breakdown of the blood brain barrier and consequent surrounding host-inflammatory response. The inflammatory response and the implied cellular and molecular events are probably responsible for seizures. Several mechanisms have been proposed for the epileptogenesis for cNCC: (1) intermittent host response to the antigen trapped in the calcium matrix as evidenced by perilesional edema and contrast enhancement [13,14], (2) perilesional gliosis, a common feature with these lesions [26,27]; and (3) recent evidence of an association between calcific NCC and hippocampal sclerosis [28].

This study suggests that CSE due to SCG or low cyst load and single cNCC is rare and has a benign course with excellent outcome. Probably this may be related to limited focal network and rapid stabilization of the associated inflammatory response with the treatment.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Declaration of Competing Interest

None of the authors has any conflict of interest to disclose

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