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Original Research Article

Study of Cryptococcal Meningitis in Telangana State

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Abstract: Cryptococcus meningitis is one of the commonest manifestations in immune compromised and immunocompetent individuals with significant morbidity and mortality. Our aim of the study was to study the clinical features, symptoms signs, laboratory investigations, and treatment outcome in Cryptococcal meningitis patients. This study was conducted over a period of 28 months. Total patients were10, with Male to Female ratio of 7:3and age ranging from 25 years to 60 years with mean age of 41.3 years. The commonest symptom was Headache in 100% followed by fever in 80% and commonest sign was neck stiffness in 80%.The risk factors were HIV infection in 70% and steroid intake in 20%.Cerebrospinal fluid (CSF) showed Cryptococcal antigen positivity in 100%,India ink positivity in 80% and CSF cultured grown Cryptococcus in 50% patients,20% patients had Disseminated Cryptococcus .All the patients were treated with Amphotericin B followed by fluconazole .90% patients responded 1 patient (10%) died. Hence Cryptococcal meningitis should be diagnosed early and treatment should be started early to prevent morbidity and mortality.

Keywords: Amphotericin B, Anti retro viral treatment (ART), Cerebrospinal fluid, (CSF), Human immunodeficiency virus (HIV), Tubercular Meningitis (TBM).

INTRODUCTION:

Cryptococcus meningeal infection is one of the commonest fungal infections affecting both immune competent and immune compromised individuals [1-3]. It is generally seen as initial acquired immune deficiency syndrome (AIDS) defining disease in 2% patients and commonly occurs when CD4 cells are less than 100/ul [4, 5]. It is one of the leading causes of mortality and morbidity in patients with AIDS [5]. The objective of the study was to study the clinical features, risk factors, investigations and treatment out come in Cryptococcus meningitis.

MATERIAL AND METHODS:

Case records of admitted patients with Cryptococcus meningitis, in General medicine department in Nizam's Institute of Medical sciences hospital which is multispecialty, tertiary care referral hospital Hyderabad, Telangana state. Were collected over a period of 28 months (from April 2014 to July 2016).

- Inclusion criteria was 1) All patients diagnosed patients with Cryptococcus meningitis, 2)Age above 12years.were included.
- Exclusion criteria was .Patients Age below 12 years were excluded.

Information from case sheets of all patients recruited for analysis was reviewed. In the history, demographic details, symptoms with the duration, loss of appetite and weight were noted. The risk factors information tabulated were Human immunodeficiency virus (HIV) infection, steroid intake and any other immunocompromised status of patient. Clinical findings specifically noted were presence of temperature, enlargement of Lymph nodes, liver,

spleen. Pleural effusion and in nervous system examination neck stiffness was noted.

The investigation reports of Hemogram, chest radiograph, abdominal ultrasonography (carried with MYLAB60 model, Esaote company from Ahmedabad), Contrast Enhanced Computed Tomography (CECT) of abdomen and chest (carried with Philips Brilliance 16 model, 16 slice CT, PHILIPS company from Netherlands),Magnetic resonance imaging (MRI) of Brain plain and contrast (1.5 TESLA SEIMENS ,GERMANY) Mantoux test, HIV ELISA, Electrocardiogram, CD 4 counts, Blood culture and CSF culture specially for Cryptococcus were ever done were documented. CSF analysis for opening pressure, protein , sugar, White blood cells(WBC), Lymphocytes, Adenosine deaminase(ADA), Cryptococcal antigen titers done, India ink for Cryptococcus were also noted.

The treatment details like medical management including surgical procedures were also noted. Antifungal antibiotics dose and duration of therapy, along with Antiretroviral treatment (ART), Anti tubercular treatment (ATT) and steroids were ever given were documented. Information on Inter costal drainage was also noted. The above data from all patients was tabulated and analyzed retrospectively. The reports of MRI Brain, CSF Cryptococcal antigen, and Cryptococcal culture study, FNAC/ biopsy of pulmonary nodule and splenic lesion were also collected (wherever they were carried out depending on clinical profile). The study was retrospective audit with no patient direct identifiers, hence consent was not taken. Hospital ethics committee was informed of the study.

STATISTICAL ANALYSIS

Microsoft office 2007 was used for the statistical analysis. Descriptive statistics like mean and percentages were used to interpret the data.

RESULTS:

Total 10 patients data(Table-1) were collected, with age ranging from 25 years to 60 years and mean age being 41.3 years and male to female ratio of 70% to 30%.The main presenting clinical feature was headache in 100%,followed by fever in 80%,vomiting in 50%,altered sensorium in 50%and blurring of vision in 10%. The commonest sign was neck stiffness in 80%, followed by hepatomegaly and spleenomegaly in 10% , and hydropneumothorax in 10% patients.40% patients had previous history of tuberculosis,50% patients were on anti-tubercular treatment(ATT) , 30% were on anti-retro viral treatment(ART),and 10% were on steroids at presentation ,

On chest radiography 10% had hydropneumothorax, 10% had solitary pulmonary nodule in right lung which was biopsied showing Cryptococcus and on ultrasound abdomen 10% had hepatomegaly, and spleenomegaly. There was hypodense lesions in the spleen, and pulmonary nodule (Figure-1) which were biopsied and showed Cryptococcus (Figure-2).MRI Brain showed basal meningeal enhancement in 50% patients, and 20% showed ring enhancement lesions. The blood culture in 10% had grown Cryptococcus. 2(20%) patients had disseminated Cryptococcus.

Table 1: Showing clinical features

Age	25 to 60 years	Mean 41.3 years
Sex Male: Female ratio	7(70%):3(3-%)	
Symptoms	Number (%)	
Fever	8 (80%)	
Headache	10(100%)	
Vomitings	5(50%)	
Altered sensorium	5(50%)	
Blurring of vision	1(10%)	
Signs		
Neck stiffness	8(80%)	
Hepatosplenomegaly	1(10%)	
Lungs	1(10%)Hydropneumothorax	
Cardiovascular system	Normal	

Table 2: Laboratory findings-Microbiology

Cerebrospinal fluid	Number (%)
India Ink positivity	8(80%)
Cryptococcal antigen	10(100%)
Culture growing Cryptococcus	5(50%)
Blood Culture	1(10%) grown Cryptococcus
Splenic Biopsy	Cryptococcus
Pulmonary nodule Biopsy	Cryptococcus

Table 3: Comparison of *CSF characteristics of Cryptococcal vs Mixed Meningitis

CSF VALUES (MEAN)	**CRYPTOCOCCAL MENINGITIS(CM) (number = 8)**	**CRYPTOCOCCAL+ TUBERCULOUS MENINGITIS (CM+TBM)(number= 2)**
OPENING PRESSURE	30mmHG	32.6mmHG
GLUCOSE	30.5mg/dl	25.5mg/dl
PROTEIN	72.8mg/dl	135.6mg/dl
TLC	22.7	98.6
LYMPHOCYTES	85.5	96.5
ADA	2.8U/L	11.2U/L
Cryptococcal Antigen Titres	1:213dilution	1:64dilution

*CSF-Cerebrospinal fluid, TLC-Total leucocyte count. ADA-Adenosine deaminase.

The cerebrospinal fluid (CSF) analysis(Table-2) was done in all 100% patients ,the CSF opening pressure in Cryptococcus meningitits(CM) group was 30mmHG compared to Cryptococcus +Tubercular meningitis(CM +TBM) group of 32.6mmHG,and glucose was 30.5mg/dl to 25.5mg/dL, protein 72.8mg/dl to 135.6mg/dl ,Total leucocyte count was 22.7 to 98.6, Lymphocyte was 85.5 to 96.5 ,Adenosine deaminase was 2.8U/L to 11.2U/L, cryptococcal antigen titre was 1:213dilution to 1:64dilution respectively in Cryptococcus to Cryptococcus + TBM group(Table-3). India ink was positive (Figure-3) in 80% patients, Cryptococcal antigen in 100% and 50% had grown Cryptococcus from CSF culture.

Fig-1: Chest radiograph showing(Arrow) pulmonary nodule in right lower lung (Biopsy showed Cryptococcus)

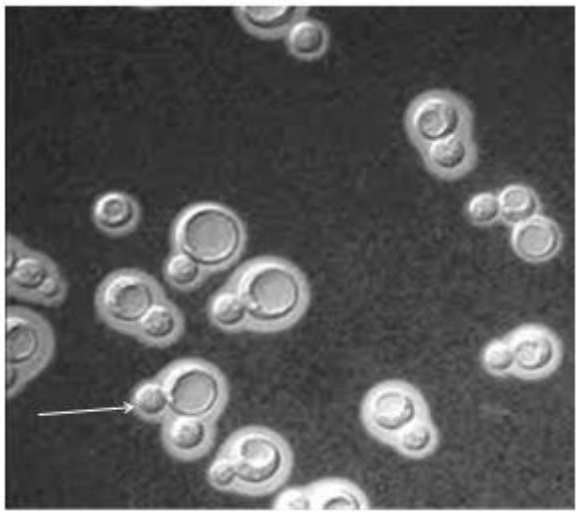

Fig-2: Showing CSF(Arrow) India ink stain budding yeast cells (Cryptococcus)

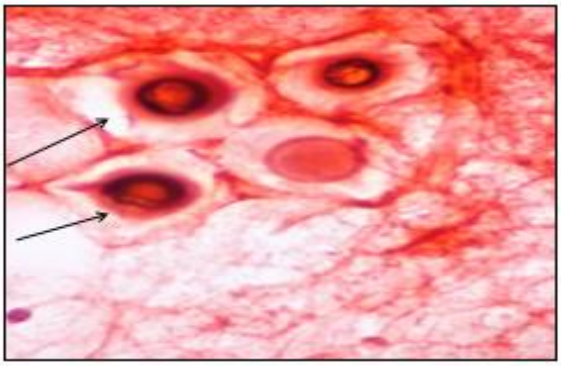

Fig-3: Fine needle aspiration biopsy of pleural based right lung nodule showing (Arrows): Clusters/singly scattered roundbodies with refractile capsule and thin covering

2(20%) patients had disseminated Cryptococcus, 7(70%) patients were HIV positive with mean CD4 count of 73. All the patients received 100% Amphotericin B (0.7mg/kg/day)for 2 weeks followed by Fluconazole 400mg/day for 8 weeks, 20% received steroids for SLE and ITP. 20% patients were on ATT and 70% on ART. 90% patient's recovered.1 (10%) patient died.

DISCUSSION:

Cryptococcus is yeast like fungus with predilection for respiratory and central nervous system [6]. In our study we had 10 patients of Cryptococcus meningitis (CM) over 28 months. Vishwanth *et al.;* [7], and Lakshmi *et al.;* [8] also had 12 patients each in there study, but Shaik *et al.;* [9] had 100 patients over 30 months. The patient age group in our study group was 25 to 60 years with mean age of 41.3 years. But Vishwanath *et al.;* [7], had age group from 28 to 52 years Shaikh *et al.;* [9] from 28 to 55 years, with mean age of 35.4 years. The Male to Female ratio of 70% to 30% similarly Shaikh *et al.;* [9] had 72% males to 28% females but Vishwanath *et al.;* [7] had 58.3% male and 41.7% females in there study.

The commonest symptom in our study was headache in 100% patients almost similarly reported by Satishchandra *et al*[6] 96%, Shaikh *et al.;* [9] 95% but less was reported by, Kalra *et al.;* [10] 80%. Chuk *et al.;* [11] 73%.The common symptom was fever in 80% patients, similarly reported by Satishchandra *et al.;* [6] Vishwanth *et al.;* [7] of 79 % and 78% respectively. But Kalra *et al.;* [10] reported 86% and Chuk *et al.;* [11] 45 %.The next symptom was vomiting in 40% patients which is similarly reported by Chuk *et al.;* [11] but Vishwanath *et al.;* [7] had in 50% patients. The next symptom was altered sensorium in our study was present in 50% patients which is similar to

Satishchandra etal[6] study but more than Chuk *et al.;* [11], Kalral *et al.;* [10], who had 28% and 26% respectively. The commonest sign was neck stiffness in 70% patients which is less than Shaikh *et al.;* [9] in 91% patients.

CSF analysis was done in all patients, CSF India ink for Cryptococcus was positive in 80% similarly reported by Vishwanath *et al.;* [7] in 83% ,but Darras-joy *et al.;* [12], Khanna *et al.;* [13], had positive in 87% ,Shaikh *et al.;* [9] in 90%and Imwidthaya *et al.;* [14] in 91%.CSF Cryptococcal antigen positivity in our study was 100% similarly reported by Imwidthaya *et al.;* [14] and Shaikh *et al.;* [9], but Khanna *et al.;* [13] had positivity of 98%, Darras-joy *et al.;* [12] had positivity of 92%.The CSF culture grown Cryptococcus in 50% patients, which is less than reported by Imwidthaya *et al.;* [14], Darras-joy *et al.;* [12] Khanna *et al.;* [13], Shaikh *et al.;* [9] reported 100% growth of Cryptococcus. The mean CSF pressure in our group was more in CM and CM+ TBM group which is similar to Vishwanath *et al.;* [7]. The mean CSF glucose in CM group was 30.5mg/dl compared to CM +TBM group of 32.6mg/dL, which differs from Shaikh *et al.;* [9] reporting mean glucose of 37mg/dl in CM and 34.7 in CM+TBM group. The mean CSF protein in present CM group was72.8mg/dl and in CM+TBM group was135.6mg/dl which is similarly reported by Shaikh *et al.;* [9]. The mean CSF total leucocyte count was 22.7 in CM group and 98.6 in CM+TBM group, but Shaikh *et al.;* [9] reported 21.1 and 97.4 in CM group and CM+TBM group respectively. The mean CSF lymphocyte count in CM group was 85.5 and in CM+TBM group was 96.5, in our study Shaikh *et al.;* [9] reported 16.6 in CM group and 86.6 in CM+TBM group.

There were 7 patients of HIV in the present group with mean CD4 of 73 which is similarly low CD4 count was reported by Khanna *et al.;* [13] Shaikh *et al.;* [9]. Disseminated Cryptococcus was seen in 20% patients both were immune competent, which is reported similarly by Shankar *et al.;* [15] among them 1(50%) patient had pulmonary involbment as pulmonary nodule similarly reported by Pappas *et al.;* [16]. 1 (50%) patient had splenic lesion in our study. There were 10% patients of SLE in our study similarly Kiertiburanakul *et al.;* [17] had 16% patients in there study. All the patients were treated for Cryptococcus meningitis with Amphotericin +Fluconazole, 90% patients recovered, which was similarly reported by Shaikh *et al.;* [9], but Satish Chandra *et al.;* [16] reported recovery of 68%.There was 10% mortality in the present study which is less than reported by Khanna *et al.;* [13] and Shaikh *et al.;* [9] of 32% and, Vishwanath *et al.;* [7] of 33.3%. Thus early diagnosis and treatment of Cryptococcus meningitis will have better recovery.

CONCLUSION:

Cryptococcus meningitis is a dreaded infection which presents similar to tubercular meningitis its paramount important to diagnose early to prevent mortality.

Limitations:

Main limitation of our study is small number of patients and being retrospective study.

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