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Neurocysticercosis: the Notorious Vanishing Ring Enhancing Lesion.

KEYWORDS: neurocysticercosis, vanishing lesion, Anti Cysticercii Antibody – CSF.

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ABSTRACT *Objectives: To evaluate patients with ring enhancing lesion (REL) and associated clinical features thereby charting out diagnosis and treatment outcome of RELs.*

Material and methods: A cross-sectional observational study of 25 patients (age >12 years), with REL on MRI brain, was done over 12 months. Headache and seizures, and signs of hydrocephalus, meningitis and focal deficits were clinically assessed. Relevant investigations were sent, and correlated with clinical features and MRI findings. Response to medical therapy (empirical or specific) was evaluated clinically and on repeat MRI after 6 weeks. Several causes of RELs like infectious, neoplastic and inflammatory were detected. Of these, only cases of neurocysticercosis are highlighted.

Results and Conclusions: Out of 25 patients, 8 (32%) had neurocysticercosis (5 males and 3 females), mostly between 21-40 years age; seizures were present in 100% and headache in 88%. Routine CSF studies were normal in 100%. Anti Cysticercii Antibody – CSF was conducted in 4 out of 8 patients and was positive in 3 of these (75% positivity). 7 of 8 patients had a single REL; size of REL in 7 of 8 patients was between 1 to 10 mm. Lesions were scattered at various sites including frontal lobe and temporal lobe (2 each), and others. A combination of anti-convulsants, anti-helminthics (Albendazole) and steroids was instituted. On repeat scan after 3 weeks of therapy, complete resolution was observed in 6 patients (75%), and calcification and regression was observed in one patient each. We concluded that neurocysticercosis has an excellent prognosis if treated appropriately.

INTRODUCTION:

Diseases causing RELs of the brain can be infectious, neoplastic, inflammatory or vascular in origin. Neoplastic etiologies include glioblastomas, low-grade gliomas, lymphomas and brain metastases. Non-neoplastic neurological disorders mimicking brain neoplasms on neuroimaging are tuberculosis, neurocysticercosis, demyelinating disorders, pyogenic abscess, toxoplasmosis, fungal infections, radiation encephalopathy, cerebral venous thrombosis and several other vasculitic disorders.(1,2) Neurocysticercosis is the commonest cause of RELs with a range of 4% to 40%, followed by tuberculosis and malignancy - primary or metastatic in that order.(3) Single lesions are more frequently reported than multiple lesions in India with 70% lesions showing a spontaneous resolution in repeat MRI. Developing countries have a higher proportion of infectious causes of RELs like tuberculoma, neurocysticercosis, brain abscess and toxoplasmosis. (4,5) Cysticercosis has been called a modern day plague very correctly due to its worldwide distribution, high incidence and occasional fatal complications. Cysticercosis is the most frequent parasitosis of the nervous system. Nevertheless, its precise incidence is not known due to lack of dependable and simple serological tests.(6) It often undergoes regression and complete resolution if apt treatment with anti-helminthics is instituted. This necessitates adequate knowledge about the clinical and radiological presentation of neurocysticercosis; therefore focus on this subset of patients out of others with RELs in this study is justified.

MATERIAL AND METHODS:

Approval from the Ethics committee, for material and methods to be used, was procured before commencing data collection. 25 patients (age 12 years and above) with REL detected on MRI brain, admitted to a teaching hospital over 12 months, were included in this cross-sectional observational study after written informed consent. Each patient was clinically assessed on the basis of following signs and symptoms:

- Headache
- Focal or Generalized Seizures or Status Epilepticus
- Hydrocephalus: papilloedema , dementia , stupor or coma
- Meningitis: neck stiffness , fever , cranial nerve palsy
- Focal deficits: monoparesis , hemiparesis

Following detailed history taking and physical examination, patients were subjected to laboratory investigations and neuroimaging (MRI brain).The clinical features, laboratory data and findings on imaging were correlated to arrive at a diagnosis. Response to therapy such as anti-epileptic drugs (1st line/2nd line) or to specific medical therapy- depending on etiology was correlated with the clinical presentations and diagnosis. Patients were followed up with brain scans

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at 6 weeks and later if required, which were correlated clinically and radiologically. The data thus obtained was entered in a spread sheet and analysed using descriptive statistics such as frequencies and percentages.

RESULTS:

As only 25 cases were studied in a span of 12 months, the incidence could not be predicted; the number being too small. Among the 25 cases, 8 patients (32%) had neurocysticercosis, which was second only to tuberculomas (48%). In our study, most of the patients showing RELs on MRI were in the age group of 21 to 40 i.e. (12 out of 25). Younger age group had a higher prevalence than the older age group. Of the 21 to 40 age group; majority (6 of 8) were diagnosed having neurocysticercosis followed by tuberculomas. While the all cause sex ratio in our study was Male: Female = 40:60, there was a slight male preponderance (5 out of 8) in cases of neurocysticercosis (Male: Female= 63:37).

In our study, all patients having neurocysticercosis had seizures (100%) [Table 1]. Only 1 (age 24 years) out of 8 patients of neurocysticercosis had a past history of (< 6 months) seizures, which indicates that in most cases seizures are directly correlated to the diagnosis of REL. 7 patients out of 8 with neurocysticercosis presented with headache (87.5%). Fever was present in only 1 out of 8 patients of neurocysticercosis. Occurrence of fever in all cause RELs was 8 out of 25 (32%). 5 of these 8 had tuberculoma. All 8 patients of neurocysticercosis in our study showed no focal neurological deficit. Out of 24% of patients who had focal neurological deficit, 3 were diagnosed with malignancy and the rest as tuberculoma.

Anti-cysticerci antibody test was sent for 4 patients of the 8 patients of neurocysticercosis. Of these, 75% cases (3 of 4) turned up positive, thus diagnosing neurocysticercosis. The diagnosis here was made on the basis of radiological and CSF analysis. In our study; as many as 76% of patients showed single lesions on MRI as opposed to 24% showing multiple RELs. [Figure 1, figure 2] Out of the 8 patients of neurocysticercosis, 7 showed single REL. Majority of these lesions were in the size range of 0-1 cm. i.e. less than 10 mm in size. Most common location of focal lesion in patients of neurocysticercosis was frontal lobe and temporal lobe (2 patients each). Other sites included parietal lobe, lentiform nucleus and thalamus. [Table 2] Our study reported frontal lobe lesions as the favoured site for RELs due to any cause.

Albendazole alongwith anticonvulsant therapy and steroids were given to all 8 patients of neurocysticercosis. Neurocysticercosis showed 75% complete resolution (6 out of 8) after a 3 weeks course of Albendazole with steroids. Calcification and regression was seen in 1 case each. [Table 3].

DISCUSSION:

Age distribution observed by Bhattacharya et al [7] in 1996 and Rudersh et al [8] in 2008 was similar to our study with commonest occurrence in the young age group (21 to 40 years). Rudersh et al [8] also concluded that neurocysticercosis was the commonest cause for RELs across all age groups. Two earlier studies by Kumar et al [9] and by Bansal et al [10] reported male preponderance for all cause RELs as seen in our study.

Recently, Gracia et al (11) in 2004 reported seizures in all 120 patients (100%) in their study and they also observed neurocysticercosis as the main cause of adult onset seizures. The percentage of seizures in RELs reported from studies by Bhattacharya et al, Rudersh et al, Kumar et al, Bansal et al, Chopra et al, Bhatia et al, varied from 14% to 96%.(7,8,9,10,12,13)

In contrast to our study which recorded headache in 87.5%, Bhatia et al [13] and Rudresh et al [8], reported a lesser frequency of headache as the presenting complaint. A study by Achappa et al [14] reported fever with headache as the commonest presenting feature in RELs; but the study population exclusively included HIV positive patients diagnosed with toxoplasma encephalitis. Bhatia et al [13] and Ahuja [3] observed focal neurological deficit in 20% and zero patients respectively in their study. We observed focal neurological deficits in 24% of our patients.

Jain et al [15] in May 2011, Kumar et al [9] and Rudresh [8] et al also observed that a single REL was present in majority of the patients. In concordance with our study which showed 76% patients with a single REL. While we reported frontal lobe lesions as the favoured site for RELs due to any cause, this was in contrast to observations made by Mitchell et al [16], Rudresh et al [8] and Chopra et al [12]. All of them reported parietal lobe as the commonest location for RELs.

Gracia et al [11] concluded that in patient with seizures due to viable parenchymal cysts, anti parasitic treatment decreases the burden of parasite, and is safe and effective. In their study, groups treated with Albendazole showed reduction in seizures and improvement/resolution of REL after 2-30 months. This was similar to our result which showed complete resolution in 75% of patients with neurocysticercosis after treatment with albendazole and steroids. Kumar et al [9] reported 15 patients whose ring lesion disappeared with anticonvulsants alone. Similarly; Bhatia et al [13] found 5 patients out of 25 which solitary micro lesions showing complete disappearance with anticonvulsants only. Wadia et al [17] had given anti-tubercular alongwith anticonvulsants treatment to all 39 patients who had RELs. Of these, 25 underwent repeat neuroimaging after 3 months. In 23 of these the REL had cleared completely. In their paper, they concluded that watching without definite treatment may be hazardous especially if patients follow up is defective.

With introduction of MRI, a large number of patients with seizures have been found to have small single/multiple RELs. Cysticercosis is a systemic infection that occurs when human being becomes the intermediate host. The incidence of invasion of brain may be upto 60%. Single or multiple cysts containing the scolices may be found in brain (figure 1 and figure 2) & spinal cord parenchyma, ventricle and subarachnoid space. Both intraparenchymal and subarachnoid cysts incite an intense inflammatory reaction that subsides following the death of the scolex approximately 18 months after infection. Cerebral cysts calcify infrequently. (18) Neurologic manifestations are common. Seizures, which may be generalized, focal, or Jacksonian, are associated with inflammation surrounding cysticerci in the brain parenchyma. Hydrocephalus results from obstruction of cerebro-spinal fluid (CSF) flow by cysticerci and accompanying inflammation, or by CSF outflow obstruction from arachnoiditis. Signs of increased intracranial pressure including headache, nausea, vomiting, changes in vision, dizziness, ataxia, or confusion, are often evident. When cysticerci develop at the base of the brain or in the subarachnoid space, they may cause

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chronic meningitis or arachnoiditis, communicating hydrocephalus, or strokes. A consensus conference has delineated absolute, major, minor, and epidemiologic criteria for diagnosis of neurocysticercosis. Absolute criterion implies definite demonstration of the parasite. This is possible by histologic observation of the parasite in excised tissue, by fundoscopic visualization of the parasite in the eye (in the anterior chamber, vitreous, or subretinal spaces), or by neuroimaging studies demonstrating cystic lesions containing a characteristic scolex. Diagnostic certainty is not always possible. Instead, a clinical diagnosis is made by combining clinical presentation, radiographic studies, serologic tests and exposure history. (19) Primary major diagnostic criteria are the neuroimaging findings suggestive of neurocysticercosis. These include cystic lesions with or without enhancement (e.g., ring enhancement), one or more nodular calcifications, or focal enhancing lesions. Cysticerci in the brain parenchyma are usually 5–20 mm in diameter and rounded. Cystic lesions in the subarachnoid space or fissures may enlarge up to 6 cm in diameter and may be lobulated. For cysticerci within the subarachnoid space or ventricles, the walls may be very thin and the cyst fluid is often isodense with CSF. Thus, obstructive hydrocephalus or enhancement of the basilar meninges may be the only finding on CT in extraparenchymal neurocysticercosis. (19)

The second major diagnostic criterion is detection of specific antibodies to cysticerci. An immunoblot assay using lentil-lectin purified glycoproteins has >99% specificity and is highly sensitive. However, patients with single intracranial lesions or with calcifications may be seronegative. With this assay, serum samples provide greater sensitivity than CSF.

Clinical criteria can aid in the diagnosis in selected cases. In patients from endemic areas who had single enhancing lesions presenting with seizures, a normal physical examination, and no evidence of systemic disease (e.g., no fever, adenopathy, or abnormal chest radiograph), the constellation of rounded CT lesions 5–20 mm in diameter with no midline shift is almost always caused by neurocysticercosis. Finally, spontaneous resolution or resolution after therapy with albendazole alone is consistent with neurocysticercosis. [19]

Minor diagnostic criteria include neuroimaging findings consistent with, but less characteristic of cysticercosis, clinical manifestations suggestive of neurocysticercosis (e.g., seizures, hydrocephalus, or altered mental status), evidence of cysticercosis outside the central nervous system (CNS; e.g., cigar-shaped soft tissue calcifications), or detection of antibody in CSF by ELISA. Epidemiologic criteria include exposure to a tapeworm carrier or household member infected with Taenia solium, current or prior residence in an endemic area, and frequent travel to an endemic area. [19]

Diagnosis is confirmed in patients with either (1) one absolute criterion or (2) a combination of two major criteria, one minor criterion, and one epidemiologic criterion.

A probable diagnosis is supported by the fulfillment of (1) one major criterion plus two minor criteria; (2) one major criterion plus one minor criterion and one epidemiologic criterion; or (3) three minor criteria plus one epidemiologic criterion. (19)

Initial management of neurocysticercosis should focus on symptom-based treatment of seizures or hydrocephalus. Seizures can usually be controlled with antiepileptic treatment. If parenchymal lesions resolve without development of calcifications and patients remain free of seizures, antiepileptic therapy can usually be discontinued after 1–2 years. For the treatment of patients with brain parenchymal cysticerci, antiparasitic drugs, including praziquantel (50–60 mg/kg daily in three divided doses for 15–30 days) or albendazole (15 mg/kg per day for 8–28 days) are favoured. Both agents may exacerbate the inflammatory response around the dying parasite, thereby exacerbating seizures or hydrocephalus as well. Thus, patients receiving these drugs should be closely monitored, and high-dose glucocorticoids should be used during treatment. [19]

We conclude that intracranial REL on MRI were more common in males & in younger age group of 20 to 40 years. Commonest presenting symptoms were seizures and headache; focal neurological deficit not seen in any patient. Neurocysticercosis (32%) was the second commonest etiology for REL preceded by Tuberculoma (48%). Majority of lesions on MRI were solitary with their commonest size range being (0-1 cm) 0-10 mm. Frontal lobe and temporal lobe were the most common site involved in this study. Symptoms and MRI scan findings can resolve with prompt treatment. Anticonvulsants form an important aspect of the treatment modality in these cases. The outcome was excellent in solitary Neurocysticercosis with 83.3% complete resolution.

Table 1: Distribution of Symptoms according to diagnosis

Symptoms	Brain Abscess	Malignancy	Neurocysti-cercosis	Toxoplasmosis	Tuberculoma	Total	%
Fever	1	0	1	1	5	8	32
Headache	0	1	7	1	8	17	68
Seizure	0	1	8	0	8	17	68
Focal Neurological Deficit	0	3	0	0	3	6	24

Table 2: Distribution of site of lesion according to diagnosis

Site	Brain abscess	Malignancy	Neurocysti-cercosis	Toxoplasmosis	Tuberculoma	Total	%
Frontal	0	1	2	0	6	09	36
Parietal	0	1	1	0	1	03	12
Occipital	0	0	0	0	1	01	04
Temporal	0	0	2	0	0	02	08
Fronto-parietal	0	1	1	0	1	03	12
Parieto-occipital	0	0	0	1	0	01	04

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Others	1	0	2	0	3	06	24
Grand Total	1	3	8	1	11	25	100

Table 3: Changes on repeat Brain Scan

Changes	Diagnosis					Total	%
	Brain Abscess	Malignancy	Neurocysticercosis	Toxoplasmosis	Tuberculoma		
No changes	0	1	0	0	3	4	16.0
Calcification	0	0	1	0	5	6	24.0
Hemorrhagic Changes	1	0	0	0	0	1	4.0
Operated	0	2	0	0	0	2	8.0
Regression	0	0	1	0	1	2	8.0
Resolved	0	0	6	1	3	10	40.0
Grand Total	1	3	8	1	12	25	100.0

Legends to figures:
Figure 1: Axial section of MRI Brain showing single neurocysticercosis lesion in right parieto -occipital region with visible scolex (arrow).

Figure 2: Axial section of MRI Brain showing multiple neurocysticercosis-Stary sky appearance

Figure 1.

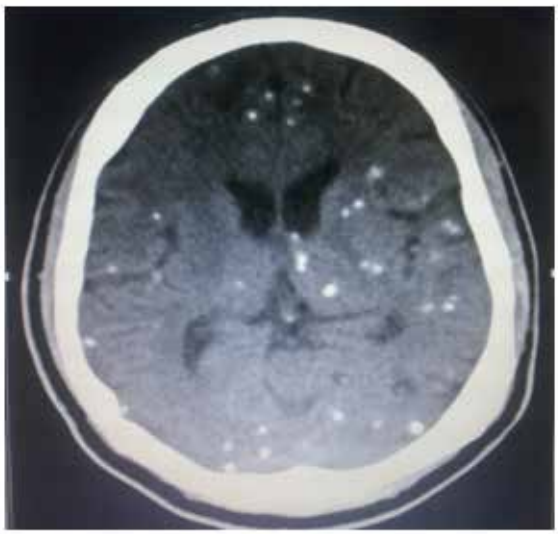

Figure 2.