Avens Publishing Group
J Clin Med Case Reports
May 2024 Volume 9, Issue 1

Candida Duobushaemulonii and Trichosporon Asahii in Hematopoietic Stem Cell Transplant Patient: A Rare Bug in Febrile Neutropenic Patient

Open Access Case Report

Journal of
Clinical & Medical Case Reports

Goutham KJ[1], Rubaina A[1], Delvin K[1], Nishit[2], Yesheswini N[2], Aswathy AN[3], and Sachin SJ[4]*

[1]*Department of clinical pharmacology ,HCG cancer Hospital, Bangalore*

[2]*Junior consultant , Department of Hematology & stem cell transplant, HCG Cancer Hospital, Bangalore*

[3]*Department of nursing, Hematology & stem transplant, HCG Cancer Hospital, Bangalore*

[4]*Group Head, Hematology & stem cell transplant, HCG Cancer Hospital, Bangalore*

Address for Correspondence:
Sachin Suresh Jadhav, Group Head Haematology & SCT HCG Cancer hospital Bangalore E-mail Id: drsachinjadhav@gmail.com

Submission: 13 April, 2024
Accepted: 16 May, 2024
Published: 20 May, 2024

Keywords: Candida duobushaemulonii; Trichosporon asahii; Aplastic anemia; Bone marrow; Stem cell transplant; Echinocandins; Azole antibiotics

Abstract

Aplastic anemia is defined by profound reduction in number of bone marrow- Hematopoietic stem cell or Hematopoietic progenitor cell. Fungal infection is the second cause of infections caused in hematopoietic stem cell transplant patients, with viral infection being first and bacterial accounts third. Candida duobushaemulonii is an emerging pathogen, given its resistance to multiple antifungal (to azoles and amphotericin B) it poses a substantial problem of causing invasive infection in immunocompromised setting. The Candida duobushaemulonii requires molecular based method for accurate identification and the conventional/ traditional biochemical method is currently inadequate. Trichosporon asahii is one of the most common species of trichosporon genus, which is a rare fatal emerging fungal infection whose occurrence has increased in immunocompromised patients with blood disease. A 58-year-old patient was diagnosed to have very severe aplastic anemia and febrile neutropenia post stem cell transplant.On basis of Sputum analysis the patient was diagnosed to have aspergillus pneumonia with High resolution computed tomography showing moderate pleural effusion and blood and urine culture revealed presence of fungal infections for which he was then started on antibiotics and antifungal. Blood Culture revealed that Candida duobushaemulonii was resistant to fluconazole and voriconazole and had a good sensitivity to echinocandins hence the patient was started on inj Anidulafungin 100 mg OD for 12 days. After 3 days the patient became hypoxic, required 2 litres of oxygen through face mask to maintain saturation, the urine and blood culture were sent in which urine culture reports showed Trichosporon asahii which was then treated with inj Anidulafungin 100 mg after which the patient was stable and afebrile. Echinocandins are more susceptible to Candida duobushaemulonii whereas azoles and amphotericin B are resistant. EarlyAnalysis of the risk factor to develop Candida duobushaemulonii and Trichosporon asahii priorto stem cell transplant is required and possibly will help in identifying this rare fungal infection by using molecular method rather than by using a traditional method and it also helps in choosing a better prophylactic antifungal.

Introduction

Aplastic anemia is defined by profound reduction in number of bone marrow- Hematopoietic stem cell or Hematopoietic progenitor cell (HSCs/HPCs) which is characterized by hypocellularity or aplastic bone marrow or an "empty" BM, which is been replaced precociously with fat cells. [1] This results in production of defective mature blood cells and peripheral pancytopenia. The incidence rate of aplastic anemia is 1-2 patients per million inhabitants per year. [2]

Although few decades ago Aplastic anemia was considered almost fatal universally, the Aplastic anemia can now be ameliorated and cured by immunosuppressive treatment or by stem cell transplantation. [3]

Hematopoietic stem cell transplant leads to various complications in post- engraftment period due to the immunosuppression caused by radiation, chemotherapy or immunosuppressive agents and type of conditioning treatment (myeloablative or reduced intensity) given prior to transplantation or presence of acute GVHD. [4,5] Were infectious complication (bacterial/viral/fungal) account for most of the morbidity and moratlity. [4] fungal infection stands second in infections (4%) caused in hematopoietic stem cell transplant patients, with viral infection being first and bacterial accounts third. [6]

C. duobushaemulonii is a long lasting but rare and unidentified/ misidentified fungal species. [7–9] Candida being genetically heterogenous forms various complex which are phenotypically identical making its accurate identification difficult. One of such complexes is Candida haemulonii, which is classified into 2 species such as C. Haemuloni sensu stricto and C. duobushaemulonii. [7,8]

C. duobushaemulonii is an emerging pathogen, given its resistance to multiple antifungal (toazoles and amphotericin B) poses a substantial problem causing more invasive infection than previously appreciated. But the species is sensitive to echinocandins. [8]

The candida duobushaemulonii requires molecular based method for accurate identification andthe conventional/ traditional biochemical method is currently inadequate and cannot identify this species accurately. [9]

> 90% of fungal infections in post hematopoietic stem cell transplant patients is caused byCandida, Aspergillosis and

ISSN: 2332-4120

Cryptococcus. Where Candida being main cause for bloodstream infection during the pre- engraftment period of hematopoietic stem cell transplant. [10] Many studies shows that Aspergillus and candida albicans is most common pathogen causing fungal infection in hematopoietic stem cell transplant in patients (where incidence of candida albicans has been decreased with prophylactic use of azole antifungals).[6] But there are no studies showing the Candida duobushaemulonii infection in post hematopoietic stem cell transplant patients.

Although the overall incidence of invasive fungal infection is 4% in hematopoietic stem cell transplant patients, but in patients with allogenic SCT the mortality rate is as high as 13%. [6] Trichosporon asahii formerly called Trichosporon bigelli is one of the most common species of Trichosporon genus, which is a rare fatal emerging fungal infection whose occurrence has dramatically increased in recent years, most frequently in immunocompromised patients with blood disease. [11–13] it is one of the causes of fatal life threatening invasive fungal infections (IFI) occurring in hematopoietic stem cell transplant recipients or in patients with cancer and neutropenia, [12] Soil and water, plants, and colonizing the human mouth, gastrointestinal tract, respiratory tract, vagina, skin, and urine can can serve as a be the major source of habitat for trichosporon species. [13]

The T. asahii has reduced susceptibility to antifungal therapy in immunocompetent and immunocompromised patients especially in patients receiving broad- spectrum antibiotics for a long period, in heavy alcoholics, or in diabetic patient even in healthy individuals [14]

Case Report

A 58-year-old male patient came to Outpatient department with complains of a non-healing ulcer on his leg and epistaxis two months back. The patient was found to have pancytopenia. Later he developed fever after which sputum analysis was done which showed aspergillus pneumonia and blood and urine culture revealed presence of fungal infections for which he was then started on antibiotics and antifungals.

Later he was shifted to our hospital, in view of severe hypoxia, the patient was shifted to ICU and was managed symptomatically. The patient was diagnosed to have very severe aplastic anemia with HB of 6.8 g/dl and febrile neutropenia. The patient was started on inj Teicoplanin, inj Ceftazidime avibactum and inj Azetreonam along with anti-fungal prophylaxis of Isavaconazole and viral prophylaxis tab acyclovir which was then changed to tab Valacyclovir. Herpes simplex virus liver showed hypo dense lesion in the liver. Bone marrow aspiration and biopsy was done which revealed hypo cellular marrow. The patient was known case of paroxysmal nocturnal hemoglobinuria and hepatitis B positive and tab Tentide AF was added for further management.

Bronchoscopy BAL was done which revealed a poly-microbial infection with Aspergillus,Staphylococcus aureus, Klebsiella pseudomonas candida, Enteriobacteriaceae. The same antimicrobials were continued throughout the ICU admission the patient received inj Teicoplanin for 17 days, inj Ceftazidime avibactum and inj Azetreonam for 14 days along with anti-fungal prophylaxis of Isavaconazole for 20 days which was then changed to tab Voriconzole and viral prophylaxis tab Acyclovir which as then changed to tab Valacyclovir 1 gm and continued. He was then planned for matched identical allogenic stem cell transplantation with his donor 9/10 match. The patient underwent stem cell infusion and achieved neutrophil engraftment on day +12 and platelet engraftment on day +15.

Table 1: Urine culture and sensitivity report for microbial infection

Gram Stain	Pus cells seen, shows gram positive budding yeast like cells
CULTURE	
organism	Trichosporon asahii (candida non albicans)
comment	Kindly corelate with clinical findings

MICROBIOLOGY REPORT	
Test name	Urine culture and sensitivity
Specimen type	urine
MB number	UC-1383/22

Table 2: Blood culture and sensitivity report for microbial infection

MICROBIOLOGY REPORT		
Test name	Blood culture and sensitivity (aerobic)	
Specimen type	Blood	
MB number	B-1371/22	
Specimen name	Central line	
CULTURE		
Organism	Candida duobushaemulonii	
ANTIBIOTIC SUSCEPTIBILITY		
Organism	Candida duobushaemulonii	
ANTIBIOTIC NAME	INTERPRETATION	MIC
AMPHOTERICIN B	SENSITIVE	0.5
FLUCYTOSINE	SENSITIVE	<= 1
FLUCONAZOLE	RESISTANT	32
VORICONAZOLE	RESISTANT	>= 8

Patient on day -2 of transplant developed febrile episodes, so cultures and molecular panel were sent. Molecular PCR and blood culture revealed Candida duobushaemulonii and urine culture showed growth of Aeromomas hydrophila and E. coli (Multi Drug Resistant), in view of febrile neutropenia the patient was started on inj Ceftazidime avibactum 2.5 g for 16 days and the patient was stable. Cultures revealed that Candida duobushaemulonii was resistant to fluconazole and voriconazole and had a good sensitivity to echinocandins hence the patient was started on injAnidulafungin 100 mg OD for 12 days. After 12 days the blood cultures showed no growth for any organisms and the patient was stable and afebrile which showed that anidulafungin monotherapy was effective enough for the treatment of candida infections.

After 3 days (day +11 of transplant) the patient became hypoxic, required 2 litres of oxygen through face mask to maintain saturation, post which repeat high-resolution computed tomography (HRCT) was done which showed interval increase in pleural effusion. The urine and blood culture were sent in which urine culture reports showed Trichosporon asahii which was then treated with inj Anidulafungin 100 mg after which the patient was stable and afebrile.

The patient was started with inj anidulafungin 100 mg OD after

ISSN: 2332-4120

the first molecular pannel report, after 5 days of treatment repeat blood cultures were obtained which did not show any organisms.Since urine culture developed Trichosporon asahii, inj Anidulafungin 100 mg OD was continued for a total of 7 days which showed a significant improvement in the patient as well as urine culture showing no growth of any organisms. hence a total course of 12 days of inj Anidulafungin 100 mg OD was effective for treatment of multi species fungal infection in blood as well as urine for a post hematopoietic stem cell transplant patient with significant improvement in patient health.

Discussion

Although few decades ago Aplastic anemia was considered almost fatal universally, the Aplastic anemia can now be ameliorated and cured by immunosuppressive treatment or by stem cell transplantation. [3] A study suggest an improved outcome can be seen in acquired aplastic anemia patients with hematopoietic stem cell transplantation when compared with conventional immunosuppressive therapy.[5]

Hematopoietic stem cell transplant leads to various complications in post- engraftment period due to the immunosuppression caused by radiation, chemotherapy or immunosuppressive agents, use of corticosteroids and type of conditioning treatment (myeloablative or reduced intensity) given prior to transplantation or presence of acute/ chronic GVHD or through catheter and central/peripheral insertion. [4-6]

These complications include myelosuppression with neutropenia, anemia, thrombocytopenia,sinusoidal obstruction syndrome (SOS), mucositis, acute or chronic GVHD, gram positive/ gram negative infections, HSV, CMV, Candida and Aspergillosis. [5,10] Were infectious complications account for most of the morbidity and mortality. [4] The recovery and reconstitution of immune system is more rapid in autologous hematopoietic stem cell transplant than in allogenic hematopoietic stem cell transplant. This is because the allogenic hematopoietic stem cell transplant Recipients undergoes a long-term immunosuppressive therapy for chronic GVHD. [4] hence, more negative outcomes of fungal infections are seen in allogenic hematopoietic stem cell transplant when compared with autologous hematopoietic stem cell transplant.[6]

C. duobushaemulonii is a long lasting but rare and unidentified/ misidentified species. [7-9] The misidentification of these species may be related to the inaccurate biochemical methods used to identify the species, thus requiring molecular based methods to guarantee its accurate identification. [7,9] According to study by Irene Jurado-Martin et al, they discovered that the isolate identified in 1996 as C. intermedia by API®ID 32C was actually a C. duobushaemulonii. [7] Neutropenia and mucosal damage present during the pre-engraftment period are risk factors to develop invasive candidiasis. As the neutropenia and mucosal skin loss recovers in post engraftment period the risk of developing candida infection decreases. [4] The incidence of fungal infections in post engraftment period can be reduced by use of prophylactic antifungal for 1 month following transplant, usually with fluconazole or voriconazole (in patients with high risk profile). [5,10] in pre- engraftment period the prophylactic antifungal treatment has been shifted from amphotericin B to itraconazole, voriconazole and echinocandins, which have shown better efficacy and decreased adverse effects. [6]

According to literature the candida species especially the complex candida species showed the reduced susceptibility to fluconazole, itraconazole and Amphotericin B, but where susceptible to echinocandins making it the best treatment options for infections caused by complex candida species. The tendency of complex species to develop resistance to azoles, echinocandins and amphotericin B increase the importance of identifying these rare or uncommon species. [7,8] Trichosporon asahii is one of the most common species of Trichosporon genus, which is a rare fatal infection whose occurrence has dramatically increased in recent years, most frequently in immunocompromised patients with blood disease. [11–13]

The growth of Trichosporon asahii was most common in urine culture (27.9%) when compared to other cultures, hence affecting urinary system most frequently (28.6%). The review shows the risk factor associated with this fungal infection was antibiotics use being highest, followed by invasive medical equipment, chemotherapy, neutropenia, bacterial infection, ICU hospitalization, glucocorticoids use, immunosuppressant and trauma being the least frequent risk factor. [11]

Conclusion

To accurately identify the species which forms complex for example Candida duobushaemulonii in our case which is one of the complexes of Candida haemulonii it is required to use molecular based method of identification. This will lead to a proper study of its prevalence, susceptibility and resistance pattern. Echinocandins are more susceptible to Candida duobushaemulonii whereas azoles and amphotericin B are resistant. Early Analysis of the risk factor to develop Candida duobushaemulonii and Trichosporon asahii prior to stem cell transplant is required and possibly will help in identifying this rare fungal infection by using molecular method rather than by using a traditional method and it also helps in choosing a better prophylactic antifungal rather than only focusing on most common fungal infections such as candida albicans or Aspergillosis.

Acknowledgement

The Authors wish to thank Department of Hematology, Department of Clinical Pharmacology,HCG Cancer Hospital.

Author Contributions

All authors helped in data acquisition, manuscript preparation, read and approved the final manuscript, and guarantees the integrity of the study.

References

1. Medinger M, Drexler B, Lengerke C, Passweg J (2018) Pathogenesis of Acquired Aplastic Anemia and the Role of the Bone Marrow Microenvironment 8: 1-10.
2. Passweg JR, Aljurf M (2013) Treatment and hematopoietic SCT in aplastic anemia 48: 161.
3. Young NS, Calado RT, Scheinberg P (2006) Review in translational hematology Current concepts in the pathophysiology and treatment of aplastic anemia 108: 2509-2519.
4. Cho S, Lee H, Lee D (2018) Infectious complications after hematopoietic stem cell transplantation: current status and future per- spectives in Korea. 33: 256-276.
5. Hematopoietic Stem Cell Transplantation - StatPearls - NCBI Bookshelf [Internet]. [cited 2022 Jun 26].

ISSN: 2332-4120

6. Rahi MS, Jindal V, Pednekar P, Parekh J, Gunasekaran K, Sharma S, et al. (2021) Fungal infections in hematopoietic stem-cell transplant patients: areview of epidemiology diagnosis, and management. Ther Adv Infect Dis [Internet]. 2021 [cited 2022 Jun 26] 8.

7. Jurado-mart I, Marcos-arias C, Tamayo E, Guridi A, Groot PWJ De, Quind G, et al. (2020) Candida duobushaemulonii : An Old But Unreported Pathogen 6: 374.

8. Ramos R, Caceres DH, Perez M, Garcia N, Castillo W, Santiago E, et al. (2018) Emerging Multidrug-ResistantCandida duobushaemuloniiInfections in Panama Hospitals: Importance of LaboratorySurveillance and Accurate Identification. J Clin Microbiol 56: e00371-18.

9. Frias-De-Leon MG, Martinez-Herrera E, Acosta-Altamirano G, Arenas R, Rodríguez-Cerdeira C (2019) Superficial candidosis by Candida duobushaemulonii: An emerging microorganism. Infect Genet Evol 75: 103960.

10. Marty FM, Baden LR (2008) Infection in the Hematopoietic Stem Cell Transplant Recipient. Hematop Stem Cell Transplant. 2008: 421-448.

11. Li H, Guo M, Wang C, Li Y, Fernandez AM, Ferraro TN, et al. Epidemiological study of Trichosporon asahii infections over the past 23 years 148: e169.

12. Sah R, Soin A singh, Chawla S, Wadhwa T, Gupta N (2019) Disseminated Trichosporon asahii infection in a combined liver-kidney transplant recipient successfully treated with voriconazole. Immunity, Inflamm Dis [Internet] 7: 125-129.

13. Sugita T (2011) Trichosporon. In: The Yeasts. Elsevier Pp: 2015-2061.

14. Go SE, Lee KJ, Kim Y, Choi JK, Kim YJ, et al. (2018) Lee DG. Catheter-related Trichosporon asahii bloodstream infection in a neutropenic patient with myelodysplastic syndrome. Infect Chemother 50: 138-143.