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Original Research Paper

Radiology

AN EVALUATION BY CT, MRI AND SEROLOGY IN THE DIAGNOSIS OF NEUROCYSTICERCOSIS IN PEDIATRIC AGE GROUP OF RURAL AREAS OF FARRUKHABAD DISTRICT, UTTAR PRADESH.

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ABSTRACT

BACKGROUND Neurocysticercosis is the most common parasitic disease of the central nervous system. The prevalence of Neurocysticercosis in some of these developing countries exceeds 10%, where it accounts for up to 50% of cases of late onset epilepsy. Seizures are the most frequent and often the only clinical manifestation of Neurocysticercosis, they occur in 70% to 90% of cases.

AIMS AND OBJECTIVE To evaluate the diagnostic significance of Neuro-imaging technique and Serology in Neurocysticercosis and to determine the intestinal carriers of the Parasite in Neurocysticercosis in Pediatric age group.

METHODS AND MATERIAL The study was done of 100 patients in Major S.D .Singh Medical College from July 2016 to June 2017 of paediatric population of age group ranging from 06 years to 16 years. CT scan and MRI are done only in the suspected cases and serology was done with ELISA, the most specific test is Enzyme Linked Immuno Electro Transfer Blot (EITB) technique.

RESULT Abnormal neuroimaging was seen in 100% of the cases whereas confirmation of diagnosis by neuroimaging alone could be made only in 36% of the cases based on diagnostic criteria. Single ring enhancing lesion was the most common finding (64%) in CT scan. The most common site of occurrence of the lesion within the brain was Parietal in 48% followed by frontal in 27%, occipital 13%, and temporal 09%. ELISA detected antibodies in 87% of the cases of Neurocysticercosis.

CONCLUSION Neuroimaging (CT scan) was abnormal in 100% of the cases. Single parenchymal lesion was the most common findings. Diagnosis could be confirmed based on CT scan only in 36% of the cases. Neuroimaging techniques, including computed tomography (CT) and magnetic resonance imaging (MRI) and serology have improved the accuracy of the diagnosis of Neurocysticercosis by providing objective evidence on the number and topography of lesions, their stage of involution, and the degree of inflammatory reaction of the host against the parasites. The sensitivity of the ELISA was higher in cases with active neurological lesion (97.5%) and in cases with multiple parenchymal lesions (94.25%).

KEYWORDS : Neurocysticercosis, Taenia solium, cysticercosis, seizures.

INTRODUCTION.

Neurocysticercosis (NCC) is the infection of brain and its coverings by the larval stage of the tapeworm Taenia solium (pork tapeworm). Encystment of larvae can occur in almost any tissue. Involvement of the central nervous system (CNS) known as Neurocysticercosis (NCC) and it is the most clinically important manifestation of the disease. NCC is caused by the tissue-invading larvae (Cysticercus Cellulosae) of the pork-tapeworm-Taenia solium. It is the most common helminthic infestation of the central nervous system. It is the most important parasitic neurologic disease and a common cause of epilepsy in Asia, Africa and Latin America, representing enormous cost for anticonvulsant and medical resources [1].Taenia solium causes two different diseases. When the adult cestode infests the human intestine, taeniasis develops, it is generally asymptomatic but the host becomes a continuous source of taenia eggs, which are expelled every day in the feces, which may then contaminate vegetables and food in areas with poor sanitary conditions. Human cysticercosis occurs by ingestion of faecally contaminated food, water or vegetables containing eggs of T. solium [2-4]. However, ingestion of infected pork only causes intestinal tapeworm infestation (taeniasis) [5].This tapeworm is a public health problem in most developing countries where pigs are raised and pork is consumed and where poverty, illiteracy and deficient sanitary infrastructure are common [3]. The main objective of this study is to find out the diagnostic significance of Neuroimaging and Serology and to detect intestinal carriers of the tapeworm. In endemic countries taeniasis/cysticercosis is extremely common and neurologically symptomatic individuals, although many represent only the tip of the iceberg [1, 6].WHO estimated that 50 million persons, predominantly from developing 10 countries, are infected with taeniasis and 50,000 people die of the disease each year [1] Cysticercosis of the central nervous system is the most important neurological disease of parasitic origin in humans.

It causes serious morbidity and in areas where T. solium is endemic, it is known to be a leading cause of epilepsy [3,5,7], which has profound social, physical and psychological consequences. NCC is the important cause of chronic epilepsy which places particular demand on the health services. Diagnostic certainty of NCC is based on combined neuroimaging studies, immunodiagnostic technique, clinical presentation and epidemiological evidence suggestive of Neurocysticercosis [8]. The clinical diagnosis is impaired by polymorphism and non-specificity of the symptoms [9, 10].Neuroimaging technique such as CT scan and MRI have attributed to more accurate diagnosis and better understanding of pathophysiology. However, only the presence of cystic lesion showing the scolex is considered pathognomonic [8]. CT scan has been claimed to have sensitivity and specificity of 95 % for diagnosing NCC [6].Immunodiagnostic techniques include detection methods for specific antibody and for circulation parasite antigen in serum and cerebrospinal fluid [11].Infection with T. solium results in specific antibody response mainly IgG class. Different techniques have been described to detect antibody to T. solium. The most specific test is Enzyme Linked Immunoelectro Transfer Blot (EITB). However in developing countries ELISA (Enzyme linked Immuno-sorbent Assay) is preferred because of better availability, simplicity and lower cost compared with EITB [12]. ELISA measures specific IgG antibody to partially purified antigen from cysticercal fluid, serum sensitivity of 75-87% and specificity of 75% has been reported [12]. Analysis of antibody

response indicated that the optimum threshold titres for seropositivity were 1:800 for the ELISA. When used with these thresholds, the ELISA gave a sensitivity, specificity, positive and negative predictive values and diagnostic efficacy of 89%, 81%, 79%, 90%, 85%, respectively [13]. Serologic test can be very useful for confirmation of neuroimaging finding for differential diagnosis of other cyst forming condition [14, 15].

Cysticercosis is a systemic illness caused by dissemination of the larval form of the pork tapeworm, Taenia solium. Encystment of larvae can occur in almost any tissue. Involvement of the central nervous system known as Neurocysticercosis (NCC) and hence, is the most clinically important manifestation of the disease. NCC is caused by the tissue-invading larvae (Cysticercus Cellulosae) of the pork-tapeworm; Taenia solium. Cysticercosis is considered the most common parasitic disease of the central nervous system [1].

TYPE OF STUDY-Cross sectional study.
PLACE OF STUDY-Major S. D. Singh Medical College, Farrukhabad.
DURATION OF STUDY-February 2016 to June 2017

MATERIAL AND METHODS

The study was done in Major S.D .Singh Medical College, Farrukhabad from February 2016 to June 2017 of paediatric population of age group ranging from 06 years to 16 years.The cases are the suspected cases of Neurocysticercosis based on clinical presentation, epidemiological evidence and positive neuroimaging findings. The patients who do not meet these criteria are excluded from the study. Newly diagnosed cases are only included in the study.

SAMPLING METHOD

Sample size of 100 Patients (aged 06 to 16 years) attending to paediatric out-Patient-Department and those admitted in Pediatric ward of Major D.Singh Medical college and Hospital are enrolled in the study. The cases are the suspected cases of Neurocysticercosis. Participants are included in the study by the order of presentation to the hospital (non-random sampling) and no restriction made as to the clinical form or stage of infection. The patients who do not meet these criteria are excluded from the study. Newly diagnosed cases are only included in the study. Our case definition for the NCC is based upon the clinical findings, epidemiological history and the diagnosis being supported by the positive neuroimaging findings (calcification or cystic lesion consistent with Neurocysticercosis). CT scan and MRI were done only in the suspected NCC cases both plane and with administration of contrast medium. The presence or absence of finding relevant to the study from the radiology reports was then derived. Specimen collection and handling of blood is collected by venepuncture. Serology (ELISA) Blood sample is taken from all the participants after being used for routine diagnostic procedure, the volume (5 ml) of blood is kept undisturbed for about 2-3 hours at room temperature; the serum is separated and preserved at -200C until use. Each bottle is given a specific code before the serology is performed. The serum from each patient is tested for cysticercal antibody by Enzyme-Linked-Immunosorbent-Assay (ELISA).

The ELISA 34 kit used is UBI MAGIWELL™ CYSTICERCOSIS for detection of IgG anticysticercal antibody. The Principal of procedure is Cysticercosis test kit is a solid phase enzyme linked immunosorbent system employing plastic wells coated with Taenia solium antigens. Incubation of serum samples in the coated wells results in the binding of anti-Taenia solium antibodies to the immobilized antigens. Subsequent addition of the enzyme conjugate, comprised of horseradish peroxidase, results in the immobilization of peroxidase in direct proportion to amount of Taenia solium antibody present in the serum sample. Unbound enzyme conjugate is washed from the wells and a substrate and chromogen solution is added. The intensity of the colour formed as a result of enzyme activity is a direct measure of the anti-Taenia solium antibody present in the serum samples and may be quantified by use of a photometric wells reader at 450 nm wavelength.

AIMS AND OBJECTIVES

To evaluate the Diagnostic Significance of Serology and Neuro-imaging technique in Neurocysticercosis and to determine the intestinal carriers of the parasite in Neurocysticercosis in pediatric age group.

1) To determine the radiological findings in suspected Neurocysticercosis cases.
2) To find out the diagnostic tools used to confirm the diagnosis of suspected Neurocysticercosis.
3) To analyse the stages and distribution pattern of cyst in Neurocysticercosis as seen in CT scan and MRI.
4) To identify the Sensitivity and Specificity of Serologic test (Enzyme Linked Immuno-Sorbent Assay-ELISA) and Neuroimaging technique (Computed Tomography (CT) scan) in diagnosing Neurocysticercosis (NCC)

RESULTS

During the study Period from July 2016 to June 2017, 100 samples of serum for serology was collected from the cases with diagnosis of Neurocysticercosis based on classification scheme proposed by Del Brutto based on CT Scan and MRI findings .Most of the patients belong to low and middle socio economic groups.

Out of 100 cases of NCC, 54% of the samples were in the age group of 6-12 years. There is steady rise in number of cases with the age. 46% of the cases occurred in age group of 12-16 years. Mean age of presentation was 10.92 S.D=2.9).

Table 1.1: Distribution of cases according to age group Age group.

Age group in year	Patients(N=100)	Percent
6-8	16	16.0
8-10	18	18.0
10-12	20	20.0
12-14	22	22.0
14-16	24	24.0
Total	100	100.0

Table 1.2: Distribution of cases according to sex.

Gender	Frequency	Percentage
Male	65	65.0
Female	35	35.0
Total	100	100.0

65% of the cases were Male and that of Female is 35%. Male to Female ratio is 1.8.

Clinical Presentation of NCC.

Within the CNS it can affect the parenchyma, subarachnoid space, or intraventricular system. Therefore, the clinical manifestations are pleomorphic and dependant on the location, number, and stage of the cysts at presentation. NCC is the leading cause of adult-onset epilepsy in areas of the world where it is endemic, particularly in Latin America, Asia, and Africa [16]. The most common presenting symptoms were Seizure (66%).Simple partial seizure being most common (56%). Other types of seizure were complex partial, Generalized and status epilepticus. Number of seizure episodes varied from single to as many as six. Features of raised intracranial tension (headache with or without vomiting) was seen in 30% cases. Other presenting symptoms include neuropsychiatric manifestation like learning disabilities, behavioural abnormality (14%). Behavioural abnormalities included abnormal speech, emotional instability, aggressive behaviour, language problem and other psychotic features. Other symptoms like focal weakness (paresis), unexplained sudden loss of consciousness in 9%. In 26% of the cases more than one presenting symptoms (combination of symptoms) was present.

Table 1.3: Presenting Symptoms of Neurocysticercosis patients

Symptoms	N(=100)
Seizures	66
Simple Partial	37(56%)
Complex Partial	13
Generalized	18
Status epilepticus	04
Features of raised intracranial tension (Headache +/- vomiting)	30
Focal neurologic deficit	12
Neuropsychiatric manifestation	14
Other Symptoms	09
Combination of symptoms	26

Acute symptoms were present for seizure disorder. Seizure occurred as a single episode, or in frequent intervals or in status. Whereas Neuropsychiatric and behavioural symptoms were usually of long durations.

Seizures due to cysticercosis usually occur when the dying cyst incites an inflammatory reaction, but has been reported in the cystic stage. For many patients epilepsy may be the sole presentation of the disease with 50%–70% of patients experiencing recurrent seizures [17,18].

C.T Features of Neurocystisercosis.

Plain and contrast enhanced computed tomography was done in all the cases. Abnormal neuroimaging was seen in 100% of the cases whereas confirmation of diagnosis by neuroimaging alone could be made only in 36% of the cases based on diagnostic criteria. Single ring enhancing lesion was the most common finding (64%) in CT scan. The most common site of occurrence of the lesion within the brain was Parietal in 48% followed by frontal in 27%, occipital 13%, temporal 09%. The other sites were cerebellar and intraventricular. Maximum diameter of lesions in CT scan was 18mm. Of these 38% of the lesions were active which showed well demarcated cyst with minimal ring enhancement on contrast CT scan. Transitional lesion was seen in 43% of the cases which showed ill defined cyst with marked ring enhancement. These cysts both active and transitional usually contain scolex within them. Scolex was positively identified in 36% of the all cases. Perilesional edema was present in 74%. Inactive calcified lesion was present in 3% of the cases.

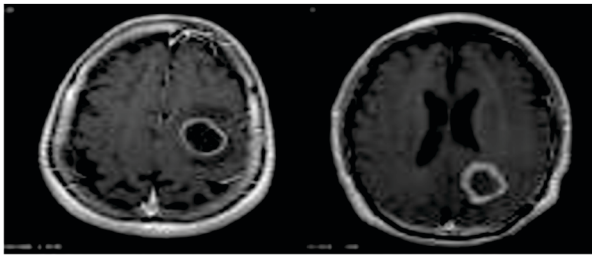

Fig:1 Single nodular ring enhancing lesion on contrast enhanced CT scan.

Table 1.4: Number of Parenchymal lesions on CT scan Head

Number of Lesions	N(100)
Single	64
Multiple	36

Table 1.5: Distribution of Intracranial Cysticercus according to CT scan

Site of lesion	N(100)
Parietal	48
Frontal	27
Occipital	13
Temporal	09
Cerebellar	02
Intraventricular	01

Table 1.6: Stages/Nature of Parenchymal Neurocysticercosis on CT scan

Nature of lesion	N(100)
Transitional	43
Active	38
Mixed	16
Inactive	03

Perilesional edema appears as a bright signal using magnetic resonance imaging (MRI) FLAIR or T2 imaging. It is almost always accompanied by enhancement around the calcified focus.

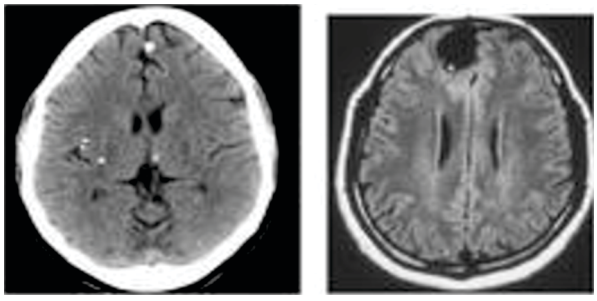

Fig: 2(a) Baseline CT scan demonstrating a dense calcification in the left frontal lobe as well as other calcifications. **2(b)** MRI image revealing vesicular cysticerci (the central dot represents the scolex).

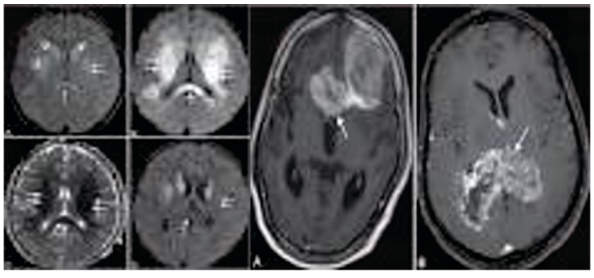

Fig: 3 (a) and (b) MRI images of Perilesional oedema.

ELISA

Cysticercus antibody was tested by ELISA in the sera of all the cases of NCC.

Only tests based on detection of antibodies specific for T. solium antigens are reliable for clinical diagnosis and epidemiologic studies. To date, these are limited to those based on the use of purified glycoprotein antigens derived from T. solium cysticerci. The current assay of choice is the electroimmunotransfer blot (ETIB) using partially purified antigenic extracts.

Table 1.6: Relationship between ELISA and number of lesion on CT Scan

		Number of lesions		Total
		Multiple	Single	
ELISA	Positive	41	46	87
	Negative	01	12	13
Total		36	64	100

The sensitivity of ELISA for serum anti-Cysticercus antibodies in cases of NCC with multiple parenchymal lesions was 94.25%, showing strong positivity in contrast to NCC with single parenchymal lesion, with sensitivity of 80.04%. Comparative studies of the sensitivity of ELISA between NCC cases with single and multiple parenchymal lesions were significant ($p<0.05$).

A major limitation of these tests are frequent false negative results in patients with single intracranial cysticerci, in which fewer than 50% test positive. Sensitivity of specific antibody assays is also relatively low in patients with only calcified cysticerci [27].

CONCLUSION

Localization of parasites in the central nervous system i.) Parenchymal Neurocysticercosis ii.) Subarachnoid Neurocysticercosis iii.) Ventricular Neurocysticercosis iv.) Spinal cord Neurocysticercosis Brain parenchymal cysticerci are usually small cysts, single or multiple, that tend to lodge in areas of high vascular supply. The process of degeneration of parasitic cysts involves a continual process that has been categorized by Escobar (1983) in four histopathological stages: 1) Vesicular, 2) Colloidal, 3) Nodular-granular and 4) Calcified. The clinical stages of NCC namely are Active, Transitional and Inactive [19]. Vesicular is active form, colloidal and granular nodular represent transitional stage while nodular calcified stage is inactive stage of NCC. CT and MRI findings of Parenchymal Neurocysticercosis depend on stages of development of the parasite within the nervous system. Neuroimaging (CT scan) was abnormal in 100% of the cases. Single parenchymal lesion was the most common findings. Diagnosis could be confirmed based on CT scan only in 36% of the cases Neuroimaging techniques, including computed tomography (CT) and magnetic resonance imaging (MRI), have improved the accuracy of the diagnosis of Neurocysticercosis by providing objective evidence on the number and topography of lesions, their stage of involution, and the degree of inflammatory reaction of the host against the parasites. ELISA detected antibodies in 87% of the cases of Neurocysticercosis.

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