## A STUDY ON THE CLINICO-RADIOLOGICAL PROFILE AND OUTCOME OF SINGLE SMALL ENHANCING LESIONS OF THE BRAIN

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ABSTRACT

### BACKGROUND

Single small enhancing computed tomography lesion is a worldwide problem, especially in tropical countries endemic for cysticercosis. It is a clinico-radiological entity & is the most common radiological abnormality seen in patients with acute onset seizures in India.

### MATERIALS AND METHODS

This study included 93 patients who attended the Neurology OPD in King George Hospital, Visakhapatnam, between February 2012 and October 2013 with new onset seizures and having a single small enhancing lesion in the brain on imaging <20 mm size. Imaging of the brain was done in all patients which included a computed tomography (CT) brain with contrast or magnetic resonance imaging (MRI) brain with contrast. The characteristics of the lesions were noted in detail.

### RESULTS

Of the 93 patients, 49 (52.68%) were males and 44.37 patients (39.78%) were in the age group of 11-20. Partial seizures with or without secondary generalization was the commonest type of seizure in 70 (75.3%) patients. 83 (89.24%) patients were diagnosed to have either definite or probable Neurocysticercosis, whereas 9 patients were diagnosed to have tuberculoma based on the clinical and imaging findings. Mean size of lesion was 10.69 mm  $\pm$  3.07. 53 (56.98%) patients had a lesion larger than 10 mm. The 9 tuberculomas had a mean size of 15 mm  $\pm$  3.47. 8 out of 9 tuberculomas were larger than 10 mm. 7 (77.7%) of the 9 tuberculomas and the probable metastasis were surrounded by moderate perilesional oedema. T2 hypointensity on MRI was seen in 6 (66.6%) tuberculomas. Thick, irregular wall was present surrounding all tuberculomas. In the 82 patients who are followed up for the subsequent visits, 63 (76.82%) patients had no recurrence of seizures during the follow up period of 3 months. 19 (23.17%) patients reported recurrence of seizure. 12 (63.15%) patients had first recurrence of seizure in the first month.

### CONCLUSION

Majority of the SSECTL are NCC & tuberculomas. Majority of the NCC are <10 mm in size with minimal perilesional oedema whereas majority of tuberculomas >10 mm with significant perilesional oedema and T2 central hypointensity on MRI. Both NCC and Tuberculomas were common in parietal lobes. The recurrence of seizures is less common in the patients with SSECTL, especially after starting AED.

### **KEYWORDS**

SSECTL, Single Solitary Enhancing Lesion, NCC, Tuberculoma, New Onset Seizures.

**HOW TO CITE THIS ARTICLE:** Gopi S, Rekha BK. A study on the clinico-radiological profile and outcome of single small enhancing lesions of the brain. J. Evid. Based Med. Healthc. 2018; 5(5), 397-403. DOI: 10.18410/jebmh/2018/81

### BACKGROUND

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Single small enhancing computed tomography lesion is a worldwide problem, especially in tropical countries endemic for cysticercosis. It is a clinico-radiological entity & is the most common radiological abnormality seen in patients with acute onset seizures in India. These lesions are reported

Financial or Other, Competing Interest: None. Submission 01-01-2018, Peer Review 12-01-2018, Acceptance 19-01-2018, Published 23-01-2018. Corresponding Author: Dr. S. Gopi, Haritha Saptagiri Plot, Opp. KGH Opp. Gate Visakhapatnam, E-mail: drgopiseepana@yahoo.co.in DOI: 10.18410/jebmh/2018/81



Seizures in association with single small enhancing CT/MRI lesions seem to be a "benign localization related epileptic syndrome" expressed in a subset of Indians genetically predisposed to seizures.

Various presumptive diagnoses such as tuberculoma, cysticercosis, neoplastic lesions, sarcoidosis, viral encephalitis, microabscesses, post ictal enhancement & vascular lesions have been considered as differential of SSECTL. The main controversy is whether these lesions are tubercular or neurocysticercal in origin.

### Aims of the Study-

1. To study the clinical and radiological profile of patients having Small, Single, Enhancing lesions of the brain with new onset seizures.

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2. To study the clinical and radiological outcome of these lesions.

## MATERIALS AND METHODS

This study included 93 patients who attended the Neurology OPD in King George Hospital, Visakhapatnam, between February 2012 and October 2013 with complaints of new onset seizures and having a single small enhancing lesion in the brain on imaging.

**Inclusion Criteria-** Patients having Single enhancing lesion on neuro imaging measuring less than 20 mm in size with new onset seizures.

## **Exclusion Criteria**

- Patients having multiple lesions on imaging
- Single enhancing lesions measuring more than 20 mm in size.
- Patients with contra indication for contrast and MRI imaging.

## **Evaluation of the Patient**

A detailed clinical history including past and family history was noted from each selected patient. 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. (According to Commission on Classification and Terminology of ILAE 1981). All the patients were subjected to a thorough general and neurological examination in view of different aetiologies for such a presentation and the details were noted in the study proforma. Informed consent was obtained from patients or their adult guardians in case of children.

**Investigations-** In each patient a complete haemogram with erythrocyte sedimentation rate (ESR), and routine biochemical tests were done. In addition, enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus and ancillary tests like chest X-ray and ultrasound abdomen were done in all.

Imaging of the brain was done in all patients which included a computed tomography (CT) brain with contrast or magnetic resonance imaging (MRI) brain with contrast. The characteristics of the lesions were noted in detail.

## **Diagnosis and Treatment-**

**Diagnosis of NCC**- Patients were diagnosed to have definite or probable neurocysticercosis if they fulfil the Revised Diagnostic Criteria for Neurocysticercosis (Del Brutto et al).

However, histologic demonstration of the parasite from biopsy of a brain lesion was not done, as this is an invasive procedure. Also, serum enzyme-linked immunoelectrotransfer blot (EITB) and cerebrospinal fluid enzyme-linked immunosorbent assay (CSF ELISA) test were not done due to non-availability of these tests in the institute and non-affordability of the patients. Thus, the diagnosis was based on clinical and radiological features.

These patients were treated with Albendazole 15 mg/kg/day for 1 week (as per Consensus guidelines for the treatment of NCC in view of reduced risk for seizure recurrence.

Parenchymal neurocysticercosis	
Vesicular cysts	
Single	Albendazole 15 mg/kg/day for 1 week, steroids used only if side-effects
	occur; or praziquantel 100 mg/kg in three equal doses
Moderate infections	Albendazole 15 mg/kg/day for 1 week, with simultaneous use of steroids.
Heavy infections (100 or more cysts)	Albendazole 15 mg/kg/day for 1 week with high doses of steroids
Degenerating (colloidal) cysts	
Single lesions	Albendazole 15 mg/kg/day for 1 week, steroids used only if side-effects
	occur; or no antiparasitic treatment
Moderate infections	Albendazole 15 mg/kg/day for 1 week with steroids
Heavy infections (encephalitis)	No antiparasitic treatment, high doses of steroids, osmotic diuretics
	(mannitol)
Calcifications	
Single or multiple	No antiparasitic treatment

Table 1. Treatment guidelines for Parenchymal Neurocysticercosis

**Diagnosis of Tuberculoma-** Patients are diagnosed to have tuberculoma based on imaging findings (Thick, irregular wall, T2 hypo intensity on MRI, adjacent meningeal enhancement, disproportionate perilesional oedema), clinical features (features of raised ICT, persistent neurological deficits, past or family history of tuberculosis) and other investigations (Raised ESR, positive Mantoux, evidence of pulmonary tuberculosis on chest X-ray). These patients were started on Anti tuberculous therapy with four drugs (INH, Rifampicin, Ethambutol, Pyrazinamide) for two months followed by treatment with two drugs (INH, Rifampicin) as per the standard guidelines (Guidelines for Treatment of CNS tuberculosis – by British Infection Society (2009) for treatment of CNS tuberculosis.

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Drug	Daily do	Route	Duration	
	Children	Adults		
Isoniazid	10-20 mg/kg (max 500 mg)	300 mg	Oral	12 Month
Rifampicin	10-20 mg/kg (max 600 mg)	450 mg (<50 kg) 600 mg (≥50 kg)	Oral	12 Months
Pyrazinamide	30-35 mg/kg (max 2 g)	1.5 g (<50 kg) 2.0 g (≥50 kg)	Oral	2 Months
Ethambutol	15-20 mg/kg (max 1 g)	15 mg/kg	Oral	2 Months

Table 2. Recommended Treatment Regimen for CNS Tuberculosis Caused by Fully Susceptible M. Tuberculosis

Along with ATT all these patients were given oral prednisolone in a dose of 1-2 mg/kg/d for 2 weeks followed by tapering over next 4 weeks.

In all patients, antiepileptic drugs were started immediately. Patients were given monotherapy, and the antiepileptic drug administered was either carbamazepine or phenytoin. Initial drug dosage was based on body weights.

All the patients are followed once in every month for 3 consecutive months. Details about the seizure control and development of any new symptoms or signs were noted at each visit. Patients house address and phone number are taken and called upon when required.

All the patients were subjected to Magnetic Resonance imaging of brain at the end of 3 months of their follow up.

Clinical outcome was assessed on the basis of recurrence of seizures, based on objective reports from patients.

The lesion was considered 'unchanged' if no change in the CT appearance of the lesion was noted. It was considered as 'regressing' if, the amount of cerebral oedema had reduced and/or the size of the lesion had altered. The 'disappearance' of the lesion was considered when the follow-up scan was reported as normal.

**Statistical Analysis-** The analysis was done using Chisquare statistics for categorical observations and t-test to compare continuous observations such as age of onset, average number of seizures and duration of illness. Chisquare was used to test the significance of differences in two groups. P value <0.05 was considered significant.

### RESULTS

Of the 93 patients, 49 (52.68%) were males and 44 (47.3%) were females. The male to female ratio was 1.1: 1.

Mean age of presentation was 21.48 yrs.  $\pm$  15.06. 37 patients (39.78%) were in the age group of 11-20. Majority of the patients (61.29%) were aged below 20 years.

The duration of illness prior to presentation was variable. Mean duration of symptoms was 17.08 days  $\pm$ 

16.74. Mean number of seizures before onset of treatment was 2.35  $\pm$  1.31.

Partial seizures with or without secondary generalization was the commonest type of seizure which was seen in 70 (75.3%) patients included in this study. GTCS in 23 (25%) patients. 3 had pure sensory seizures; whereas 19 had focal motor seizures without secondary generalization. 8 (8.6%) patients had Todd's palsy which lasted for less than 24 hrs in all.

Fever was present in 9(9.6%) patients.

4 (4.3%) patients had anorexia and weight loss in the recent past.

Past history of tuberculosis was present for 4 (4.3%) patients and 3 (3.6%) had history of contact with tuberculosis.

General examination revealed cervical lymphadenopathy in 1 patient and Neurofibromas were present in 1. Subcutaneous nodules were not seen in any of the patients.

Fundoscopy was normal in all and none had evidence of ocular cysticercosis.

2 (2.4%) were tested positive for HIV-1 serology. Chest X-ray showed evidence of pulmonary tuberculosis in 4 patients. One patient had biopsy proven lung carcinoma.

Contrast Enhancing CT of the brain was done in 21 (22.58%). 65 (69.89%) were subjected to Contrast Enhancing MRI. In the remaining 7 (7.52%) patients, plain CT was done initially which was followed by contrast MRI.

83 (89.24%) patients were diagnosed to have either definite or probable Neurocysticercosis, whereas 9 patients were diagnosed to have tuberculoma based on the clinical and imaging findings. In one patient diagnosis of metastasis was considered in view of diagnosis of carcinoma of lung.

### Neurocysticercosis Vs Tuberculoma Baseline Characteristics

The base line characteristics like age distribution, male to female ratio and mean number of seizures before presentation were almost similar in patients with NCC and tuberculomas.

Parameter	NCC (n-83)	Tuberculoma (n-9)	Total (n-93)
Male: Female	43:40 (1.07:1)	5:4 (1.2:1)	49:44 (1.11:1)
Age			
Range	2-78	7-35	2-78
Mean	21.92 ± 15.2	17.44 ± 7.82	21.48 ± 15.06
Majority – 11-20	31 (36.9%)	6 (66.6%)	37 (39.78%)

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Seizures				
Duration				
Range	3-75 20-90		3-90	
Mean	$14.38 \pm 13.98$	41.66 ± 21.56	$17.08 \pm 16.74$	
Number				
Range	1-8	1-6	1-8	
Mean	2.24 ± 1.3	$2.8 \pm 1.4$	$2.35 \pm 1.3$	
Туре				
SPS sec gen	40 (48.33%)	4 (44.4%)	45 (48.3%)	
GTCS	18 (21.68%)	5 (55.5%)	23 (24.73%)	
SPS	22 (26.5%)		22 (23.65%)	
CPS	3 (3.63%)		3 (3.2%)	
Parameter	NCC (n-83)	Tuberculoma (n-9)	Total (n-93)	
Other Symptoms				
Headache	21 (25.3%)	6 (66.6%)	27 (29.03%)	
Vomiting	3 (3.6%)	5 (55.5%)	8 (9.6)	
Fever	5 (6.02%)	4 (44.4%)	9 (10.84%)	
Anorexia &WL		4 (44.44%)	4 (4.3%)	
Past h/o TB		4 (44.44%)	4 (4.3%)	
Contact with TB		3 (33.3%)	3 (3.22%)	
Investigations				
High ESR	8 (9.6%)	7 (77.7%)	15 (16.12%)	
HIV		2	2	
Pul. TB on CXR		4	4	
Table 3. Baseline Characteristics of NCC & Tuberculoma				

### **Radiological Features**

**Site of Lesion-** More than half of the patients, i.e. 51 (54.83%) had lesions in parietal lobe. Frontal lobe in 23 (25.8%). Occipital and temporal lobes were least common sites to be involved.

Site	NCC	Tuberculoma	Metastasis	Total
Frontal	20	2	1	23 24.7%)
Fronto-parietal	7	2	0	9 (9.67%)
Parietal	48	3	0	51 (54.8%)
Parieto-occipital	1	1	0	2 (2.15%)
Occipital	3	1	0	4 (4.3%)
Temporal	4	0	0	4 (4.3%)
Total	83	9	1	93
Table 4. Site of Lesion				

**Size of the Lesion-** The size of the lesion ranged from 6-19 mm. Mean size of lesion was 10.69 mm  $\pm$  3.07. 53 (56.98%) patients had a lesion measuring larger than 10 mm or more in size. The 9 tuberculomas had a mean size of 15 mm  $\pm$ 3.47. 8 out of 9 tuberculomas were found to be larger than 10 mm in size.

**Perilesional Oedema-** The amount of perilesional oedema was found to be mild (restricted to the cerebral lobe involved) in 62 (66.6%) patients. 10 (10.7%) patients had no evidence of perilesional oedema. 7 (77.7%) of the 9 tuberculomas and the probable metastasis were surrounded by moderate perilesional oedema.

Parameter	NCC (83)	Tuberculoma (9)	Total (n-93)
Site			
Frontal +Parietal	75 (90.3%)	8 (88.8%)	83 (89.2%)
Size			
Range	6-16 mm	8-19	6-19 mm
Mean	10.18 mm ± 2.5	$15 \pm 3.742$	10.69 mm ± 3.07
>10 mm	37 (44.5%)	8(88.8%)	53 (56.98%)
Perilesional edema			
No	10 (12.04%)		10(10.7%)
Mild	62 (74.69%)		62 (66.6%)
Moderate	11 (13.25%)	7 (77.7%)	19 (20.4%)
Severe		2 (22.2%)	2 (2.15%)
Table 5. Size & Perilesional Oedema in NCC & Tuberculoma			

**Enhancement-** 79 (84.94%) of the 93 patients had ring enhancing lesions.

 $69 \mbox{ out of these were NCC}, 9 \mbox{ were tuberculomas and } 1 \mbox{ was metastasis.}$ 

46 (55.42% of NCC) patients had ring enhancing lesions which had an eccentric dot (scolex).

Disc (nodular) enhancement was observed in 14 cases of NCC (15.05%).

T2 hypointensity on MRI was seen in 6 (66.6%) tuberculomas.

Thick, irregular wall was present surrounding all tuberculomas.

**Outcome-** 11 (11.82%) of the 93 patients were lost to follow up.

### **Clinical Outcome**

In the 82 patients who are followed up for the subsequent visits, 63 (76.82%) patients had no recurrence of seizures during the follow up period of 3 months. 19 (23.17%) patients reported recurrence of seizure. 12 (63.15%) patients had first recurrence of seizure in the first month.



Chart 1. Clinical Outcome

### **Radiological Outcome**

Complete disappearance of the lesion was noted in 52 (63.41%) of the 82 patients who had a follow up imaging. All the lesions which disappeared completely were initially diagnosed as NCC. 19 (23.17%) patients had regression of the lesion. Out of these NCC was the initial diagnosis for 11 patients and tuberculoma for 8.



Chart 2. Radiological Outcome

### DISCUSSION

More than half (61.2%) were 20 or less years of age. Majority of patients (39.7%) were in the second decade of life. Similar results were found in several previous studies.<sup>1,2,3</sup> But the mean age of presentation was 21.48 years, probably because of inclusion of wide range of patients aged from 2 to 78 years. Similar findings were observed in previous studies by Sharma et al<sup>2</sup>, Bansal et al<sup>4</sup> and Murthy et al.<sup>5</sup>

The duration of symptoms before presentation was found to be highly variable according to many authors, ranging from 3 days to 6 months or even more.<sup>5</sup>

In the present study, the duration of seizures ranged from 3 days to 3 months with a mean of 17.08 days. Similar

findings were observed in the studies by Sethi et al  $^{\rm 5}$  , Kumar et al. $^{\rm 6}$ 

Mean number of seizures before presentation was 2.35 in present study, which was similar to the result observed in studies by Sharma et  $al^2$ , Gupta et  $al^7$  and Yadnopaklov et  $al.^8$ 

Partial seizures with or without secondary generalization was the commonest type of seizure associated with these lesions according to many authors.<sup>1,2,4,5,7,8,9</sup> In this present study, we also observed that partial with or without secondary generalization was the commonest type accounting for seizures in majority (75.2%) of the patients irrespective of the location of the lesion.

Focal motor seizures were the commonest type of partial seizure. Pure sensory seizures were present 2 of the patients and similar finding was reported by Chopra et al<sup>10</sup>

Headache was the next common symptom complained by 29% of patients in our study. Sotelo et al<sup>11</sup> reported that 43.4% of 753 patients with SSECTL. This could be due to inflammation surrounding the organism or post ictal inflammation.

Past history of tuberculosis was present for 4 (4.3%) patients and 3 (3.6%) had history of contact with tuberculosis. This may warrant for a thorough search for evidence of tuberculosis in these patients.

Finding subcutaneous nodules in patients with solitary cysticercus granuloma is a distinct rarity. Chopra et al<sup>10</sup> did not discover in any of the 122 patients. None of our patients had subcutaneous nodules.

In view of the above clinical findings and imaging features like thick, irregular wall with significant perilesional oedema causing midline shift (in 2 patients), and T2 hypointensity in MRI (in 6 patients), 9 patients were considered to have a diagnosis of tuberculoma. The two HIV positive patients had past history of pulmonary tuberculosis and the imaging findings were suggestive of tuberculoma. In one patient, who had carcinoma lung, the lesion was considered as solitary metastasis.

The peri rolandic area which includes the frontal and parietal lobes is the commonest site for these lesions. According to many authors.<sup>1,2,5,7,8</sup> parietal lobe is the commonest site followed by frontal lobe. In our study involvement of parietal lobe accounted for 54.8%, followed by frontal lobe (24.7%).

Both NCC and Tuberculomas were common in parietal lobes. This could be explained by the fact that lesions in other locations might not be symptomatic and the territory middle cerebral artery is preferred site for these granulomas because of the haematogenous spread.

The SSECTL is by definition less than 20 mm in size and the usual size ranges from 6-15 mm. In this study mean size of the lesion was 10.69 mm with a range of 6-19 mm.

According to the study by Chandy et al,<sup>12</sup> all the histologically proven NCC were of less than 20 mm and all the tuberculomas were greater than 20 mm in size.

In the present study, the 9 probable tuberculomas had a mean size of 15 mm. 8 out of 9 accounting for 88.8% tuberculomas were found to be larger than 10 mm in size whereas 44.5% of NCC granulomas were more than 10 mm in size. Sharma et al<sup>2</sup> reported that 76% of NCCs were of less than 10 mm size.

In a study of biopsy proven lesions, Chandy and Rajshekhar.<sup>12</sup> reported that 96% of cysticerci had a regular outline, contrasting 5 out of 6 tuberculomas which were irregular in outline.

In present study all the reported tuberculomas had thick, irregular wall.

Vesicular lesions and calcified lesions are usually not associated with perilesional oedema. The degenerating stages like colloidal stage and granular nodular stage are associated with mild to moderate perilesional oedema as these represent the stages of dying larvae which produces surrounding inflammation. Tuberculomas produce intense inflammatory reaction.

In this study 87% of NCC had mild to moderate perilesional oedema and 10 were found to have no perilesional oedema. Singh et al.<sup>1</sup> reported mild to moderate oedema in 61% and absence of oedema in 27% of 75 patients.

In present study 7 (77.7%) of the 9 tuberculomas were surrounded by moderate perilesional oedema and the remaining 2 had severe perilesional oedema producing midline shift probably suggesting more intense inflammation caused by the tuberculomas. The probable metastasis was surrounded by moderate oedema.

Desai and Bhatia <sup>13</sup> observed that finding central hypo intensity in the T2 weighted MRI is more suggestive of tuberculoma rather than a solitary cysticercus granuloma which will have increased intensity on T2. The T2 hypo intensity in tuberculoma was thought to be due to macrophage activity and high lipid content. Finding a mural nodule in the MRI which suggests presence of scolex is more suggestive of a cysticercus granuloma.

In our study 6 (66.6%) out of 9 tuberculomas had central T2 hypointensity.

These lesions, after contrast administration show either ring or disc (nodular) type of enhancement depending on the stage of the granuloma. Finding the scolex has been highly variable in different studies. Sharma et al<sup>2</sup> observed that 67% of the lesions showed ring enhancement with eccentric nodule, while 21% lesions were ring enhancing lesions without scolex. Disc enhancing lesions were present in the remaining 12%. Whereas in another study by Singh et al<sup>1</sup>, ring enhancing lesion with eccentric dot was found in only 10% and disc enhancing lesions constituted 9%.

In present study, 55.4% of cysticercus granulomas were ring enhancing with eccentric dot. Disc enhancing lesions were observed in 15%.

The recurrence of seizures is less common in the patients with SSECTL, especially after starting AED as these represent one of the acute symptomatic illnesses. In a study by Singh et al<sup>1</sup> the authors reported seizures did not recur in 86% of patients at the end of 1 yr. Majority of the patients who had a recurrence of seizure had in the first month after starting AED.

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Similar findings were observed in our study, where 76.8% patients had no recurrence of seizures during the follow up period of 3 months which was statistically significant (p-<0.05).

The most remarkable feature of single enhancing lesions observed on CT scanning is their complete spontaneous disappearance in the majority of patients, as well as their occasional significant reduction in size in others.

The rate of disappearance of lesion has ranged from 22 to 100% at 12 weeks after detection  $^{14}$ .

In a prospective study of 210 patients, Rajshekhar et  $al^{15}$  observed that at 3 months only 19% of lesion had completely resolved; at 1 year approximately 63% had disappeared.

In our study, complete disappearance of the lesion was noted in 52 (63.41%) of the 82 patients who had a follow up imaging after 3 months.

### CONCLUSION

Majority of the SSECTL are NCC & tuberculomas. Majority of the NCC are <10 mm in size with minimal perilesional oedema whereas majority of tuberculomas >10 mm with significant perilesional oedema and T2 central hypointensity on MRI. Both NCC and Tuberculomas were common in parietal lobes. The recurrence of seizures is less common in the patients with SSECTL, especially after starting AED.

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