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Case report

Infective endocarditis caused by Candida glabrata : A case report

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Abstract

Candida glabrata is unicellular yeast which is a common cause of Candidiasis reported worldwide. It is primarily a commensal of the gastrointestinal tract. This is a case report of an 18 year male who came to the hospital with breathlessness at rest (NYHA class IV), orthopnea and fever for last six months. He was diagnosed with a bicuspid aortic valve 12 years back. On examination, he was febrile and the apex beat was in left 6th intercostal space in mid-clavicular line. Split S_2 and a to and fro murmur was present in right upper sternal border and neo-aortic area. Trans-oesophageal echocardiography revealed bicuspid aortic valve with aortic root abscess and dissection of aortic root. Aortic valve replacement was done. Excised aortic valve and blood culture revealed growth of Candida glabrata which was resistant to Caspofungin in vitro. But according to various sources, the use of CLSI breakpoints for caspofungin is not recommended because of high modal variability. The patient later improved on Caspofungin treatment and was subsequently shifted to voriconazole.

Keywords: Candida glabrata, Infective endocarditis, Caspofungin

Introduction

Candidemia is the most common fungal bloodstream infection. Candida glabrata is the third most common cause of candidiasis. It is a haploid unicellular yeast which is primarily the commensal of the oral cavity and intestines but was designated as a pathogen by Wikham in 1957. Candida glabrata infection is becoming more common nowadays due to use of broad spectrum antifungal treatment, immunosuppression or prolonged hospital stay[1,2]. It is also an important nosocomial infection transmitted by hands of healthcare workers. It is difficult to treat and therefore has high mortality rates[3]. It has intrinsic or acquired resistance to azoles and genes such as YPK1 and KTR2 has been implicated. Now resistance to echinocandins and Amphotericin B has been reported[2]. We report a case of infective endocarditis caused by Candida glabrata which showed resistance to echinocandins in vitro but he responded to caspofungin treatment clinically.

Case report

A 18 year male presented at this superspeciality hospital with breathlessness at rest (NYHA class IV) which persisted even on lying down. Patient was having fever on and off for past six months.

On admission his weight was 50 kg and his height was 165 cm.

On examination, he was febrile (temperature :100.4^{0}F), with tachycardia (PR=110/min), his vitals were normal. There was no cyanosis, jaundice or edema. Lungs were clear. Precordial examination revealed apex beat in left 6th intercostals space in mid-clavicular line. Normal S1 and S2 was split. Consistent click was present. To and fro murmur was present in right upper sternal border and neo-aortic area. Rest of the systemic examination was unremarkable.

Laboratory investigations were as follows: CRP=12mg/L, ESR=34mm at 1st hour, Hb=12.3g/dl, TLC=14000/mm^3 , DLC= P_{55} L_{30} E_{10} M_5 B_0 .

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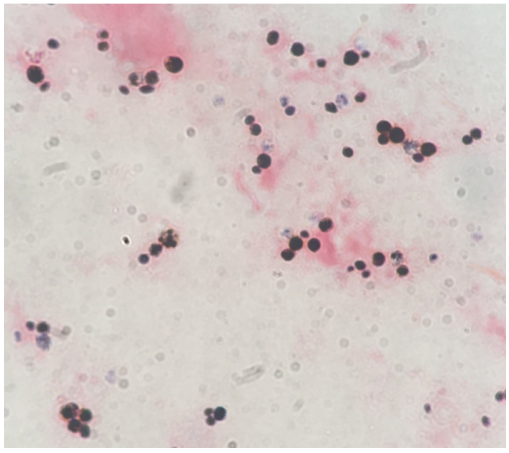
He was diagnosed with a bicuspid aortic valve 12 years back. Since then he had been experiencing breathlessness on performing ordinary activities (NYHA II). The patient had Hepatitis B infection for which he was on treatment for past two years. The present laboratory investigations showed that he was HBsAg negative.

He was admitted in a private hospital two months back with complaints of breathlessness at less than ordinary activities (NYHA IV) and fever for past 2-3 months. Trans-oesophageal echocardiography revealed bicuspid aortic valve with aortic root abscess and dissection of aortic root. Blood culture for fungus revealed growth of Candida spp., for which he was given Voriconazole for a month. However due to lack of facilities for aortic valve replacement in that setup, he was referred to our superspeciality hospital.

On day 2 of admission, blood for fungal culture was sent. On day 5 of admission, the aortic valve replacement was done. The valve was excised along with the vegetations and was sent for culture. Gram stain of the valve tissue revealed few pus cells along with oval gram positive yeast cells around 2-4µm in diameter(Figure 1). Both blood and aortic valve were cultured on Sabouraud's dextrose agar which revealed smooth glistening cream coloured colonies (Figure2). Subculture on Chromagar revealed pink to purple colonies (Figure 3). Further speciation and Antifungal susceptibility testing was done at Microbiology Department, AIIMS, New Delhi. The etiological agent was identified as Candida glabrata which was sensitive to Fluconazole, Amphotericin B, Voriconazole and Posaconazole and was resistant to Caspofungin and Micafungin. But according to various sources, the use of CLSI breakpoints for caspofungin is not recommended because of high modal variability[9]. Caspofungin was started soon after surgery on day 5 along with broad spectrum antibiotic cover and was continued for 15 days.

On Day 8, the patient was mobilised and arterial line, mid drain and foley's cather were removed. The patient was afebrile since then and subsequent blood cultures after 2 weeks were sterile. He was discharged after 2 weeks and was then shifted to oral Voriconazole which was taken for 6 weeks.

GRAM STAIN OF AORTIC VALVE -oval gram positive yeast cells of 2-4µm diameter (FIGURE 1)



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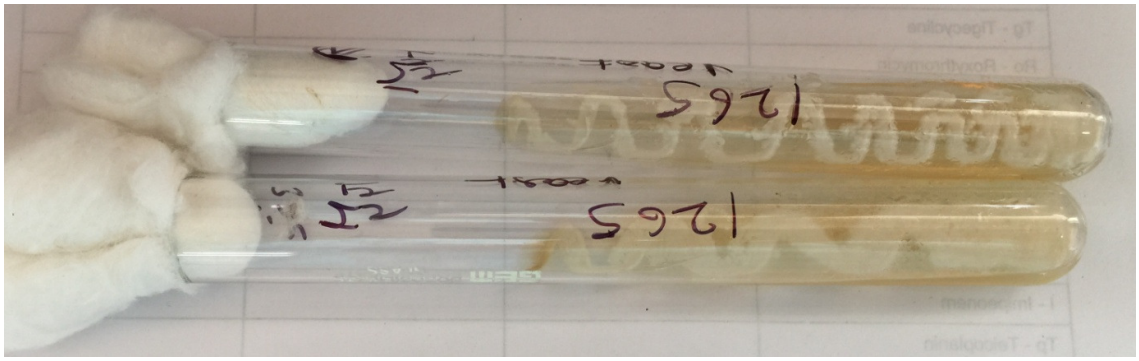
GROWTH ON SDA- smooth glistening cream coloured colonies (FIGURE 2)



GROWTH ON CHROMAGAR – showing pink colonies of Candida glabrata (FIGURE 3)

Discussion

The risk factors for Candida glabrata infections include prior hospitalisation (within 90 days), waning immunity or gastrointestinal surgery[4]. The patient had acyanotic congenital heart disease i.e. bicuspid aortic valve that was diagnosed at 6 years of age. Since 2 years he was on medication for Hepatitis B virus. The underlying heart disease and HBV infection predisposed the patient to infective endocarditis caused by Candida glabrata.

Due to the high mortality associated with infective endocarditis and previous known experiences, the combination of valvular replacement and anti fungal therapy has become the standard approach. However, even with surgical therapy recurrent candida endocarditis has been documented[5]. Echinocandins are the first line treatment for infective endocarditis or candidemia caused by Candida glabrata. Transition to Fluconazole and Voriconazole should be done after the organism is found to be susceptible by in vitro testing[6]. In a study by Lye et al have reported a case of 72 year old man diagnosed with Candida glabrata prosthetic mitral valve endocarditis was treated successfully with fluconazole for 14 days plus caspofungin for 34 days. This patient was continued on oral fluconazole and remained well on follow up at 11 months[7].

According to the SENTRY Antimicrobial Surveillance Program (2006–2010) and Centers for Disease Control and Prevention population-based surveillance (2008–2010), echinocandins resistance was seen in 8-9.3% of isolates[8]. CDC and others have reported increases in bloodstream infections

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caused by echinocandin resistant Candida sp., majority of which were Candida glabrata. Echinocandin resistance is thought to be acquired from prior exposure to echinocandins and mediated through mutations in the FKS genes. This is a problematic situation as very few treatment options are left for Candida glabrata. The alternative drug Amphotericin B is very toxic and poorly tolerated.

There are reports that majority of patients who were resistant to echinocandins had received the same drug earlier[9]. This patient had not received caspofungin before antifungal treatment was started. Susceptibility of caspofungin tested for Candida glabrata has shown a great amount of modal variability (0.031 to 0.5µg/ml) and has therefore lead to the reporting of higher number of resistant isolates. Hence the use of CLSI caspofungin MICs for Candida glabrata is not recommended[10]. Inspite of in vitro resistance to Caspofungin in this case, patient responded well to it and gradually improved.

Acknowledgement:

The strain was identified and anti-fungal susceptibility testing was done at Department of Microbiology, AIIMS, New Delhi.

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