Short Communication

Cognitive and Behavioral Profile of Treatment-Naïve Children Aged 6–14 Years with Neurocysticercosis from North India

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Abstract

Background: Neurocysticercosis (NCC) produces a progressive organic brain damage by altering brain function with alterations in memory, difficulties in learning, and behavioral changes. The present study was designed to compare the cognitive and behavioral profile of school-going children aged 6–14 years with newly diagnosed NCC with their age-matched controls. **Materials and Methods:** A descriptive cross-sectional study was conducted among children aged 6–14 years with newly (<7 days) diagnosed NCC. Age- and gender-matched typically developing children with minor illness attending outpatient facility served as control. Intelligence and behavioral assessment were performed using Malin's Intelligence Scale for Indian Children and Childhood Behavior Checklist (CBCL) (school age version CBCL/6–18). CBCL *T*-scores were computed and scores < 60 were considered as normal, 60–63 as borderline, and > 63 as clinical range. **Results:** A total of 35 cases and 35 controls were enrolled. Baseline demographic characteristics were comparable between the two groups. Verbal intelligence quotient (IQ) scores were comparable between the cases (96.14 [10.23]) and controls (100.17 [10.89]) (P = 0.11). The behavioral assessment revealed normal *T*-scores (<60) in both the groups. **Conclusions:** The study revealed comparable IQ and normal behavioral profile of treatment-naïve children with recently diagnosed NCC to their age-matched peers. Further studies with larger sample size and longitudinal study design are required to evaluate the role of NCC on cognition and behavior in Indian children.

Keywords: Behavior, cognition, intelligence, neurocysticercosis

Introduction

Neurocysticercosis (NCC) is one of the most common causes of acquired epilepsy in India. Prevalence of active epilepsy related to NCC ranged from 1.3 to 4.5/1000 population.[1] It has been estimated that NCC-associated active epilepsy caused an annual median loss of 12.03 billion Rupees in India.[2] The majority of children present with seizures in North India.[3] Uncommon presentations of NCC include cognitive impairment, behavioral disturbances, depression, and extrapyramidal manifestation.[4]

Patients with NCC showed significant impairment in executive function, verbal, nonverbal memory, constructive praxis, and verbal fluency when compared to healthy controls.[5] However, there was no correlation of cognitive scores with number and localization of lesion on magnetic resonance imaging brain.[5] Few believe that parasite induces expression of several genes in the central nervous system of the host, which encode protein or neuropeptide involved in the regulation of behavioral process.[6]

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Learning disability (28%), behavioral changes (12%), and psychomotor involution (8%) were observed among Brazilian children with NCC.[7] In a study by Prasad *et al*.,[8] it was observed that children aged 6–18 years with NCC had significantly more behavioral problems than healthy controls. However, behavioral and cognitive problems in children could be influenced by the type of seizure, duration of seizure, and nature of antiepileptic drugs. Hence, the present study was designed to compare the intelligence and behavioral problems of treatment-naïve children aged 6–14 years, diagnosed with NCC with their age- and gender-matched healthy peers.

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Materials and Methods

Study design and study population

A cross-sectional study was conducted among school-going children aged 6–14 years with newly diagnosed NCC (<7 days) based on the revised neuroimaging criteria.[9] Age- and gender-matched typically developing children with mild respiratory or gastrointestinal illness attending outpatient facility served as control. Children with recognized static or progressive neurological illness and/or those on antiepileptic drugs (for >7 days) or any psychotropic drugs were excluded from the study. Institutional Ethical Committee approval was obtained before the commencement of the study. Written informed consent was obtained from parents/caregivers.

Study tool and measurements

Eligible study participants were enrolled sequentially in the study. Demographic and clinical details including type of seizure and their neuroimaging findings were recorded. Investigator had no role in deciding the choice of investigation or in the management plan which was executed as per the hospital unit policy. The behavioral assessment was performed on Childhood Behavioral Checklist (CBCL).

CBCL (6–18 years) is a tool which provides age- and sex-standardized assessment of a child's behavior. It consists of 120 questions answered by parents or caregivers. Each response was recorded on a Likert scale: 0 – not true, 1 – somewhat or sometimes true, and 2 – very true or often true. CBCL provides a total behavior problem score and two second-order factor scores: internalizing problems and externalizing problems. *T*-scores were computed for both internalizing (emotionally reactive, anxious/depressed, somatic complaints, and withdrawn) and externalizing problems (attention problems and aggressive behavior). CBCL *T*-scores were computed and scores <60 were considered as normal, 60–63 as borderline, and >63 as clinical range.

Intelligence was assessed using Malin's adaptation of Wechsler Intelligence Scale called Malin's Intelligence Scale for Indian Children (MISIC). Verbal intelligence (intelligence quotient [IQ] score) was computed based on a component of MISIC which includes information, comprehension, arithmetic, similarities, vocabulary, and digit span test.

Statistical analysis

A convenience sample of 35 children with newly diagnosed NCC and 35 age- and gender-matched controls was recruited for the study. All data were entered in Microsoft Excel 2000 version. Categorical variables were expressed as numbers (percentage) and continuous variables as median (IQR) or mean (standard deviation [SD]). IQ scores and *T*-scores of CBCL were compared between the groups using Student's *t*-test or Mann–Whitney U-test. $P < 0.05$ was considered as statistically significant.

Ethics

The project was approved by the Institutional Ethical Committee and written informed consent was obtained from parents/caregivers of the study participants.

Results

Mean (SD) age of the enrolled children was comparable among cases (9.26 [2.35] years) and controls (9.51 [2.56] years) ($P = 0.66$). Baseline demographic characteristics were comparable between the cases and controls [Table 1]. Among the 35 cases of NCC, 16 (45.7%) had generalized seizures and rest 17 (54.3%) had focal seizures. The majority 29 (82.8%) of the enrolled cases had a single lesion of NCC and rest 6 (17.2%) children had more than one lesion. Only 4 (11.4%) had a calcified lesion, and rest had active inflammatory NCC. Distribution of the most prominent lesion was in the frontal 11 (31.4%), parietal 19 (54.2%), temporal 3 (8.5%), and occipital 2 (5.7%) lobe of the brain.

Verbal intelligence scores were comparable between the cases and controls [Table 2]. Mean (SD) *T*-scores in both cases and controls were in normal range (*T*-scores <60). However, for statistical purpose, when *T*-scores were compared between the cases and controls, the former had significantly higher scores in somatic complaints, withdrawn, and attention problems, leading to higher scores on externalizing, internalizing, and total problems [Table 3]. However, considering the normal range of *T*-scores in both the groups, the statistical significance of this difference has no clinical relevance.

Discussion

This study revealed comparable intelligence and behavioral profile of treatment-naïve children diagnosed with NCC to their age-matched peers. NCC has been implicated in cognitive impairment, behavioral, and other neuropsychiatric manifestations in adults and children.[5,6,8,10] NCC is an endemic infection that manifests clinically only when the host develops

Table 1: Comparison of baseline characteristics of study participants (cases and controls)

Baseline characteristics	Cases ($n=35$), *n* (%)	Controls ($n=35$), *n* (%)	*P*
Male gender	18 (51.4)	15 (42.8)	0.63
Rural background	20 (57.1)	21 (60)	0.81
Literate parents	27 (77.1)	24 (68.5)	0.42
Employed	17 (48.6)	19 (54.2)	0.64
Monthly income (<10,000)	14 (40)	13 (37.1)	0.75
Water supply (pipe)	30 (85.7)	29 (82.8)	0.74
No sanitation	3 (8.6)	4 (11.4)	0.69
Nonvegetarian diet	14 (40)	16 (45.7)	0.63
Pork eaters	9 (25.7)	11 (31.4)	0.59
Eating unwashed vegetables	6 (17.1)	7 (20)	0.76
Eating outside food	4 (11.4)	3 (8.5)	0.85

Table 2: Various domains of intelligence quotients in cases and controls

Parameter	Mean (SD)		*P*
	Cases	Controls	
Information	91.8 (12.42)	97.43 (15.1)	0.09
Comprehension	109.37 (22.41)	114.49 (19.68)	0.31
Arithmetic	97.2 (15.76)	93 (12.45)	0.22
Analogies	101.03 (15.08)	107.49 (17.85)	0.11
Vocabulary	90.94 (16.60)	96.64 (13.35)	0.11
Digit span	94.21 (12.51)	94.29 (10.65)	0.93
Verbal IQ	96.14 (10.23)	100.17 (10.89)	0.11

IQ=Intelligence quotient, SD=Standard deviation

Table 3: Comparing childhood behavior checklist *T*-scores of cases (children with neurocysticercosis) and controls

Subscale	*T* score		*P*
	Cases	Controls	
Emotionally reactive	51.1 (3.8)*	50.3 (0.2)*	0.17
Anxious/depressed	50.8 (2.1)*	50.2 (0.6)*	0.08
Somatic complaints	53.2 (6.4)*	50.6 (1.9)*	0.01
Withdrawn	51.4 (3.2)*	50.1 (0.6)*	0.03
Attention problems	51.9 (3.8)*	50.1 (0.2)*	<0.01
Aggressive behavior	50.5 (2.1)*	50.0 (0.1)*	0.11
Internalizing problems	51.6 (2.5)*	50.2 (0.5)*	<0.01
Externalizing problems	51.2 (2.4)*	50.2 (0.2)*	<0.01
Total problems	51.8 (1.6)*	50.1 (0.4)*	<0.01

**T*-scores <60 are considered in normal range

an inflammatory response to the parasite.[2] This raises serious concerns on the prevalence of silent or asymptomatic NCC in endemic areas. It is rather difficult to determine such a prevalence considering the limited role of serological tests for NCC.[11] Moreover, it is obviously not feasible to screen everyone for NCC by neuroimaging in the endemic zone. The present research was conducted to address the concern of possible association of learning difficulties and cognitive and behavioral problems among school-going children to raising the burden of NCC.

NCC is known to be the most common cause of focal epilepsy in Indian children.[3] The study design was conceptualized on treatment-naïve children with NCC. This circumvents the possible role of duration of epilepsy, nature of antiepileptic drug, and psychological issues related to the diagnosis of epilepsy on cognition and behavior. A cutoff of 7 days was adopted for the duration of an antiepileptic drug, giving leverage to stabilization of the child following seizure secondary to NCC.

The verbal intelligence scores were statistically comparable in the present study although there was a trend of lower scores in the domain of information, comprehension, analogies, and vocabulary subscales. Our study findings are consistent with the previous study by Prasad *et al*.,[8] where the total IQ scores were comparable between children with NCC, children with idiopathic epilepsy, and healthy controls. On domain-wise analysis, authors have reported that children with NCC lagged behind in domains of concept formation; analysis, synthesis, and reasoning; verbal ability; and memory and spatial ability.[8]

In a study by Forlenza *et al*.,[12] cognitive decline has been reported among 87.5% of adults with NCC. Ciampi de Andrade *et al*.[5] found that treatment-naïve patients of NCC had significant impairment in executive function, verbal and nonverbal memory, constructive praxis, and verbal fluency when compared to healthy controls. In another study by Rodrigues *et al*.,[10] both groups of patients with calcified NCC and active NCC were found to have impairment in a single domain or had a cognitive impairment with no dementia.

A meta-analysis of population-based studies revealed the prevalence of intellectual disability in India to be 10.37/1000 population.[13] In a study by Diagana *et al*.,[14] cognitive impairment was detected in 8.4% of 227 adults screened in a community from Ecuador known to endemic for *Taenia solium*. Authors have attributed this impairment to the endemicity of cysticercosis. However, in the Indian context, perinatal–neonatal event remains the predominant cause of intellectual disability, irrespective of endemicity for a large number of infections including *T. solium*.[15]

In a study by Prasad *et al*.,[8] children with NCC had significantly more behavioral problems in the domain of anxious-depressed, withdrawn, somatic problems, and rule-breaking behavior. Although we observed significantly higher *T*-scores in the same domains, none of the scores were in clinical or subclinical range. Behavioral disturbances in Indian children are predicted by the presence of nuclear family (odds ratio [OR] = 1.89), working status of the mother (OR = 2.71), financial problems at home (OR = 13.32), and low socioeconomic status (OR = 3.73).[16] We believe that children in the present study setting belong to family with the rich agricultural background, concept of joint family, and homemaker mothers. This could probably attribute to lower burden of behavioral problems in their children as observed.

The strengths of the present study include controlled study design, a true representation of rural background, and the inclusion of treatment-naïve children with NCC. However, the study is very limited by the small sample size included. Furthermore, the cross-sectional study design does not permit any definite conclusion. Further studies with larger sample size and longitudinal study design are required to evaluate the role of NCC on cognition and behavior in Indian children.

Clinical implications of this neutral effect of NCC on cognition and behavior of school-going children could be varied. Cognitive disturbance and behavioral problems in children who have been detected to have NCC on neuroimaging are more likely to be coincidental rather than causative. Few authors believe in the complete workup of children and adults with cognitive and behavioral disturbances including autoimmune, paraneoplastic, and vasculitic workup.[17] These

study findings could possibly allay the fear of epidemiologist who has attributed behavioral changes and suboptimal learning and intelligence of school-going children to the endemicity of *T. solium*.

Conclusions

The study revealed comparable intelligence and normal behavioral profile of treatment-naïve children with recently diagnosed NCC to their age-matched peers. Further longitudinal studies with larger sample size are required before concluding that NCC has no effect on cognition and behavior of school-going children.

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Conflicts of interest

There are no conflicts of interest.

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