Original Research Article

The clinical profile ofring-enhancing lesions among children below 12 years presenting with epileptic and non-epileptic manifestations in a tertiary care hospital

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Abstract

Background: Single ring-enhancing computed tomography lesions are commonly seen in young patients presenting with acute symptomatic seizures. It has also been observed in many varieties of non-epileptic manifestations. The present study was conducted to evaluate the clinical profile and incidence of ring-enhancing lesions in contrast-enhanced computerizedtomography (CECT) scan in children presenting with seizures focal neurological deficits and other non-seizure CNS manifestations.**Methods:** A cross-sectional study was conducted on48 children in the age group of 0 to 12 years with a history of seizures (GTCS, simple partial (SP), complex partial (CP), and simple partial with secondary generalization (S. P+S.G)), focal neurological deficits and other non-seizure CNS manifestations. Detailed clinical examinationalong with of Neurocysticercosis (NCC) and tuberculoma diagnosis were made using CECT scan. IBM SPSS version 22 was used for statistical analysis. **Results:** Majority of the children were above 5 years of age (79.16%) and presented with single lesion (77.08%). Majority were diagnosed with 30 (62.50%) NCC, followed by tuberculoma 6 (12.50%), and 12 (25%) had unknown aetiology. Seizures alone were observed in 38 (79.16%) cases, 9 (18.74%) had seizures and non-epileptic manifestations like episodic headache, focal deficit and raised intracranial tension. All the tuberculoma patients had decreased edema on follow-up andmost of the NCC cases (32.14%) had calcifications.**Conclusion:** NCC is the most common non-seizure CNS manifestations presenting with a single ring-enhancing CT lesion among children. Differentiating between all these ring-enhancing lesions is essential as misdiagnoses can cause grave danger to life.

Keywords: NCC, Tuberculoma, Seizures, Ring enhancing lesions, CECT

Introduction

A seizure is a widespread problem encountered in the pediatric population. Worldwide 65 million people have a seizure at least once in their lifetime, among which 30% occur in children. Neuroimaging forchildren is done only for selective indications such as partial seizure, unprovoked seizure, late new-onset seizure, and trauma. [1]Single ring-enhancing computed tomography lesions are commonly seen in young patients presenting with acute symptomatic seizures.It is an abnormal radiologic sign-on neuroimaging appearing as hypo-dense or iso-dense disc or target lesion with perifocal oedema. [2]Clinical presentation in a child with seizure and radiologic ring-enhancing lesion includesmonoparesis, hemiparesis, severe headache, ataxia, raised intracranial tension and cranial nerve palsy.[3] The exact pathological nature of ring-enhancing lesions has not been verified as biopsy of such lesions are carried out only in isolated cases. Various presumptive diagnoses such as tubercular lesions and neurocysticercosis are identified as the two most common aetiologies.[3]Tubercular lesions are a tumour likemass of typical tubercular granulomatous disease, which produces symptoms of a space-occupying lesion.[4]In a study by Bhargava et al[2], found thatlesions disappeared after treating with anti-tuberculosis drugsin patients withring-enhancing lesions.[5]Sethi et al. reported that these lesions showed a spontaneous resolution, and they were popularly termed as “disappearing lesions".[6]Neurocysticercosis (NCC) of the central nervous system (CNS) is caused by the larval stage of the pork tapeworm *Taenia solium*. Many cases of solitary enhancing lesion caused by NCC are seronegative because the parasite is already dead or because a single parasite does not elicit a strong antibody response. Hence, these aetiologies pose a significant diagnostic challenge.[7]It has been observed that many varieties of non-epileptic manifestations other than seizure are presented with single ring-enhancing lesions on the CT scan. Until date, no study has been conducted on the clinical presentations of ring-enhancing lesions with a varied etiological diagnosis. Hence, the objectives of the present study are:1) to evaluate the clinical profile and incidence of ring-enhancing lesions in contrast-enhanced computerized tomography (CECT) scan of the brain in children between 0 and 12 years of age group presenting with seizures focal neurological deficits and other non-seizure CNS manifestations; and 2) to determine the incidence of neurocysticercosis, tuberculoma and GTCS manifesting in CECT brain scan.

Material and Methods

A cross-sectional study was conducted in the department of paediatrics at a tertiary medical hospital from June 2019 to September 2020. A total of 48 cases were included in the study by convivence sampling.All children in the age group 0 to 12 years with a history of seizures (GTCS, simple partial (S.P), complex partial (C.P), and simple partial with secondary generalization (S.P+S.G)), focal neurological deficits,and other non -seizure CNS manifestations were included in the study. All children born with neural tube defects,and children with pre-existing neurological disorders (cerebral palsy, hydrocephalus, post-trauma cases) were excluded from the study. The study was approved by the institutional ethics

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review board and all patients who have given informed written consent were enrolled in the study.

Methodology

Detailed clinical examination and investigations such as complete blood picture (CBP), erythrocyte sedimentation rate (ESR), Mantoux test (Mx Test),chest x-ray(CXR)were obtained.A CECT brain scan was done in all the cases.Neurocysticercosis was assessed using Diagnostic Criteria and Degree of Diagnostic Certainty for Human Neurocysticercosis proposed by Del Brutt. Those patients who met the criterium of "definitive diagnosis" were identifies as neurocysticercosis cases. The diagnosis of tuberculoma was confirmed on CT scan when the patient had following clinical findings: lesion size > 20 mm, irregular borders, midline shift, plain CT-isodenselesion, contrast enhancement of lesion, moderate to severe perifocal edema and basal meningeal enhancement.

Follow-Up: All patients were treated symptomatically. The patients with seizures started with antiepileptic drugs. The patients having tuberculoma were put on anti-tubercular therapy with steroids. The patients with neurocysticercosis were treated with albendazole and prednisolone for three days. Repeat CT scan was advised after 12 – 20 weeks of initial CT scan.Various types of convolutions and aetiologies were considered as primary outcome variables. Age groups and clinical factors were considered as other explanatory variables. Categorical outcomes were compared between study groups using the Chi square test /Fisher's Exact test. A p value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

Results

A total of 48 subjects were included in the final analysis.A total of 48 children with ring-enhancing lesions were studied in which 19 (39.58%) were males and 29(60.42%) were females.Majority of the children were above 5 years of age (79.16%) and presented with single lesion (77.08%). Most ofthe patients presented with seizures alone 38(79.16%), 9 patients(18.74%) had seizures and non-epileptic manifestations like episodic headache, focal deficit and raised intracranial tension (ICT) and only 1(2.08%) subject had episodic headache (2.08%). The NCC diagnosis was made in 30 (62.50%) cases, tuberculoma was confirmed in 6(12.50%) cases, and 12(25%) cases had neither NCC nor tuberculoma, hence were included in the undetermined group. (Table 1)The study shows that CPS is the most common type of seizure presentation (34.04%) in 5 to 12-year age group, followed by GTCS (21.27%). However, simple partial with secondary generalization and CP were more common (6.38%) in the >2 – 5-year age group. The youngest subject was a 2-year-old who presented with GTCS. In NCC, the most common presentation was complex partial seizures (50.00%). Likewise, in tuberculoma cases, complex partial seizures, GTCS, the simple partial seizures were observed(33.33%). (Table 2)Seizures (83.33%) were the most common manifestations among subjects diagnosed with NCC. The clinical features observed in NCC subjects were headache, focal neurological deficit, raised ICT. Single lesions were reported in 19 (51.35%) of NCC, and 6 (16.22%) oftuberculoma, and 12 (32.43%) with undetermined aetiology. Majority of the cases in 9 to 12 years age group were diagnosed with NCC (60.88%), followed by undetermined etiology (34.78%). There were no significant difference in the incidence of NCC and tuberculomawith regard to age and gender. (Table 3)Only 28 cases (58.33%) came for follow up, of which 4 had Tuberculoma, 20 had NCC and 4 had unknown aetiology.All the tuberculoma patients had decreased oedemaon follow-up. Majority of NCCcases (32.14%)had calcifications. All four cases with multiple lesions received eight days of albendazole with steroids before getting discharged. Among 16 patients with single lesions, follow up CT scan showed 50% disappearance of the lesions. (Table 4)

Table 1: Summary of baseline characteristics (N=48)

Baseline characteristics	Summary
Age group	
0 – 2 years	2 (4.16%)
>2 – 5 years	8 (16.66%)
>5 – 12 years	38 (79.16%)
Gender	
Males	19 (39.58%)
Females	29 (60.42%)
Clinical Presentations	
Seizures alone	38 (79.16%)
Seizures with raised ICT	7 (14.60%)
Seizures with Focal Deficit	1 (2.08%)
Seizures raised ICT and Focal Deficit	1 (2.08%)
Episodic Headache, Focal deficits, Raised ICT	1 (2.08%)
No. of lesions in CT scan	
Single	37 (77.08%)
Two Lesions	9 (18.75%)
More than two Lesions	2 (4.16%)
Etiology of the ring-enhancing lesion	
Neurocysticercosis (NCC)	30 (62.50%)
Tuberculoma	6 (12.50%)
Undetermined	12 (25.00%)

Table 2: Types of convulsions in various age groups &etiology (N=48)

	Generalized tonic-clonic seizure (GTCS) n (%)	Simple partial (SP) n (%)	Complex partial (CP) n (%)	Simple partial with secondary generalization n (%)	Subtle seizures n (%)
Total	**14**	**8**	**19**	**6**	**-**
Age groups (N=48)					
0 – 2 years	2 (4.25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
>2 – 5 years	2 (4.25%)	0 (0%)	3(6.38%)	3(6.38%)	0 (0%)

>5 – 12 years	10 (21.27%)	8 (17.02)	16 (34.04%)	3 (6.38%)	0 (0%)
Etiology of ring enhancing lesion					
NCC	8 (26.66%)	3 (10.00%)	15 (50%)	3 (10%)	0 (0%)
Tuberculoma	2 (33.33%)	2 (33.33%)	2 (33.33%)	-	0 (0%)
Undetermined	4 (33.33%)	3 (25%)	2 (16.66%)	3 (25%)	0 (0%)

No statistical test was applied-due to 0 subjects in the cell

Table 3: Comparison of demographic and clinical parameters across etiology of the ring-enhancing lesion (N=48)

	No. of Cases	NCC (N=29)	Tuberculoma (N=6)	Undetermined (N=12)	P value
Clinical Presentation					
Seizure Alone	38	25(83.33)	2(33.33)	11(91.66)	
Seizures with raised ICT	7	3 (10.00)	3(50.00)	1(8.33)	
Seizures with Focal Neurological Deficit	1	1(3.33)	0 (0%)	0 (0%)	
Seizures with Focal Neurological Deficits and raised ICT	1	0 (0%)	1(16.66)	0 (0%)	*
Clinical Features					
Headache, Focal neurological deficit, Raised ICT	1	1(3.33)	0 (0%)	0 (0%)	
Number of Lesions					
Single	37	19 (51.35)	6 (16.21)	12 (32.43)	
2 Lesions	9	9(100.00)	0 (0%)	0 (0%)	*
More than 2	2	2 (100.00)	0 (0%)	0 (0%)	
Age (Years)					
0 – 4	7	3 (42.85)	1 (14.28)	3 (42.85)	
5 – 8	18	13 (72.22)	4 (22.22)	1 (5.55)	0.099
9 -12	23	14 (60.88)	1 (4.34)	8 (34.78)	
Gender					
Female	29	18 (62.06)	4 (13.99)	7 (24.13)	0.094
Male	19	12 (63.15)	2 (10.52)	5 (26.31)	1

**** No statistical test was applied-due to 0 subjects in the cell***

Table 4: Comparison of the outcome at discharge across etiology of the ring-enhancing lesion (N= 28)

Outcome at discharge	Tuberculoma(4) n (%)	NCC (20) n (%)		Undetermined(4) n (%)	Total
		Single(16)	Multiple(4)		
No Change	0 (0%)	1(6.25%)	1(25%)	0 (0%)	2(7.14%)
Decreased Edema Size	4 (100%)	1(6.25%)	0 (0%)	1 (25%)	6(21.42%)
Calcification	0 (0%)	6(37.50%)	3(75%)	0 (0%)	9(32.14%)
Disappeared	0 (0%)	8(50%)	0 (0%)	3 (75%)	11(39.28%)

**** No statistical test was applied-due to 0 subjects in the cell***

Discussion

Brain ring-enhancing lesions remains to be a diagnostic challenge as they have a wide range of differential diagnoses.In the present study, neurocysticercosis30 (62.50%)is the main etiological factor for single enhanced lesions.Majority of the participants had complex partial seizures 38 (79.16%).Most of the children, 38 (79.16%), were in the age group of 5 to 12 years in the study. Our study is in line with the study by Adhikari et al where maximum cases of seizures were seen in an age group of 11-15 years. Another study by Bhaskar et al. among seizure 50 cases,most children were in the age group of 6 to 10 yrs. In the present study,females were primarily affected with 29 (60.42%) single small enhancing CT lesions. Among females, 18 (62.06%) had neurocysticercosis, 4 (13.99%) had tuberculoma, and 7 (24.13%) had unknown aetiology. In a study by R.K Garg, there were 61.53% males, whereas Goulatia et al. reported 57.58% of females,similar to the present study. [2,8]In the current study, the most common presentation of the ring-enhancing lesion wascomplex partial seizures 19(39.5%), followed by generalized tonic-clonic seizure (GTCS)14(29.1%), simple partial seizures 8 (16.6%), simple partial with secondary generalization 6(12.5%). Complex partial seizures were observed in 50% of the cases with neurocysticercosis. Our study corroborates with the study conducted by Singh et al. who reported complex partial seizures as the most common seizures in their study (53.27%).[9] Previous studies by Kumar et al[4],and Thakur et al[10] also found that partial seizures were the most common type of seizures. However, in a study by Sanchez[11]et al. have shown that GTCS as the most common seizure (63.8%) than the focal seizures.Neurocysticercosis 30 (62.50%)is the main etiological factor for single enhanced lesions, followed by 6 (12.50%) tuberculoma, 12 (25.00%) with unknown aetiology.Rajashekar et al. reported the incidence of NCC as 49%, tuberculoma as 11.8% and 23.5% had undetermined parasitic granulomas in their study.[12] R.K. Garg reported incidence of NCC as 80% among those presented with seizures with single enhancing lesions. [2] Mathew J Chandy et al. in their study of small single-enhancing lesions, the diagnosis was done by biopsy and found that 28% had NCC.[13] In developing countries, most of these single-enhanced lesions are caused by NCC or tuberculosis with differential diagnoses being challenging to ascertain. This is because the clinical and imaging features are similar. Common characteristics of cysticerci are round in shape, 20 mm (or smaller) in size, and with ring enhancement or visible scolex. Tuberculomas, by contrast, are usually irregularly shaped, solid, and greater than 20 mm in size. They are often associated with severe perifocal edema and focal neurological deficits.In the present study, one patient with neurocysticercosis presented with headache, focal neurological deficit, and raised ICT. In a study by Arsenic et al., presented that 12.15% had an episodic headache with the focal deficit.[14] In a study by Wendy G. Mitchell, onlyone patient, had a headache with visual symptoms, and eight patients had seizures with

associated focal deficits. None of the patients in their study had raised ICT. The reason can be explained that theinflammatory changes of the lesions and surrounding brain parenchyma could extend into intracranial blood vessels and meninges as a result of the blood-brain barrier disruption. In our study, the NCC lesions had decreased oedema 1(6.25%), calcifications 6(37.50%)and 8(50%) had disappeared lesion. Chopra et al. highlighted that childhood NCC hada low incidence of calcification and explained that it requires almost ten years for calcification.[15]However, in the study by V Karla et al., none of their patients showed calcification in follow up[16] In contrast, Percy et al. found that 80% of childhood NCC were calcified.[17]The main drawback of the study was a limited sample size, which hampers the generalisability of the results. The study had not reported about the antiepileptic drug management (AED) of such cases. Future research on magnetic resonance spectroscopy (MRS) and diffusion-weighted images (DWI)can help in identifying the aetiology and prevents delay in treatment initiation.

Conclusion

NCC is the most common non-seizure CNS manifestations presenting with asingle ring-enhancing CT lesion among children. The differential diagnosis of non- epileptic neurological syndromes such as NCC and tuberculosis should be considered among Indian patients for appropriate treatment plan. Differentiating between all these ring-enhancing lesions is essential as misdiagnoses can cause grave danger to life.

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