

Invasive fungal infection by *saprochaeta capitata* in an immunocompromised child- a case report from cancer hospital in Pakistan

Seemal Aslam,¹ Salma Muhammad Abbas,² Nida Safdar³

Abstract

Saprochaeta Capitata is an emerging fungus known to cause life-threatening infections in immunocompromised patients. Here, we describe the case of a 4-year-old male child seen in Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, after obtaining informed consent from the parents. He had Pre-B ALL (acute lymphoblastic leukaemia) and contracted this infection during induction chemotherapy. With the use of dual antifungals, he was able to survive this otherwise fatal fungal infection.

Keywords: *Saprochaeta capitata*, invasive fungal infection, dual antifungal therapy, immunocompromised.

DOI: 10.47391/JPMA.9506

Submission completion date: 16-03-2023

Acceptance date: 26-08-2023

Introduction

Saprochaeta Capitata and *Saprochaeta Clavata* are urease-negative, non-fermenting, ascomycetes yeast. In contrast to *Trichosporon* whose distribution is worldwide, *Saprochaeta* has been found mostly in Europe. *Saprochaeta Capitata* is a ubiquitous yeast found in soil, water, and dairy products and is also recovered from the human respiratory and gastrointestinal tract¹. Previously *Saprochaeta Capitata* was known as *Geotrichum Capitatum*, and *Blastoschizomyces Capitatus*. At present correct taxonomic name for this fungus is *Saprochaeta Capitata*.

With the advancement in the treatment strategies for cancer and bone marrow transplantation, rate of opportunistic infections has increased and identification methods to the species level have improved with techniques such as Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) Mass Spectrometry, M13 microsatellite PCR (Polymerase Chain

.....
^{1,2}Department of Infectious Diseases, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, ³Department of Microbiology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.

Correspondence: Seemal Aslam. Email: seemal.aslam01@gmail.com

ORCID ID. 0009-0008-6902-7531

Reaction), and gene sequencing².

From our subcontinent, few cases have been described in India^{3,4}, but to our knowledge, this is the first case to be reported from Pakistan.

Case Report

A 4-year-old boy presented on 20-10-2022 in Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, with history of intermittent fever recorded up to 38.6°C, associated with bleeding from mouth, progressive pallor, and non-inflammatory joint pains. Prior to the presentation, he was given steroids and methotrexate for his joint pains for a period of 6 months. All treatments were stopped 2 months before presenting to us. On his initial examination, he was pale, had cervical lymphadenopathy, splenomegaly, and a left testicular enlargement.

His baseline total leucocyte count was $34 \times 10^3/\mu\text{L}$ (Normal $4.52-10.93 \times 10^3/\mu\text{L}$) with 95% blast cells and 5% lymphocytes (20.2-40%). Bone marrow flow cytometry showed 86% of total cellular events expressing CD45+, CD58++, CD10++, CD19+, CD34++, CD81++, CD66c+ and CD38 variables (- to +). This population was negative for CD20 and all other antigens, suggesting a diagnosis of Pre-B ALL. His baseline blood culture and CSF studies were negative for any infections. Echocardiography and ultrasound abdomen was normal. However, an ultrasound of scrotum showed left moderate hydrocoele, and slightly enlarged testes, although both testes were unremarkable for any invasive lesion. His chemotherapy started with 3 drug inductions per Regimen A of UKALL 2019 Guidelines.⁵

Induction chemotherapy included Intrathecal 12 mg Methotrexate on Day 1, 0.885 mg, intravenous Vincristine on day 2, 590 mg intramuscular Pegaspargase on day 4. He was having daily fever spikes with a maximum fever recorded up to 39.5°C. We initially started Piperacillin/tazobactam 1270 mg Q6 hourly empirically.

On Day 4, he developed grade 2 mucositis for which Fluconazole 40 mg once daily was started. On the 5th day, he became neutropenic (absolute neutrophil count <500) and started having more frequent fever spikes. On induction day 6 and febrile neutropenia day 1, gram-



Figure-1: Yeast-Like Colonies: Creamy-White and Moist, on Sabouraud Dextrose Agar (SDA).

negative rods were detected in the blood culture. Patient was shifted to intravenous Meropenem 290 mg Q 8 Hourly from Piperacillin/tazobactam. On induction Day 7, yeast was identified in the blood. On Sabouraud Dextrose agar, it showed white to cream coloured colonies (image 1).

Under the light microscope, it showed arthroconidia and hyphal elements as shown in (image 2).

His aspergillus galactomannan assay was 1.06 index. Intravenous Amphotericin B 13 mg once daily was started. Colistin was added on day 9 as gram negative rods were finally identified as E Coli resistant to carbapenems. He was given intravenous Vincristine 0.885mg on the same day as a part of induction chemotherapy.

Blood cultures from the day 8th, 9th, 10th grew E coli with similar resistance pattern. The yeast in the blood was finally identified as *Saprochaeta Capitata*. The identification was done using Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry (MS). After identification of *Saprochaeta Capitata*, we added Voriconazole, 100 mg Q12 hourly and workup for source was started. CT scans of sinuses, chest, abdomen, and pelvis were done. There was complete opacification of bilateral maxillary, ethmoid and sphenoid sinus, but there were no bony erosions or air fluid level suggestive of fungal infection. On chest CT scan, consolidation patches in the lower lobe of the right lung and upper lobe of the left lung were seen, although bronchoalveolar lavage did not reveal any organism, fungal hyphae, or any inflammatory cells. His echocardiography was performed again, which was also unremarkable.

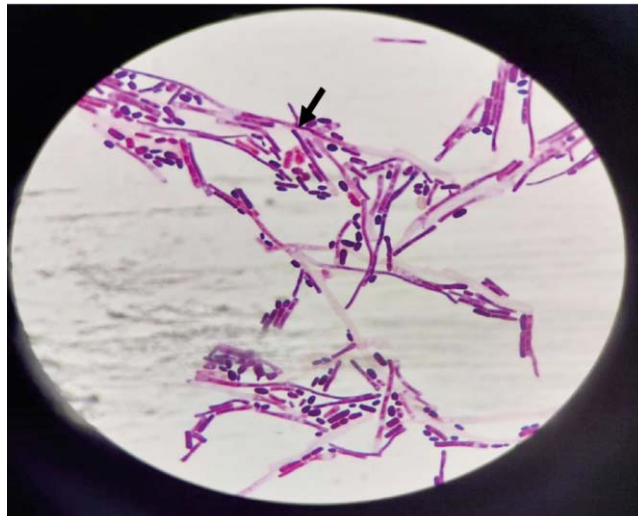


Figure-2: Variable-Length Rectangular Arthroconidia with Rounded Ends, Some Transitioning to Spherical Shape (Black arrow).

Up to this point, patient was having daily with multiple spikes up to 39°C, but 24 hours after starting Voriconazole fever started to space out, initially 24 hours gap, and then a 48 hours afebrile period. Before starting Voriconazole, 2 more blood cultures grew *Saprochaeta Capitata* while being on Amphotericin, but after adding Voriconazole no more yeast cultured from his blood. We continued this combination therapy for 14 days after his 1st negative blood culture. And continued Meropenem with Colistin to clear E coli from his blood cultures.

Antral sinus lavage was also planned later which revealed necrotic material with septate hyphae but fungal culture was negative. Keeping this finding in mind, Voriconazole alone was continued for this fungal sinusitis after clearing *Saprochaeta Capitata* from his blood with combination of antifungals.

Day 15 intrathecal methotrexate was stopped due to septicaemia and fungaemia. He received on day 16 Vincristine and on day 18 gaspargase. Dexamethasone tapering, as a part of induction chemotherapy was started early on day 22 due to sepsis. Later he showed good response to chemotherapy. His end of induction MRD (minimal residual disease) was negative, and he was discharged from hospital. Patient was admitted later with osteomyelitis caused by E coli that was also successfully treated. Currently consolidation chemotherapy is planned for him as per Regimen A of UKALL 2019 guidelines.

Discussion

To the best of our knowledge, this is the first case report of *Saprochaeta Capitata* infection from Pakistan. Invasive fungal infections are increasingly diagnosed in

immunocompromised patients. In contrast to candida species and mould like aspergillus, *Saprochaeta Capitata* rarely causes invasive fungal infections. It is commonly detected in haematological malignancies (70%) especially in patients with prolonged neutropenia (absolute neutrophils count < 500 mm³). Its pathogenesis is like other candida species yet it has some distinguished features. Like candida, it can colonize skin, gastrointestinal and respiratory tract but unlike candida infection, it is intrinsically resistant to echinocandins⁶. It most commonly infects lungs and can present in a variety of ways like productive cough and dyspnoea. Radiological features are variable and may include pleural effusion, ground glass haze, pulmonary infiltrates or parenchymal micronodules. Lung involvement is less commonly seen in candidiasis. Nodules can also be seen in other organs like liver and spleen. Skin lesions include generalised maculopapular rash, or erythematous nodules or papules. Galactomannan assay is often positive in *Saprochaeta* infections.⁷

Our patient also had haematological malignancy and persistent fever which was not responding to antibiotics. He had respiratory involvement as evident by his CT scan of the chest but bronchoalveolar lavage did not reveal any yeast growth. This could be best explained by the fact that we had commenced our patient on Amphotericin B by that time. Our patient had indwelling catheters which has an association with invasive candidiasis, however its association with *Saprochaeta Capitata* invasive infection has seldom been reported. Its diagnosis requires advance diagnostic methods which may not be readily present at all centres. Clinical features consistent with invasive candidiasis but not responding to Caspofungin can be highly suggestive of invasive *Saprochaeta Capitata*.

There are no formal guidelines for the management of *Saprochaeta Capitata* invasive infections yet. It is intrinsically resistant to Echinocandins. There is considerable data suggesting that it well responds to combination of Amphotericin B and azoles⁸. However, resistance to Amphotericin B and Itraconazole has been reported in literature⁹. Contrary to this fact, Voriconazole has good efficacy against this infection as it is a recommended treatment in literature¹⁰. This is much consistent with our case; fever did not respond to Amphotericin B and on starting Voriconazole, the infection was cleared.

Conclusion

Invasive spirochaetal capitata is an opportunistic infection commonly found in haematological

malignancies and carries high mortality. Diagnosis requires sophisticated molecular assay which may not be readily available. Voriconazole in combination with Amphotericin is the preferred regimen for these infections up till now.

Consent: Written consent was obtained from the parents of the patient for publishing the case.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Duminuco A, Vetro C, Maugeri C, Mauro E, Palumbo GAM, Parisi MS, et al. *Saprochete capitata*: Emerging Infections from Uncommon Microorganisms in Hematological Diseases. *Hematol Rep* 2022;14:67-72. doi: 10.3390/hematolrep14020011.
2. Keene S, Sarao MS, McDonald PJ, Veltman J. Cutaneous geotrichosis due to *Geotrichum candidum* in a burn patient. *Access Microbiol* 2019;1:e000001. doi: 10.1099/acmi.0.000001.
3. Pamidimukkala U, Kancharla A, Sudhaharan S, Gundeti S, Mandarapu S, Nagalla VK, et al. Isolation of the Rare Opportunistic Yeast *Saprochaete capitata* from Clinical Samples-Experience from a Tertiary Care Hospital in Southern India and a Brief Review of the Literature. *J Clin Diagn Res* 2017;11:DC36-42. doi: 10.7860/JCDR/2017/30339.10669.
4. Bansal N, Devarajan V, Ghafur K A, Sethuraman N, Sree V L. Breakthrough *Saprochaete Capitata* infections among patients with hematological malignancies. *Leuk Lymphoma* 2018;59:1762-3. doi: 10.1080/10428194.2017.1402306.
5. Children's Cancer and Leukaemia Group (CCLG). Acute lymphoblastic leukaemia (ALL). [Online] 2019 [Cited 2023 October 23]. Available from URL: <https://www.cclg.org.uk/Acute-lymphoblastic-leukaemia-ALL>
6. Sasi S, Parakadavathu R, Abukhattab M, Hashim SM, Al-Maslamani M. Disseminated Geotrichosis in Prolonged Neutropenia. *J Case Rep* 2020;10:116-9. DOI: 10.17659/01.2020.0031.
7. Bonini A, Capatti C, Parmeggiani M, Gugliotta L, Micozzi A, Gentile G, et al. Galactomannan detection in *Geotrichum capitatum* invasive infections: report of 2 new cases and review of diagnostic options. *Diagn Microbiol Infect Dis* 2008;62:450-2. doi: 10.1016/j.diagmicrobio.2008.08.008.
8. Lignieres G, Guitard J, Alby-Laurent F, Rambaud J, Bigot J, Morand K, et al. Antifungal combination therapy for invasive fungal infections in a paediatric oncology and haematology department: A retrospective analysis of practice. *J Mycol Med* 2022;32:101276. doi: 10.1016/j.mycmed.2022.101276.
9. Dannaoui E, Lortholary O, Raoux D, Bournoux ME, Galeazzi G, Lawrence C, et al. Comparative in vitro activities of caspofungin and micafungin, determined using the method of the European Committee on Antimicrobial Susceptibility Testing, against yeast isolates obtained in France in 2005-2006. *Antimicrob Agents Chemother* 2008;52:778-81. doi: 10.1128/AAC.01140-07.
10. Girmenia C, Pagano L, Martino B, D'Antonio D, Fanci R, Specchia G, et al. Invasive infections caused by *Trichosporon* species and *Geotrichum capitatum* in patients with hematological malignancies: a retrospective multicenter study from Italy and review of the literature. *J Clin Microbiol* 2005;43:1818-28. doi: 10.1128/JCM.43.4.1818-1828.2005.