

Does CSF antibodies assay help in differentiating neurocysticercosis from tuberculoma?

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Abstract

Introduction: Two common causes of ring/disc enhancing lesions in CT scan or MRI scan of brain are Cysticercosis and tuberculoma. It is often difficult to know the cause in a patient with ring/disc lesions. The gold standard being tissue diagnosis, which is often not done or not practical due to procedural complications and most of these lesions carry a benign course. The present study was undertaken to test the sensitivity and specificity of CSF antibodies in Definitive cases of Neurocysticercosis and Tuberculoma.

Materials and Methods: A Cross-sectional descriptive study was conducted with a sample size of 50 patients. The duration of study was for 2 years. Consecutive patients visiting the neurology department with complaints of seizures, headache and focal neurological deficit and their neuroimaging demonstrating a ring/disc enhancing lesions, suggesting either a Cysticercosis or Tuberculoma were included. Patients were subjected to a detail clinical history and examination. Complete hemogram, complete blood chemistry, HIV serology and Neuroimaging either MRI or CT brain were done.

Lumbar puncture was done in all patients if there were no contraindications. CSF analysis for antibodies against antigens of cysticercosis and anti-tubercular antibodies were done. Antibody estimation is done by ELISA method.

Results: There were 52 patients in the study of which 26 patients were diagnosed as Neurocysticercosis and 11 patients as Tuberculoma. In all 26 patients with Cysticercosis CSF was showing less than 4 cells with normal glucose and protein. Out of 11 patients with tuberculoma only one patient CSF study was abnormal. CSF Elisa for anticysticercal and antitubercular antibodies were done in all patients and were negative in all them.

Conclusion: CSF ELISA test for anticysticercal antibody and anti tubercular antibody test has a low sensitivity and is not helpful in the diagnosis of ring enhancing lesions in the brain.

Keywords: Neurocysticercosis, Tuberculoma, CSF Antibodies.

Introduction

It is common in our clinical practice to detect ring/disc enhancing lesions in CT scan or MRI scan of brain while evaluating a patient with seizures, headache and/or focal neurological deficit.

It is often difficult to know the cause in a patient with ring/disc lesions of the brain. Two common causes are Cysticercosis and tuberculoma. The gold standard being tissue diagnosis, which is often not done or not practical due to procedural, complications and most of, these lesions carry a benign course. Various features are considered in arriving at a possible/probable diagnosis like associated clinical findings, neuroimaging, serological studies of serum and CSF.

Objective of the study

To test the sensitivity and specificity of CSF antibodies in Definitive cases of Neurocysticercosis and Tuberculoma.

Materials and Methods

Study was conducted at Department of Neurology; from a tertiary care university-affiliated Hospital from South India. The study period was for two years between April 2007 to March 2009 and a sample size of 50 patients were considered to be included in the study.

Study Population: Consecutive patients visiting the neurology department with complaints of seizures, headache and focal neurological deficit and their neuroimaging demonstrating a ring/disc enhancing lesions, suggesting either a Cysticercosis or Tuberculoma were included.

Study design: Cross-sectional descriptive study.

An informed consent was obtained from the patients. Patients were subjected to a detail clinical history and examination. Detailed skin examination was done for subcutaneous nodules. Fundus was examined by an ophthalmologist for choroidal tubercles or cysticercal lesions. Complete hemogram, complete blood chemistry, HIV serology and Neuroimaging either MRI or CT brain were done.

CSF Study

Lumbar puncture was done in all patients if there were no contraindications. CSF analysis was done for cell count, cell type, protein glucose, AFB stain and culture sensitivity fungal stain & culture sensitivity, malignant cells. CSF analysis for antibodies against antigens of cysticercosis and anti-tubercular antibodies were done. Antibody estimation is done by ELISA method.

Case Definitions

Neurocysticercosis

In the study, cases were diagnosed as Neurocysticercosis based on Del Brutto et al¹ criteria and also by diagnostic criteria proposed by Rajashekhar and Chandy.²

Tuberculoma

Tuberculoma of the brain were diagnosed if patient had any one of the following

1. Evidence of tuberculosis elsewhere in the body.
2. Close contact with tuberculosis patients and
3. Neuroimaging characteristics like size more than 20mm, severe perilesional edema and target lesion as suggested by Rajashekhar et al.
4. Diagnosis is confirmed by biopsy or other organ involvement or strongly positive Mantoux.

Statistical Analysis

All analysis was performed with SPSS 12.0 (SPSS Inc, Chicago, IL).

Continuous variable is expressed as mean±SD or as median (Range) if it is non- uniformly distributed. Categorical data is expressed in proportions. The study was approved by the ethical committee.

Results

In the present study 52 patients with Ring / Disc enhancing lesions of Brain were studied. There were 22males & 30 females (M: F Ratio 1:1.45), of these there were 26 patients who were diagnosed as Neurocysticercosis and 11 patients as Tuberculoma. The mean age was 28.8years.

The most common presentation was seizure (76%), partial with secondary generalization being the commonest (45%), followed by headache (17%) and focal deficit (3.8%).

Anemia was observed in 15.4% of patients and the mean ESR was 27.1mm. Mantoux test was positive in 7.7%.

The Demography, clinical, Lab investigation findings are mentioned in table 1 and 2.

CSF study

Lumbar puncture was done in 44(84.6%) patients and other 8 patients didn't agree for Lumbar puncture. In all 26 patients with Cysticercosis CSF was showing less than 4 cells with normal glucose and protein.

Out of 11 patients with tuberculoma only one patient CSF study was abnormal, in him.

CSF cell count was 20 cell / mm³, all were lymphocyte predominant with low glucose <45mg/dl & increase in protein.

CSF Elisa for anticysticercal and antitubercular antibodies were done in all 37 patients and were negative in all them.

Table 1: Demographic and clinical characteristics

Features	NCC (n=26)	Tuberculoma (n= 11)
Age yrs (mean)	28	25
Sex (M:F)	1:1	1:4.5
Presented with Seizures	23	5
Mean duration of seizures (days)	90.7	102.5
Mean Number of attacks	2.2	5.2
Mean duration of headache Head ache	27	20.5
Past history of TB	3	1
Focal Neurological deficits	3	5

Table 1: Salient lab values

Lab Investigation	NCC (n=26)	Tuberculoma (n=11)
Hb gm% (mean)	13.4	10.1
AEC (mean)	258	220
ESR mm/hr (mean)	17	62.5
Mantoux	0	2

Discussion

Review of published literature on Serological tests in the diagnosis of neurocysticercosis reveals that the CSF ELISA sensitivity for IgG and Ig Manticysticercal antibody is reported to be 76% and 87% and specificity of 92% and 93% respectively by Corona et al.³ Ahuja et al⁴ from India reported that in their 38 patients with disappearing CT lesion, serology was positive for

cysticercosis in 12 patients and for tuberculosis in two patients. However, Chopra et al⁵ reported that CSF cysticercus serology was negative in all the 122 cases of "Vanishing CT lesions".

Rajashekhar et al⁶ studied the serum of 18 patients with SPECTL, using the immunoblot assay for cysticercus antibodies and it was positive in only one

patient even though biopsy had features of Cysticercosis in 12 patients.

In our study also, of the 26 patients with cysticercosis of brain, CSF antibodies were negative when tested by ELISA method. Sensitivity of the ELISA test decreases considerably when parenchymal cysts are not in contact with the subarachnoid space⁷ (Rosas). The lower sensitivity of cysticercal ELISA test is probably related to the parenchymal location and lower antigenic load in these patients.

Other method of detecting antibodies is by Immunoblot technique performed in serum samples, it is based on the detection of anticysticercal antibodies to one or more of the seven lentillectin purifies structural glycoprotein antigens from the larval cysts of *T. solium*. It has a sensitivity of 98 per cent and specificity of 100 per cent in patients with more than one live cyst or subarachnoid disease.⁸ However immunoblot test is not freely available. This test has been claimed to have a high diagnostic precision⁹ (ito et al).

Most of the studies published about serological tests are in case of TBM, however case reports in isolated tuberculoma were negative in identifying mycobacterium by ELISA. Detection of specific mycobacterium antigen or antibody in CSF would certainly be of considerable help to a clinician in arriving at a definitive diagnosis of TB of the brain. The variations in sensitivity and specificity of many immunoassays have resulted in a lack of confidence among clinicians in immunodiagnosis of cerebral TB. These variations may be because of: (i) The use of different antigenic sources, such as total bacterial sonicate extract, culture filtrate, partially purified antigens, monoclonal antibody-based immunoaffinity purified or recombinant antigens (ii) Use of different immunoassays, such as hemagglutination, enzyme linked immune sorbent assay (ELISA), immunofluorescent assay (IFA), radio immunoassay (RIA), immunoblot assays and T cell-based gamma-interferon release assay (iii) The host's immune response.¹⁰ In our study also in patients with tuberculoma CSF study for Mycobacterial antibodies were negative in all eleven patients.

Conclusion

CSF ELISA test for anticysticercal antibody and anti tubercular antibody test has a low sensitivity and is not helpful in the diagnosis of ring enhancing lesions in the brain. Recommendation from this study is that it is not useful to perform CSF serological studies in patients with ring enhancing lesions when there are no clinical or imaging features of meningitis.

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Abbreviations

AEC: Absolute eosinophil count
 CT: Computerized tomography
 CSF: Cerebrospinal fluid
 ELISA: enzyme linked immune sorbent assay
 ESR: Erythrocyte sediment rate
 IFA: immunofluorescent assay
 Hb: Hemoglobin
 HIV: Human immunodeficiency virus
 IgG: Immunoglobulin G class
 IgM: Immunoglobulin M class.
 MRI: Magnetic resonance imaging
 NCC: Neurocysticercosis
 RIA: radio immunoassay
 SD: Standard deviation
 SPSS: Statistical Package for the Social Sciences.
 SSECTL: Single small enhancing CT lesions
 TB: Tuberculosis
 TBM: Tubercular Meningitis.

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