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Single small enhancing computed tomographic (CT) lesions in Indian patients with new-onset seizures. A prospective follow-up in 75 patients

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This study was planned to observe the clinical and radiological course of single small enhancing CT lesions in Indian patients presenting with new-onset-seizures. In this study, 75 patients with new-onset seizures and a single enhancing CT lesion were prospectively followed up for 1 year. All patients fulfilled the criteria of cysticercus granuloma. The repeat CT scans were performed 2 months after the first CT scan. Antiepileptic drug therapy was the only form of treatment given. The majority of patients were below 20 years of age. Simple partial seizure, with or without secondary generalization, was the commonest type of seizure encountered in these patients. In follow-up CT scans 84% of patients showed either disappearance or regression in the size of lesion. The proportion of patients showing complete disappearance of CT lesions was 0.73 (95% CI, 0.61–0.80). In 11 (15%) patients the lesions were calcified. In nine patients, in whom the lesion had persisted or regressed, another follow-up CT scan (6 months after the second scan) revealed either complete disappearance or calcification of the lesions. The majority (86.6%) of patients remained seizure free for 1 year after starting antiepileptic drugs. Ten patients experienced seizure recurrences within the first month of therapy. The proportion of patients who remained seizure free was 0.86 (95% CI, 0.76–0.92). Four patients experienced seizure recurrence even after complete disappearance of CT lesions. In the majority of patients the lesions disappeared spontaneously and in a few the lesions calcified; hence these patients did not require anticysticercal therapy. Antiepileptic therapy was helpful in controlling further recurrences of seizures in most of the patients. A few patients experienced seizures even after disappearance of CT lesions.

Key words: cysticercosis; neurocysticercosis, epilepsy, tuberculoma granuloma, computed tomography.

INTRODUCTION

Single enhancing CT lesions (Fig. 1) are a common imaging abnormality in Indian patients with new-onset seizures[1–4]. Histopathological studies[5] suggest that single enhancing CT lesions, in the majority of patients, represent dying cysticercus larva. Another, less common, cause of these lesions are tuberculomas. Several retrospective studies have observed that these lesions resolve spontaneously[3,6]. In several other studies[7–9] these lesions have been treated with anticysticercal drugs, however, with conflicting results. The objective of the present study was to prospectively observe the clinical and radiological course in these patients.

MATERIALS AND METHODS

This prospective study included 75 consecutive patients of new-onset seizure disorder with a contrast CT scan showing a ring/disc-enhancing lesion. These patients were attending Neurology/Medicine outdoor clinics of Sir Sunder Lal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, between July 1997 and February 1999. All these patients presented within 7 days of onset of seizure disorder and were immediately (within 48 hours) subjected to plain and contrast CT scans. The patients selected fulfilled the clinical and radiological criteria suggestive of cysticercus granuloma[10] (Table 1).

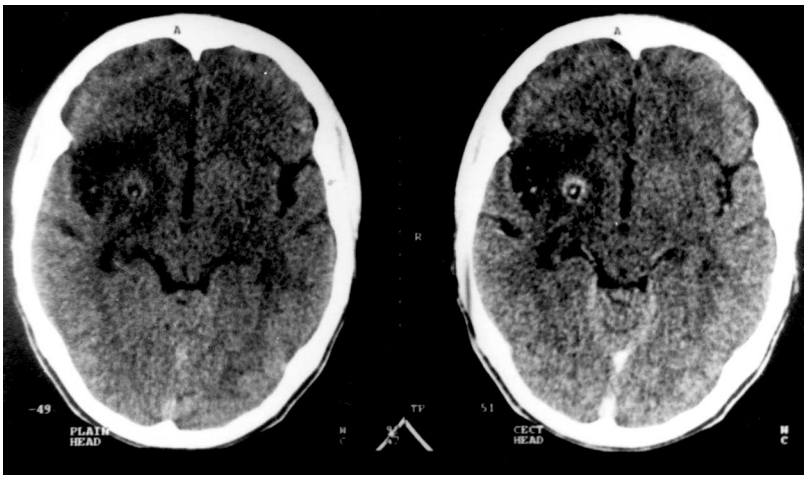

Fig. 1: Plain and contrast-enhanced cranial computed tomography showing a ring enhancing CT lesion along with perifocal oedema.

Table 1: Diagnostic criteria for cysticercus granuloma[10].

Clinical criteria
1. Seizures (partial or generalized) should be the initial symptom.
2. There should no features of persistent raised intracranial pressure.
3. There should be no history of progressive neurological deficit.
4. There should be no evidence of active systemic disease.
CT criteria
1. CT scan should only show a solitary, contrast-enhancing lesion.
2. The lesion should measure less than 20 mm in maximal dimension.
3. Oedema may or may not be present, but is not severe enough to produce a shift of midline structures.

PATIENT'S EVALUATION

Each selected patient was subjected to a detailed neurological examination. An eyewitness account of seizure episodes was obtained either from a relative or a friend. Seizures were classified as per the International League Against Epilepsy Classification of seizure types. In each patient, routine haematological and biochemical parameters were obtained. In addition, enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus (e.g. toxoplasmosis) and chest X-ray (e.g. secondary metastasis) were performed to exclude other possible causes of similar CT morphology. A 21-channel electroencephalography was also performed in each patient.

In 60 patients *in vitro* qualitative determinations of anti *Taenia solium* antibodies in serum were performed by using solid- phase ELISA employing plastic wells coated with *Taenia solium* antigen. Forty healthy age matched controls were also subjected to ELISA for *Taenia solium* antibodies. The results were classified as positive and negative. Positive specimens yielded optical density absorbency readings greater than 1.404 at the 450 nm wavelength of the photometric well reader (package insert).

TREATMENT AND FOLLOW-UP

In all patients antiepileptic drugs were started immediately. Patients were given monotherapy, and the antiepileptic drug administered was either carbamazepine or phenytoin (Table 1). Initial drug dosage was based on body weights. In situations of seizure recurrence and/or respective antiepileptic drug toxicity, appropriate dosage adjustments were performed. Therapeutic drug monitoring of antiepileptic drugs was not done. None of the patients was treated with anticysticercal treatment.

Patients were followed up at fortnightly intervals for the first 2 months, and then, at intervals of 3 months, patients were prospectively followed up for a total of 1 year. Follow-up CT scans were performed 8 weeks after the initial CT scan. Visual analyses of CT scans were performed by an independent observer (a radiologist who was not familiar with the clinical status of the patients). The lesion was considered 'persisting' if no change in the CT appearance of the lesion was noted. It was considered as 'regressing' if, on visual analysis, the amount of cerebral oedema had reduced and/or the morphology of the lesion had altered. The 'disappearance' of the lesion was considered when the follow-up CT scan was reported as normal. The lesions were considered 'calcified' when a hyperdense lesion was seen on a plain CT scan at the same place where the original enhancing lesion was situated. In patients in whom the enhancing CT lesions did not disappear at 2 months, another follow- up scan was obtained after 6 months of further follow-up.

Table 2: Clinical characteristics of patients with single enhancing CT lesions and seizures ($n = 75$).

1.	Age (year)	
	Mean	15.46 ± 7.73
	< 10	20 (26.6%)
	10–20	45 (60.0%)
	> 20	10 (13.3%)
2.	Sex	
	Male	45 (60.0%)
	Female	30 (40.0%)
3.	Mean duration of illness (days) (mean $\pm$ SD)	8 ± 3.5
4.	Seizure patterns	
	Single seizure	5 (6.6%)
	Seizures in clusters	57 (76.0%)
	Recurrent seizures	10 (13.3%)
	Status epilepticus	3 (4.0%)
5.	Todd's palsy	6 (8.0%)
6.	Mean of number of seizures before start of treatment (mean $\pm$ SD)	3.9 ± 3.5
7.	Antiepileptic drugs given as monotherapy	
	Carbamazepine	61 (81.3%)
	Phenytoin	14 (18.6%)
8.	Electroencephalography	
	Normal	57 (76.0%)
	Generalized slowing	4 (5.3%)
	Focal slowing	10 (13.3%)
	Focal spikes	4 (5.3%)

STATISTICAL ANALYSIS

The follow-up observations were also presented in proportions and one sample *z*-test for proportion was used to analyse the level of significance. Wherever required the data were also analysed by using a chi-squared test, and a P value < 0.01 was considered significant.

RESULTS

There were 75 patients who fulfilled the inclusion criteria during the study period. The majority of patients (86.6%) were 20 or less years of age. The male and female ratio was 3 : 2 (Table 2). Simple partial seizures with or without secondary generalization were the commonest type of seizures (69.3%) associated with single enhancing CT lesions (Table 3). In 76% of the patients seizures occurred in clusters (multiple seizures within 24 hours), only 10 patients reported recurrent seizures before the start of antiepileptic therapy (Table 2). Routine electroencephalography was found to be unrewarding and was normal in 76% of the patients. A significantly higher number of patients ($P < 0.01$) had a positive ELISA test for anti *Taenia solium* antibodies in comparison to controls. The sensitivity and specificity of the ELISA test was 60% and 72.5%, respectively (Table 4).

Table 3: Various seizure types seen in patients with single enhancing CT lesions ($n = 75$).

Seizure types	No.	%
Simple partial	25	33.3
Simple partial with secondary generalization	27	36.0
Complex partial	5	6.6
Complex partial with secondary generalization	1	1.3
Generalized tonic–clonic	17	22.6

Table 4: Positive ELISA test for anti *Taenia solium* antibodies in patients with seizures and single enhancing CT lesions, and controls.

	No.	%	
Patients ($n = 60$)	36	60.0	
			($x^2 = 15.35$, $P \leq 0.01$)
Controls ($n = 40$)	11	27.5	

In the first CT scans, in approximately 10.6% of the patients, an enhancing eccentric dot-like structure suggestive of scolex of cysticercus larva was also seen inside the ring lesions (Fig. 1). In 9.3% of the patients, the lesions were disc enhancing.

Table 5: Incidence of various imaging abnormalities in patients with single enhancing CT lesion ($n = 75$).

	No.	%
Type of lesion		
A. Ring enhancing	68	90.6
without eccentric dot	60	80.0
with eccentric dot	8	10.6
B. Disk enhancing	7	9.3
Amount of oedema		
Absent	27	36.0
Mild	39	52.0
Moderate	7	9.3
Severe	2	2.6
Location of lesions		
Frontal	9	12.0
Fronto-parietal	5	6.6
Parietal	42	56.0
Parieto-occipital	11	14.6
Occipital	4	5.3
Temporal	2	2.6
Parasagittal	2	2.6

Single enhancing CT lesions were more common in posterior parietal regions. In 76% of patients these lesions were in parietal and occipital regions. In two patients lesions were present in the parasagittal region, both patients had post-ictal Todd's palsy, weakness was more marked in the lower limbs of these patients. Approximately half of the patients had mild oedema (restricted to the cerebral lobe involved). Only

two patients had severe cerebral oedema (producing midline shift). Seven (9.3%) patients had moderate oedema (oedema involving the adjacent cerebral lobe) (Table 5).

Follow-up CT scans performed 2 months after the initial CT scan showed either complete disappearance (Fig. 2) or regression in the size of the lesions in the majority (84%) of patients. The proportion of patients showing complete disappearance of CT lesions (follow-up CT scans were normal) was 0.73 (95% CI, 0.61–0.82, $P = < 0.01$). Lesions were calcified in 11 (14.6%) patients (Fig. 3). In only one patient the lesion remained unchanged (Table 6). Of nine patients in whom the lesion had persisted, or regressed, a repeat CT scan 6 months later showed complete disappearance in six patients and calcification of the lesion in three patients.

Table 6: Changes seen in follow-up CT scans after two months ($n = 75$).

Changes in lesions	No.	%
A. Disappeared[a]	55	73.3 ($P \leq 0.01$)
B. Not disappeared[b]	20	26.6
calcified	11	14.6
regressed	8	10.6
unchanged	1	1.3

[a] Normal follow-up CT scan; [b] abnormal follow-up CT scan.

Table 7: Seizure recurrence in patients with single enhancing CT lesion after starting antiepileptic drugs during the 1 year follow-up ($n = 75$).

	No.	%
A. Patients with no recurrence	65	86.6 ($P = < 0.01$)
B. Patients with recurrence	10	13.3
No. of recurrences		
1–3	7	70.0
4–6	2	20.0
> 6	1	10.0
Time of first recurrence		
During first month	8	80.0
After 6 months	2	20.0
Correlation with CT findings		
Normal CT	4	40.0
Abnormal CT[a]	6	60.0

[a] Persistence or regression or calcification of CT lesions.

The proportion of patients who did not experience another seizure after starting antiepileptic therapy until completion of 1 year of treatment was 0.86 (95% CI, 0.76–0.92, $P = < 0.01$). Only 10 patients experienced seizure recurrence during the follow-up period of 1 year. Most of the patients (who had seizure recurrence) experienced their first recurrence within 1 month of follow-up. Four patients experienced seizure recurrence despite complete disappearance of CT lesions (Table 7).

DISCUSSION

In this study, we observed that single enhancing CT lesions frequently affected younger patients; these patients presented as acute new-onset seizure disorder. Simple partial seizures with or without secondary generalization are the commonest seizure type seen in these patients irrespective of location of CT lesions. We also observed that the seizures tended to occur in clusters.

In the brain, a cysticercal cyst passes through four stages in its natural evolution. In the ‘vesicular’ stage the viable cyst contains invaginated larva bathed in translucent fluid. The cyst is encapsulated and there is little tissue reaction. On CT the ‘vesicular’ form of cysticercosis appears as a non-enhancing lesion without oedema. Eventually, in circumscribed and hypodense response to the host’s immune reaction against the parasite the cyst shows hyaline degeneration and early mineralization. The cysts fluid changes to whitish, jelly-like material and the capsular membrane thickens. Inflammatory changes develop in the cyst wall and surrounding brain parenchyma. This ‘colloidal’ stage produces on CT a ring-enhancing lesion, initially with perilesional vesogenic oedema. As the lesion continues to regress, the cyst size is reduced and the cyst membrane further thickens. The cyst contents are transformed into coarse granules, due to mineralization with calcium salt. This is the ‘granular-nodular’ stage, which is seen as a disc-enhancing lesion in CT scans. Ultimately the cyst becomes completely mineralized—the ‘calcified stage’—and a nodular hyperdense lesion is seen in non-contrast CT scans[11,12]. Patients having a parenchymal cysticercal lesion become symptomatic when the cyst becomes acutely inflamed and this results in seizure clusters and frequent early recurrences. With resolution of inflammation in and around cystic lesions, the possibility of seizure recurrence also decreases. Murthy and Subha Reddy[13] in their recent article observed that in the majority of patients seizures do not recur, even after withdrawing the antiepileptic drug, after the lesion has disappeared. In our study we could not confirm this observation. However, four patients experienced seizure recurrence even after complete resolution of the CT lesions. Possibly, focal cerebral gliosis, as a result of healing the inflammatory lesion, can also have epileptogenic potential. In a retrospective study by Murthy *et al.*[14] similar findings were observed. Seizures did not recur in 162 (61.8%) of 262 patients with single enhancing CT lesions after initiation of antiepileptic therapy. Seventy-four patients continued to have seizures for some time (median, 2 months) before remission. In

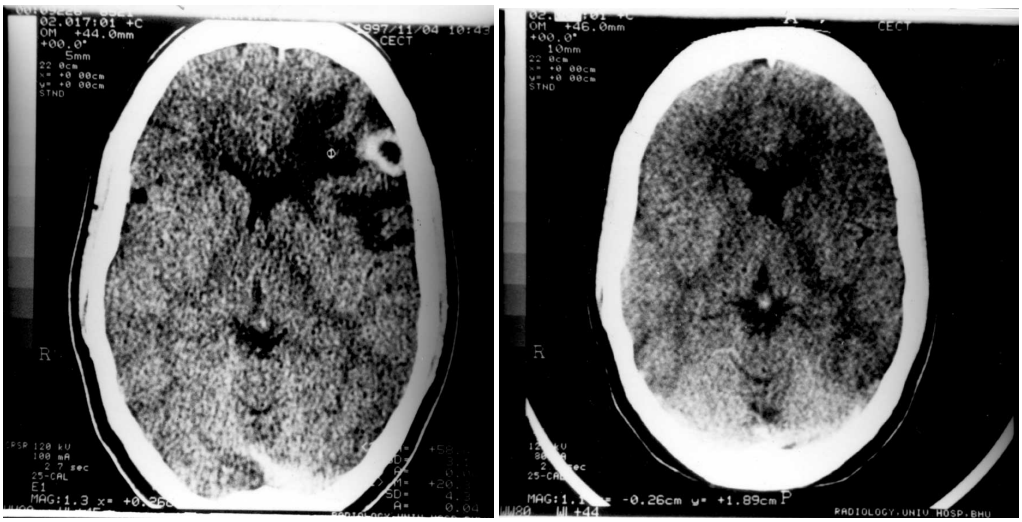

Fig. 2: (*a*) A ring enhancing CT lesion with eccentric scolex; (*b*) follow-up scan after 2 months showing complete disappearance of the lesion and oedema.

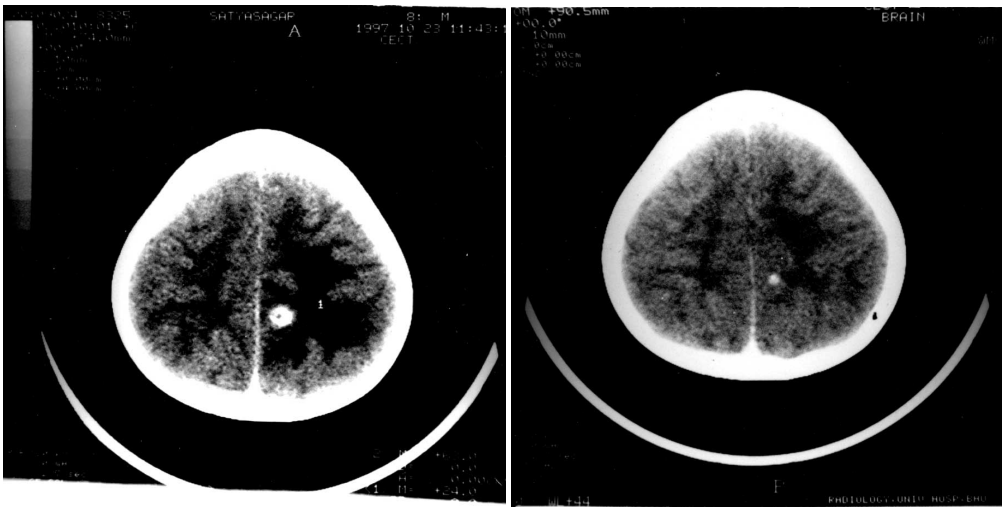

Fig. 3: (*a*) Ring enhancing CT lesion; (*b*) plain CT scan after 2 months showing calcification of the same lesion.

the remaining 26 (10%) patients seizures continued to recur (median, 8 months), and seizure remission was achieved following cysticercal therapy. Antiepileptic drugs were discontinued in 206 patients after a seizure-free period of $\geq$2 years. In all these patients the CT lesions had resolved on follow-up CT scans. In this study[14] only two patients experienced recurrence of seizures. In one of these patients, the repeat CT scan showed a gliotic scar at the site of previous lesion. The mean follow-up period was 31.4 months (range 14–73 months).

Initially tuberculomas were considered as a possible cause of single enhancing CT lesions[1], at present it is believed that tuberculosis is the cause only in a minority of patients[10]. Moreover, tuberculomas are very unlikely to resolve spontaneously.

There is enough evidence to suggest that anti-cysticercal drugs (praziquantel and albendazole) are of value in the management of active parenchymal cerebral cysticercosis[12]. However, there are conflicting views[7,9] about the role of anticysticercal drugs in the management of single enhancing CT lesions. Our study clearly suggests that in the majority of patients these lesions disappear spontaneously within 2 months of the onset of seizure disorder. Therefore, these patients do not require administration of anticysticercal drugs.

Rajshekhar recommended anticysticercal drugs for lesions that persisted in follow-up CT scans even after 12 weeks. Our study further suggests that even these patients do not require any treatment because many of the persisting lesions (if they do not disappear), as per Escobar's stages of natural evolution, are destined to become calcified.

In conclusion, the observations from our study suggest that single enhancing CT lesions in patients with new-onset seizures are benign in nature and tend to disappear spontaneously within 2 months. Antiepileptic monotherapy is effective in controlling the seizures and recurrences are infrequent. A few patients may experience seizure recurrence even after disappearance of the CT lesions.

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