Candidal meningitis in disseminated candidiasis by *Candida tropicalis* - A rare case report from India

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Abstract

Introduction: Candida spp. are the normal flora of human body and do not cause CNS disease unless there is some immune disturbance. The prevalence of non albicans species differed significantly in various geographic areas. Candida tropicalis is a species that is now recognized as an important pathogen of debilitated individuals.

Case Report: A 70 year old female complaining of altered sensorium since 7 days with neck stiffness. The patient was also had white plaques in the oral cavity and pharynx. MRI scan showed bilateral cerebral infarcts in pre and post central gyral regions and left thalamus. Thick curvilinear leptomeningeal enhancement along the bilateral parietal regions. Gram stain of centrifused CSF, throat swab showed presence of gram positive, yeast budding cells. Growth was curdy white on Saboraud's dextrose agar and was negative for germ tube test. Blue colored colonies were obtained on Candida chrome agar and considered as Candida tropicalis. HIV status was negative. The patient was administered intravenous liposomal amphotericin B along with regular insulin, levitiracetam lobazam, pheytoin and potassium supplementation along with I.V. fluids. She was discharged from hospital with fluconazole maintenance dose.

Conclusion: Candida tropicalis is now recognized as an important pathogen of debilitated individuals. Subclinical candidal colonization can make the individual more prone to develop systemic infection and disease. Candida tropicalis infects meningeal layers, brain parenchyma and also involves vasculature of brain. Even though Systemic infections with Candida tropicalis may occur as terminal complications, timely evaluation, accurate diagnosis, administration of specific and supportive treatment gives good prognosis.

Keywords: Candida tropicalis, Disseminated, Meningoencephalitis, Amphotericin B.

Introduction

Candida is a large genus of Ascomycetous yeast, consisting of about 150 species, and more than 20 species are clinically important.[1] Candida spp. are the normal flora of human body and do not cause CNS disease unless there is some immune disturbance such as malignancy, steroid and broad spectrum antibiotics treatment, HIV infection, organ transplantation, diabetes, metabolic dysfunction, extremes of age and exposure to invasive procedures.[1-5] Due to the commensal nature of Candida species, most of the times it is found to be a cause of endogenous infection.[6] All candida spp. cause diseases ranging from superficial infections such as oral thrush to invasive disease.[7] Invasive fungal infections have been reported in recent years in 26% of chronically and intensively immuno suppressed patients. Most infections are caused by C.*albicans*, the shift towards treatment resistant non albicans candida (NAC) species is evident in recent years.[5] The prevalence of non albicans species differed significantly in various geographic areas. Candida glabrata was the most frequently isolated species in Western countries whereas C. tropicalis predominated in Asia.[8] A substantial proportion of candidal infections are associated with biofilm formation, especially on the surface of implanted medical devices.[9] Candida tropicalis is a species that is now recognized as an important pathogen of debilitated individuals.[5] Even though rare disseminated Candida tropicalis infections have been reported in inimmunocompromised patients.[10] Here in we report a case of disseminated Candida tropicalis infection in a diabetic, old female, who presented with meningoencephalitis.

Case Report

A 70 year old female came to our hospital as outpatient, complaining of altered sensorium since 7 days. Co existing medical history included that she is a known diabetic (type 2 diabetic mellitus) and hypertensive since many years and taking medication. Before to the present complaint she was having dry cough for one month. She had taken anti bacterials (ceftriaxone 2 gm, twice a day for 3-4 days) as prescribed by local physician. On examination she had neck stiffness and meningeal signs. The patient had white plaques in the oral cavity and pharynx. To evaluate further she was admitted in the hospital at Kammineni neuro care, Kadapa, Andhra Pradesh. On the day of admission she had cluster of seizures (generalized tonic clonic seizures for one day followed by right focal seizures – face, eyelids and upperlimb for 2 days) .Complete blood picture showed leucocytosis (13000cells/µl) with increased lymphocyte count (48 cells/µl), increased ESR and other parameters were normal. Urine examination showed 15 - 20 cells/ high power field and presence of sugar. Random blood sugar level was 270 mg/dl, serum creatinine – 0.9 mg/dl. MRI scan showed bilateralcerebral infarcts in pre and post

central gyralregions and left thalamus. Thickcurvilinear leptomeningeal enhancement along the bilateral parietal regions and central, precentralsulcal regions with adjacent nodular enhancement. To confirm the involvement of meninges and brain parenchyma and to know the infective agent, lumbar puncture was done under aseptic conditions and cerebro spinal fluid was collected in sterile containers. CSF sample was milky. Laboratory investigations revealed presence of 17 cells/cumm and all were lymphocytes; increased sugar level and protein level was normal. CSF, urine, blood, throat swabs were collected and were sent for microbiology investigations. Gram stain of centrifused CSF, throat swab showed presence of gram positive, yeast budding cells and no pseudo hyphae along with inflammatory cells. For CSF sample, Negative staining and Zeihl–Neelsen staining were negative for capsulated organisms and for Mycobacterium tuberculosis respectively. From all the above clinical samples same growth was obtained. Growth was small, white, opaque colonies on blood agar and curdy white colonies on Saboraud's dextrose agar after 18 - 24 hours of incubation at 37°C. Gram stain from the colonies showed gram positive yeast like budding cells. The isolates from the samples were negative for germ tube test.[11] Then the isolates were considered as non albicans candida species. The isolates were further inoculated on Candida chrome agar (Hi media) for speciation and incubated over night at 37°C. Blue colored colonies were obtained from the inoculated plates and were considered as Candida tropicalis. The patient was also tested for HIV status and it was negative. All the laboratory investigations were performed by following standard operative procedures. The patient was administered intravenous liposomal amphotericin B (3.0 mg/kg/ day) for 4 days along with regular insulin, levitiracetam - 1000 mg/day, lobazam – 20 mg/day, pheytoin 300 mg/day in divided doses and potassium supplementation along with I.V. fluids. Regular monitoring was done with blood sugar, serum creatinine, electrolytes and urine output. Serum creatinine was increased (3 mg/dl). Hence amphotericine dose was decreased to 1 mg/kg /day and continued for further 10 days along with fluconazole. Even though there is high mortality as per available literature, patient responded to treatment and started improving clinically. She was discharged from hospital with fluconazole maintenance dose and advised to follow up. She attended the hospital after 3 months. Slight elevation of lymphocytes was observed in differential count. Urine, throat swab and CSF samples were sent to microbiology lab for culture and sensitivity. No growth was obtained from all the above samples.

Discussion

Infection of the central nervous system is usually described under three clinically descriptive headings: meningitis, encephalitis and local suppuration. However, two or rarely three may co- exist, the most frequent combination is meningitis with encephalitis.[2] Clinical presentation of CNS infection by Candida species can be meningitis, meningoencephalitis, and brain abscess.[12]

Candida species pathogenic for humans are also encountered as commensals of humans, particularly in the mouth, stool and vagina.Among the species of Candida, Candida albicans is well known pathogen. There are also non albicans Candida species those are commensals and also as opportunistic organisms. Of all these non albicans Candida species, Candida tropicalis is a species that is now recognized as an important pathogen of debilitated individuals.Subclinical candidal colonization can make the individual more prone to develop further colonization in other mucosal areas, GIT mucosal region and can also disseminate into the blood circulation,[13] which is the most common mode of infection to CNS.[2,14] Fungal meningitis develops insidiously over a period of severaldays or weeks.[12]

In this case the patient was a poorly controlled diabetic and had been administered with broad spectrum antibiotics & prednisolone. Dry cough and chest pain might be due to involvement of respiratory system with the organism. The above factors facilitated the organism to cause disseminated infection. The change from a commensal to a pathogen has been related to altered expression of the virulence factors like secretion of as partyl proteinase 5 and 9, serine proteinases, ability to adhere to host tissue and secretion of other hydrolytic enzymes (phospolipases) together with a debilitation in host defense mechanisms.[5,10] Enzymes such as aspartyl proteinases and help the organism to invade tissues.[15] and helps the organism to cross blood brain barrier.[12]

In the present case Candida tropicalis was isolated from the clinical samples – urine, throat swab, blood and CSF. This represents that candedemia was because of endogenous source of infection. CNS was infected by haematogenus spread. The organism infected meningeal layers, brain parenchyma and also involved vasculature of brain which led to thrombosis and infarction of brain parenchyma. Because of this the patient had multiple focal seizures and complicated further. Soon after admission the patient was on oral Fluconozole. After confirming the diagnosis as candidal meningitis the patient was treated with liposomal amphotericin B (3 mg/kg/day). The most common adverse effect with this anti fungal is nephrotoxicity and is dose related.[16] Hence her serum creatinine was tested periodically and it was elevated. The dose of the drug was decreased as per the renal clearance of creatinine. Fluconozole was also administered as it is having good penetration to brain and CSF.[17] Even though Systemic infections may occur as terminal complications in severe generalized disease, timely evaluation, accurate diagnosis, administration of

specific and supportive treatment made her to discharge from hospital in good condition. As the patient has received fluconazole maintenance therapy, colonization of the organism was cleared and culture of urine and throat swab were negative for the organism after three months.

Conclusion

Candida tropicalis is now recognized as an important pathogen of debilitated individuals. Subclinical candidal colonization can make the individual more prone to develop systemic infection and disease. Candida tropicalis infects meningeal layers, brain parenchyma and also involves vasculature of brain. Even though Systemic infections with Candida tropicalis may occur as terminal complications, timely evaluation, accurate diagnosis, administration of specific and supportive treatment gives good prognosis.

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