Case Report

A Case of Cryptococcal Meningitis in Hiv positive patient in A tertiary care hospital in Kancheepurum district, Tamilnadu, India

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Abstract

Cryptococcal meningitis has been reported in recent years as major life threatening opportunistic infection associated with HIV with a leading cause of mortality ranging from 7 – 15 % around the world & 6% in United States of America. Approximately 25 – 30 % overall mortality rate is encountered in patients suffering from Cyrptococcal meningitis. Among the survivors 40% have significant neurological disorders like loss of vision, decreased mental function, hydrocephalus, cranial nerve palsies with relapse occurring in 25% of cases. It frequently presents as subacute meningitis and is a sporadic infection that affects both immunosuppressed patients (50%) and nonimmunosuppressed patients. This is the first case of cryptococcal meningitis reported in our Hospital in a HIV positive patient reported in our area – Rathinamangalam – Kancheepuram district – during a span of 2 years case study 2013 to 2014.

Key words: Meningitis, Cryptococcus neoformans, Human immune deficiency virus

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Introduction

Cryptococcal meningitis has been reported in recent years as major life threatening opportunistic infection associated with HIV with a leading cause of mortality ranging from 7 – 15 % around the world and 6% in United States of America [1]. Among the survivors 40% have significant neurological disorders like loss of vision, decreased mental function, hydrocephalus, cranial nerve palsies with relapse occurring in 25% of cases [2].

Cryptococcus is yeast like fungus, round to oval in shape with a large polysaccharide capsule ranging from 1 to 30 micron when cultivated in lab [3] and in natural environment it is smaller and poorly encapsulated. There are four capsular types A, B, C and D. Weathered pigeon droppings commonly contain serotypes A or D (*Cryptococcus neoformans*). It has been isolated from litter around the trees of the species *Eucalyptus camaldulesis* and *E. tereticornis* isolates have been so far typed as serotype B. It is the only pathogenic species of human. Var gatti (serotype B and C) has a limited geographic distribution and affects immunocompetent male host in their second decade on life predominantly. Human infection s is contracted through inhalation [4]. *Cryptococcus neoformans* is isolated from the nasopharynx of 50% of the AIDS patients with cryptococcosis and not isolated from AIDS patients without cryptococcosis, supporting inhalation as the mode of entry. Crytococcal meningitis is the AIDs defining illness in 88% of patients.

The median survival without antifungal therapy is 14 days, range (0- 233days). CNS invasion is secondary to haematogenous infection or may represent reactivation of the disease. The time of onset of symptoms for diagnosis ranges from days to months [5].Infection usually presents as a sub acute process. We report a case of cryptococcal meningitis since 60 % of patients with cryptococcosis present as cryptococcal meningitis and is higher in AIDS patients causing 6,00,000 deaths annually particularly in resource limited countries [6].

The predisposing factors are AIDS with CD4 cell count less than 200 cells / microliter, Hodgkin's disease, diabetes and in patients receiving corticosteroids or immunosuppressants. It is usually reported in patients with advanced stage of immunosuppressant with a

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median CD4 cell count below 50 cells / microliter [7]. Incubation period is 14- 25 days. It can cause pulmonary, cutaneous, osseous and visceral cryptococcosis. Diagnosis is made by identifying the organism or its antigen in C.S.F, urine and in blood.

Case Report

A 35 year old farmer by profession was admitted to our medical outpatient department with a complaint of weakness of all the four limbs, gradual in onset and progressive for the past one month associated with low grade fever also for one month.

He had neck pain for past 1 month, visual disturbances on and off, difficulty in bringing the food to mouth - 5 days. On examination, the patient is disoriented, partially responded to commands.

He had signs and symptoms of meningitis, convergent squint and bilateral rectal muscle palsy. Muscle power was 3/5 in all the four limbs. Facial nerve was normal. Sensations were intact and bladder & bowel function were normal.

Routine blood investigations viz., blood sugar, TC, DC, smear study, serum electrolytes, urea, creatinine reports were done and found to be normal. ESR alone was raised. CT plain scan was normal and x-ray chest NAD.

Lumbar puncture fluid was sent to central laboratory with a note that fluid was under increased pressure and with a provisional diagnosis of Tuberculous meningitis. Biochemical analysis of the fluid showed increased protein of 130/ dL and decreased sugar to 18 mg /dL.

Microbiological & pathological investigations were performed.

As a routine, the wet mount preparation carried out which showed the presence of round to oval cells some in budding stage.

Gram stain preparation also revealed the same as round to oval yeast like cells some in budding stage on an average 1-2 cells / oil immersion field (Figure 1).

The India ink preparation was done. A small drop of centrifuged deposit of CSF placed on a glass slide with a drop of India ink with the cover slip on and was observed under 10x and 100x.

Thick walled spherical to oval yeast like cells with a clear halo around was seen and few among them showed budding stage (Figure 2). Provisional diagnosis of crytococcal meningitis was made. The diagnostic yield of C. neoformance in C.S.F. by India Ink preparation is 87- 89%, by C.S.F. fungal culture is 87- 95 % & by blood culture is 75- 100%. [8]

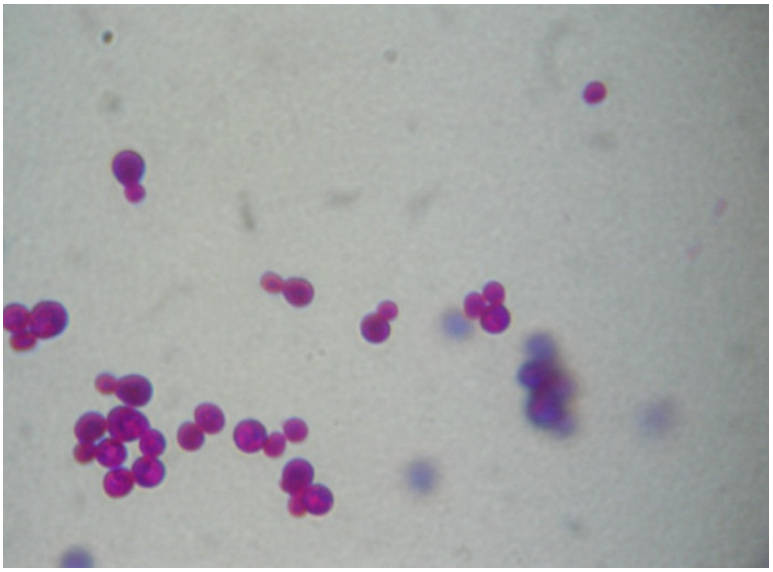

Fig1: Gram's staining of CSF showing budding yeast cells

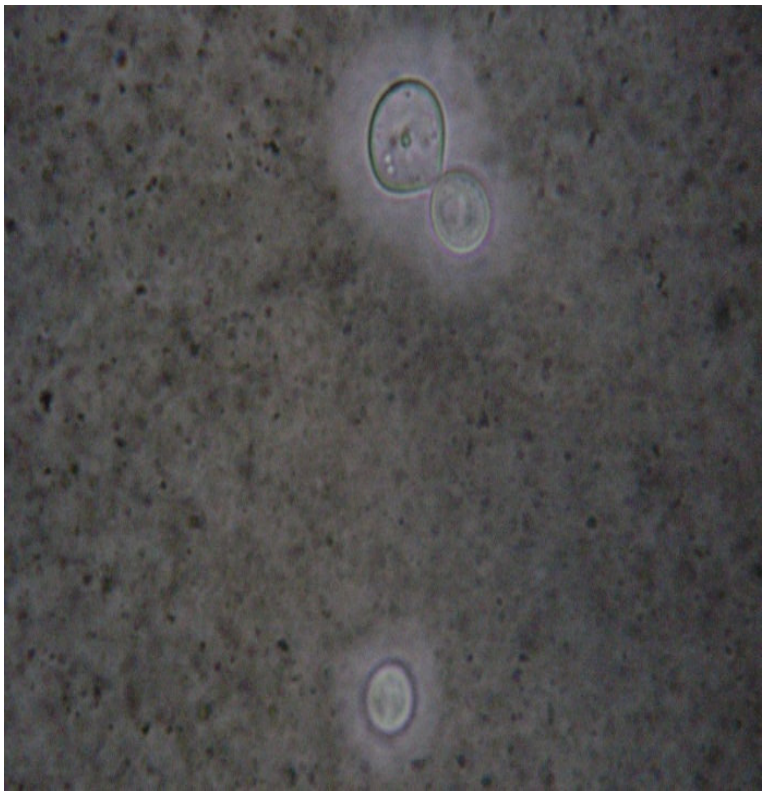

Fig 2: India ink preparation of CSF showing capsulated oval yeast like budding cells

Fig 3: CSF fungal culture showing the growth of *Cryptococcus neoformans*

Patient serum was subjected to HIV testing initially done by rapid test and confirmed positive by routine ELISA HIV antigen detection. CSF deposit was cultured on SDA incubated at $25^{O}C$ for 72 hrs. After 48 hrs it showed smooth white flat, irregular colonies which turned mucoid on third day (Figure 3).

They were identified as *Cryptococcus neoformans* based on gram's stain, cryptococcal capsular polysaccharide stain, urease production, nitrogen assimilation, sugar fermentation and mice pathogenicity test as per standard methods. CSF deposit also sent for antigen detection by latex agglutination test (LAT) which confirmed the diagnosis.

LAT for detection of cryptococcal capsular polysaccharide antigen is a reliable and rapid method for diagnosis of *Cryptococcal neoformans*.

Other investigations like sputum culture for bacterial organisms, Gram's stain smear of sputum, smear for AFB, urine wet mount, motion examination were carried out to rule out other opportunistic infection since the patient is HIV positive .

There was no evidence of other opportunistic infection. Adrenal gland CT scan was done to evaluate the size and consistency of it to rule out adrenal insufficiency which occurs secondary to cryptococcal invasion [8]. CT scan revealed a normal study.

Patient was started on antifugal drug amphotericin B 1 gm I.V. bd and fluocytosine 1 gm I.V. bd. Due to HIV positivity the patient was transferred to Government Tuberculosis and Thoracic Medicine, Tambaram, Sanatorium, Chennai, Tamil Nadu, India where he expired on the third day inspite of adequate treatment.

Discussion

Prevalence of cryptococcosis varies from place to place. According to Kisenge et al. [9] and Kumar et al. [10] India ink preparation is positive in 60% and 70 – 90 % of AIDS patient respectively. Crytococcus infection is more common in male than female probably due to the difference in exposure rather than the host susceptibility [11].

India ink preparation and culture methods are complementary to each other though differences were observed in many studies and both were therefore recommended for an effective diagnosis of cryptococcosis.

The cellular reactions and chemical changes in CSF usually resemble those seen in tuberculous meningitis and hence diagnosis is based on the isolation of organism from the clinical specimen and demonstration of the same after culture.

The frequent clinical presentation of cryptococcosis is meningitis. Cryptococcal meningitis ranked second in frequency among the infectious agents causing neurological disease in AIDS patients.

It is detected in 50% of cases with India ink preparation in cerebrospinal deposit. Detection of cryptococcal antigen in spinal fluid has 90% sensitivity and also is very specific.

Out of 5442 patients who has been screened for HIV in our institution during a span of 2 years (2013 – 2014), 22 patients were positive for HIV which turned out to be 0.40% in our area .This percentage of HIV positivity more or less coincides with the study conducted in India, for a period of 3yrs 2009 – 2012 (0.31% in adults).

All positive patients were screened for various opportunistic infections and this is the first Crptococcal meningitis case that is reported in and around Kancheepuram district.

Conclusion

From our study it is inferred that cryptococcosis is rife in AIDS patients. As the symptoms are not pathognomonic and to minimize the death toll in AIDS affected patients, routine checkup should be integrated with management of AIDS.

We recommend that laboratory diagnosis of cryptococcal infection should be performed in all HIV patients and anti retrovirus treatment to be intensified so that the risk of cryptococcosis is reduced in such cases.

References

1. Speed B, Dunt D. Clinical & host differences between infections with the two varieties of Cryptococcus neoformans. Clin Infect Dis.1995; 21(1):28 – 36.

2. Jain N, Wicks BL , Keller Sm, Fu J, Kesadevall A, Jain P *et al* .Molecular epidemiology of Cryptococcus neoformans strains in India. J Clin Microbiol. 2005: 43(11): 5733- 5742.

3. Aberg JA, Powderly WG. Cryptococcosis. Adv Pharmacol 1997; 37: 215-51.

4. Sukroongreung S, Eampokalap B, Tansuphaswadikul S, Nilakul C, Tantimavanich.S. Recovery of Cryptococcus neoformans patients. Mycopathologia 1998;143(3) :131-134.

5. Mitchell TG, Perfect JR. Cryptococcosis in the era of AIDS – 100yrs after the discovery of Cryptococcus neoformans. Clin Microbiol Rev 1995; 8(4): 515-48.

6. Park B.J,Wannemuehler.K.A,Marstan B.J, Govender N, Pappas P.G, Chiller T.M, Estimation of the current global burden of cryptococcal meningitis among persons living with HIV /AIDS. AIDS. 2009; 23(4): 525- 530.

7. Van der Horst CM, Saag MS, Cloud GA, Hammil RJ, Grabill.R. Sobel JD.Treatment of Cryptococcal meningitis associated with AIDS. N Engl J Med 1997; 337(1): 15-21.

8. Abhilash KPP, Mitra S, Arul JJJ, Raj PM, Balajii V, Kannangai R, Thomas SA, Abraham OC. Changing paradigm of Cryptococcus meningitis: An eight year experience from a tertiary hospital in South India. Ind J Med Micro, 2015;33 (1) 25 – 29.

9. Perfect JR. Crptococcosis. Infect. Dis .Clin. North Am .1989 (1); 3:77 -102.

10. Kisenge PR, Howkins AT, Marvo V.P, Mchele JPD,SwaiNS, Muller A, Houpt ER. Low CD4 count plus coma predicts Cryptococcal Meningitis in Tanzania. BMC Infect Dis 2007; 7:39-43 doi: 10.1186/1471-2334-7-39.

11. Kumar S , Wanchu A, Chakrabarti A, Sharma A, Bambery P *et al* . Cryptococcal meningitis in HIV infected experience from a north Indian Tertiary care center. Neurol India 2008; 56(4): 444- 449.

12. Prasad KN, Agarwal J, Nag VL, Varma AK, Dixit AK, Ayyagari A. Cryptococcal infection in patient with clinically diagnosed meningitis in a tertiary care centre. Neurol India. 2003 Sep;51(3):364-6.

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