New Microbiologica, 46, 4, 400-406, 2023, ISSN 1121-7138

CASE REPORT

18S rRNA sequencing and homology analysis of post-traumatic bloodstream infection with *Saprochaete clavata* (*Magnusiomyces clavatus*) and a case report

Wei Jia, Guang Chen, Wanxiang Li, Jie Ma, Xue Zhao

Department of Clinical Laboratory, Weifang People's Hospital, Weifang, Shandong Province, China

SUMMARY

We present a case of bloodstream infection with *Saprochaete clavata* following an abdominal steel impact injury in a 52-year-old man, whose non-healing abdominal wound was also highly suspected of being caused by *Saprochaete clavata*. *Saprochaete clavata* is a very uncommon fungal pathogen. Our case is distinctive in that previous reports have typically involved immunocompromised, malignant, or leukemic patients. In contrast, our case involved a middle-aged man in good health who had ileal perforation repair for gastrointestinal perforation. Post-surgery, *Saprochaete clavata* was isolated from the incision exudate and blood samples. The pathogen was characterized and the drug sensitivity test was performed, and based on their results a clinical treatment plan was devised. The combination antifungal treatment comprising voriconazole and caspofungin significantly controlled the patient's infection and gradually healed the wound. Therefore, early isolation and characterization are essential because invasive fungal diseases have a high death rate.

Received July 27, 2023 *Accepted* December 01, 2023

INTRODUCTION

Saprochaete clavata, formerly known as *Geotrichum clavatum* and now referred to as *Magnusiomyces clavatus*, is a rare fungal pathogen characterized by its arthrosporic yeast-like filamentous fungus nature. Medical researchers have identified *Saprochaete clavata* as an emerging pathogen primarily affecting immunocompromised, malignant, or leukemic patients (Buchta *et al*., 2019; Del Principe *et al*., 2016). The mortality rate associated with *Saprochaete clavata* infections has been reported to be 60%-80% (Stanzani *et al*., 2019). This fungal pathogen is predominantly reported in Europe, possibly attributed to contaminated dairy products or medical devices (Vaux *et al*., 2014). *Saprochaete clavata* can be isolated from various sites in the human body, including blood, sputum, bronchoalveolar lavage fluid, sterile body parts, and the digestive tract (Menu *et al*., 2020), making individuals susceptible to invasive fungal infections (IFIs). This report focuses on a patient with a bloodstream infection caused by *Saprochaete clavata*. The biological characteristics of the strain were investigated, followed by 18S rRNA sequencing and analyses. Overall, this study's findings provide valuable insights into microbiologic testing and clinical diagnosis of *Saprochaete clavata* infections.

Key words:
Saprochaete clavate, bloodstream infection, 18S rRNA sequencing.

Corresponding author:
Xue Zhao
E-mail: WFRYWSW@163.com

CASE REPORT

Case information and strain source

A 52-year-old man in good physical condition, no history of infectious diseases including hepatitis and tuberculosis, and no close contact with individuals with such conditions, was admitted to our hospital. The patient's vaccination records were carefully maintained locally, and no missed vaccinations or adverse reactions were observed. Additionally, the patient showed no history of food or drug allergies, surgical procedures, or blood transfusions. Moreover, the patient had not travelled to or resided in domestic or foreign regions with a high risk of outbreaks within three weeks prior to onset of the disease. Additionally, no documented instances of contact with diseased or deceased livestock or poultry were found, the patient did not consume unclean food, and worked at a construction site. The patient had a persistent cutting pain in the left lower abdomen following an injury from a rebar hitting his abdomen; the trauma showed the characteristics of a closed blunt-force-impact injury. He did not exhibit symptoms such as nausea, vomiting, haematemesis, tarry stool, abdominal distension, diarrhoea, or consciousness disorder. Plain abdominal

radiographs taken at a local hospital showed no abnormalities. However, after 2 days, the patient experienced unbearable abdominal pain that was considerably worse than before, affecting the entire abdomen and accompanied by vomiting of gastric contents. An emergency abdominal computed tomography scan performed at an external hospital revealed a significant amount of free gas in the abdomen, suggestive of gastrointestinal perforation. Furthermore, a high likelihood of small bowel rupture was recorded in the epigastric region, indicating peritonitis and abdominopelvic effusion. After emergency surgery, intraoperative investigation showed that the rupture was 1.5 cm in diameter and was located approximately 100 cm from the ileocecal region. Consequently, the patient underwent surgery for ileal perforation repair and abdominopelvic cavity drainage. He was postoperatively transferred to the intensive care unit (ICU; external unit) for the management of infectious shock, acute diffuse peritonitis, ileal perforation repair, hypoproteinaemia, and acute renal insufficiency. Ascitic fluid was cultured to check the presence of *Klebsiella pneumoniae*, and blood cultures were negative. He received relevant treatments, including ventilator-assisted respiration with endotracheal intubation, the combination of imipenem with vancomycin for anti-infection (exact dosage unknown), blood transfusion, and continuous renal replacement therapy. After 3 days, the patient developed a fever (39.1°C), dyspnoea, progressive decrease in oxygen saturation, and loss of consciousness. As a result, he was transferred to our ICU for immediate intervention. He required extracorporeal membrane oxygenation due to acute respiratory distress syndrome to improve oxygenation and reduce lung burden.

When the patient was admitted to the hospital, blood cultures were negative and the abdominal surgical incision dressing was dry; however, the surgical incision was at a high risk of infection because of the occurrence of acute diffuse peritonitis. Slight remission was observed after anti-infective and symptomatic treatment using the combination of biapenem (0.6 g, q12h, 1 day), tigecycline (50 mg, q12h, first dose 100 mg, 39 days), and vancomycin (0.25 g, q6h, 4 days). On the 16th day of hospitalization, extracorporeal membrane oxygenation (ECMO) was discontinued, and the patient was again in critical condition with a high fever of 39.2°C, a pulse rate of 122 beats/minute, and 27 respirations/minute. Blood cultures suggested a fungal-induced bloodstream infection, with a fungal D-glucan test result of 190 pg/ml (reference: <60 pg/ml) and an *Aspergillus* galactomannan serum index of 2.34 (with a value of <0.5 indicating a negative result). The patient's abdominal incision was opened, the pus obtained from the abdominal surgical incision exudate culture exhibited mixed growth, involving *Klebsiella pneumoniae*, yeast-like fungi (identified by mass spectrometry as consistent with blood culture results), and *Viridans streptococcus*. The combination antifungal treatment comprising voriconazole (intravenous, 200 mg q12h, 3 days; nasal administration, 200 mg bid8, 13 days; oral, 200 mg bid8, 20 days) and caspofungin (intravenous, first dose 70 mg, 50 mg qd8h for 22 days) significantly controlled the patient's infection. Blood cultures were negative after administering the antifungal drug combination for five consecutive days, followed by twice at one-week intervals. The patient was admitted to the hospital with a central venous catheter (CVC), which was replaced every two weeks for two consecutive times, and culture results for the tip removed from the CVC were negative. The patient was hospitalized for 88 days. At the time of discharge, granulation growth was observed at the incision, with the closed skin edge on the left side and the unhealed right side of about 2 cm, which required long-term medication changes to heal. Approximately 23 days after discharge, the outpatient follow-up showed that the incision had healed.

Our purpose in reporting this case is to provide a reference for laboratory identification and clinical treatment. We have received and archived written patient consent forms in this study, along with approval by the ethics committee of Weifang People's Hospital, Weifang, Shandong, China, for the use of specimens from human patients.

Fungal cultures

On hospital day 16, blood samples were collected from the patient and cultured using a bilateral two-bottle strategy with the Mérieux blood culture

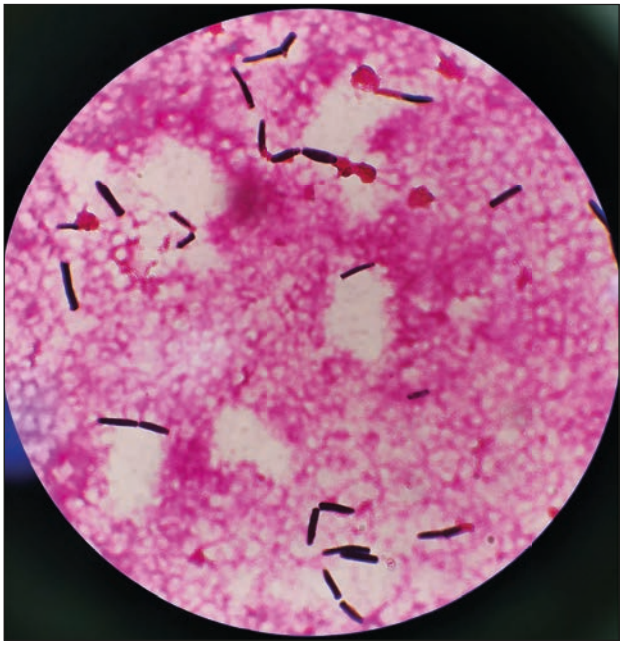

Figure 1A - *Morphology of Saprochaete clavata colonies from blood smears in positive bottles (Gram staining ×1000).*

Figure 1B - *Saprochaete clavata colonies on the Columbia blood agar plate (48 h).*

device (3D/ALERT). After 35 h, the culture of the left aerobic bottle showed a positive result. Subsequently, gram staining microscopic examination of blood smears was performed (*Figure 1A*). The organism exhibited atypical fungal morphology. The strain was then transferred to Columbia blood agar, *Candida* chromogenic agar, and Sabouraud's agar plates. After 48 h of incubation, colonies on the Columbia blood agar plate appeared as a white cottony growth (*Figure 1B*). Colonies on the *Candida* chromogenic agar exhibited a white, dry appearance with a slight pinkish-purple colour (72 h) (*Figure 1C*). On the Sabouraud's agar plate, colonies exhibited a white, ground glass-like appearance after 72 h (*Figure 1D*). Gram staining microscopic examination was performed again (*Figure 1E*), revealing the presence of fungal arthrospores with round or rectangular ends.

Routine identification and sensitization tests

Strain identification was carried out using VITEK MS automatic microbiological mass spectrometry detection system (bioMérieux, Marcy-l'Étoile, France) following the instrument's standard operating procedures. The strain was identified as *Saprochaete clavata* with a 99.9% confidence coefficient (*Figure 2*). Antifungal drug susceptibility testing using the bioMérieux yeast-like fungi drug susceptibility kit (broth dilution method) revealed the following results: 5-fluorocytosine, 4 µg/ml; amphotericin B, 0.5 µg/ml; fluconazole, 2 µg/ml; itraconazole, 0.125 µg/ml; and voriconazole, 0.125 µg/ml. Quality control strains of Candida albicans ATCC 14053, Candida krusei ATCC 6258, and Candida parapsilosis ATCC 22019 were included.

18S rRNA sequencing

Sequencing of the 18S rRNA amplification product resulted in a 1639 bp sequence (*Figure 3*). Subsequently, a BLAST alignment was performed on the NCBI database using the accession number MK834559.1. The alignment showed 100% similarity between the 1639 bp sequence and *M. clavatus* strain GEOT-23.

Figure 1C - *Saprochaete clavata colonies on the Candida chromogenic plate (72 h).*

Figure 1D - *Saprochaete clavata colonies on Sabouraud dextrose agar (72 h).*

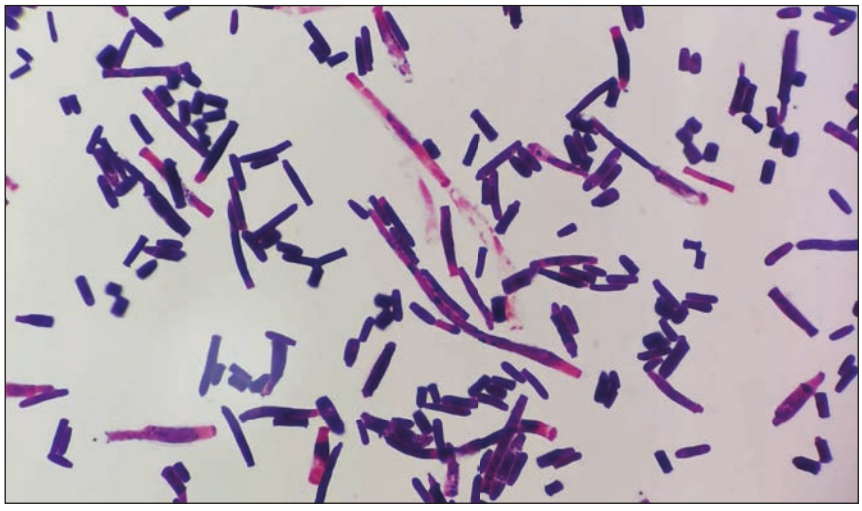

Figure 1E - *Gram staining of Saprochaete clavata hyphae and arthroconidia.*

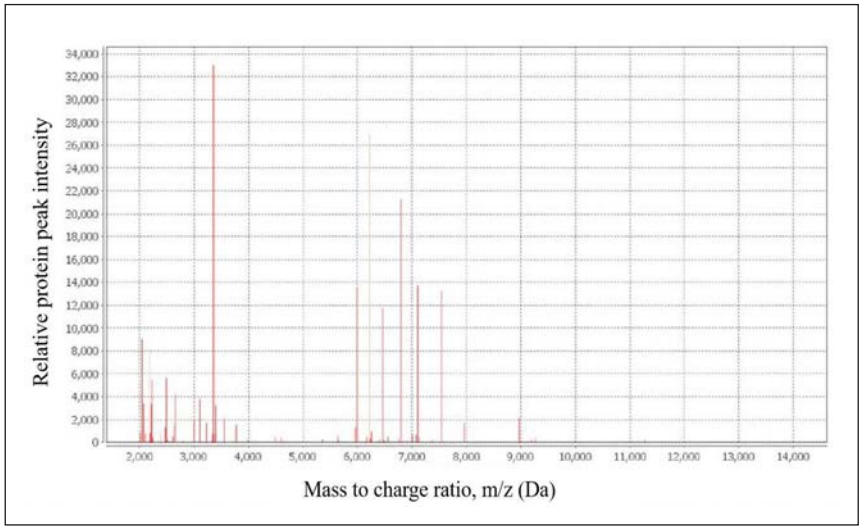

Figure 2 - *Matrix-assisted laser desorption ionization time-of-flight mass spectrometry analysis.*

ATCTGGTTGATCCTGCCAGTAGTCATATGCTTGTCTCAAAGATTAAGCCATGCATGTCTA
AGTATAAGCGTTATACAGTGAAACTGCGAATGGCTCATTAAATCAGTTATAGTTTATTTG
AAGATAATAACCATTAGGATAACCGTGGTAATTCTAGAGCTAATACTTGCTTCTAGGCTT
TATTAGATATGAATCACAATAACTTCAGATCGTTCTGACGCTTCATTCAAATTTCTGCCC
TATCAGCTAGATGGCAAGGTATTGGCTTGCCATGGCAGCAACGGGTAACGGGGAATTAGG
GTTCGATTCCGGAGAGGGAGCCTGAGAAACGGCTACCACATCCAAGGAAGGCAGCAGGCG
CGCAAATTACCCAATCCCGACACGGGGAGGTAGTGACAATAAATAACAATGCGGGGCCTA
TGGTCTTGCAATTGGAATGAGAACACGATAAATAGGTTAACGAGGAGCAAAAAGAGGGCA
AGTCTGGTGCCAGCAGCCGCGGTAATTCCAGCTCTTTTAGTGTATATTAAATTTGTTGCA
GTTAAAAAGCTCGTAGTTGATATTCGGGGGATGGAACTTCTTTATTGAGGTTTCCTGAAC
CTAGGTCTGTATATTTGCAGACCAGTTACTTTGAGAAAATTAGAGCGCTTAAAGCAGTCA
TTGAATACGTTAGCATGGAATAACAATAGGACGACGTTTCTCTTGTGGGAACATCGTAAT
TGATTAAAAGGGACAGTCGGGGGCATCAGTATTCAGGAGCTAGAGGTGAAATTCTTAGAT
TTCCTGAAGACTAACTAATGCGAAAGCATTTGCCAAGGATGTCTTCATTAATCAAGAACG
AAAGTTAGGGGATCGAAGACGATCAGATACCGTCGTAGTCTTAACAGTAAACTATGCCGA
TAGAGTGGAGGATGGACTATTTAATCTATTCTCCGCTCAAGCGAAAGCAGTTGGTTCTGG
GGGGAGTATGGTCGCAAGGCTGAAACTTAAAGGAATTGACGGAAGGGCACCACCAGGAGT
GGAGCCTGCGGCTTAATTTGACTCAACACGGGGAAACTCACCAGGTCCAGACACAATGAG
GATTGACAGATTGAGAGCTCTTTCAAGATTTTGTGGGTGGTGGTGCATGGCCGTTCTTAG
TTGGTGGAGTGATTTGTCTGCTTAATTGCGATAACGGACGAGATTTTGGCGAGCAGTTGG
TGAAGTTACATTTTGTAGCGGATCCGTCTACTCGGACAGCTGATGCAAATCAGAGGAAGC
GAGGCAATAACAGGTCTGTGATGCCCTTAGACGTTCTGGGCCGCACGCGCGCTACACTGA
CTCGGTCAGCGAGATCCTTTGTTTAGCAACACGGGGGAACTTGTAAACCGGGTCGTGCTG
GGGATAGAGCCTTGCAATTATTGCTCTTGAACGAGGAATTCCTAGTAAGCGCAAGTCATC
AGCTTGCGTTGATTACGTCCCTGCCCTTTGTACACACCGCCCGTCGCTACTACCGATTGA
ATGGCTTAGTGAGGGTTTTGGAGAGCTTTTGAAGTAGGGCAACCTACCTCATATGCTCAA
AGATAGACAAACTTGGTCATTTAGAGGAAGTAAAAGTCGTAACAAGGTTTCCGTAGGTGA
ACCTGCGGAAGGATCATTC

Figure 3 - *18S rRNA gene sequences of the 1639 bp clinical isolate.*

Homology results: the phylogenetic tree

The clinical isolate was designated as ZJ-1. The 18S rRNA sequences of ZJ-1 were submitted to GenBank and subjected to sequence homology alignment using the BLAST online tool. Ten 18S rRNA sequences were selected, including sequences obtained in this study and related sequences from previous studies, with homology greater than 95%. The *Yarrowia lipolytica* sequence (MW281693) was used as the outgroup. The multiple-sequence alignment and phylogenetic tree construction were performed using the neighbour-joining method with the K2P model executed in MEGA 7.0. The resulting phylogenetic tree was visualized and annotated using FigTree v1.4.2 software.

The phylogenetic tree of *Saprochaete clavata* and related taxa was constructed using the neighbour-joining method, including 10 sequences from 7 species within the *Magnusiomyces* genus. The tree exhibited a stable topology, divided into two distinct clades, with the outgroup *Yarrowia lipolytica* (MW281693) at the base. Strain ZJ-1 (*Magnusiomyces clavatus*), located at the top of the tree, formed a sister clade with *Magnusiomyces clavatus* (MK834559) and then clustered with *Magnusiomyces capitatus* (NG070302). The clade located at the base of the phylogenetic tree was divided into two subclades, with *Magnusiomyces tetraspermus* and *Magnusiomyces magnusii* clustering in one subclade. The two *Magnusiomyces ingens* strains clustered together and then formed another subclade by clustering with *Magnusiomyces ovetensis* and *Magnusiomyces starmeri*, respectively. The phylogenetic tree is presented in *Figure 4*.

Mass spectrometry identification confirmed 100% homology between *Saprochaete clavata* and the sequencing result of *Magnusiomyces clavatus*. A literature review indicated that the fungal nomenclature of this species has undergone several changes due to modifications in fungal terminology. The original name, *Geotrichum clavatum*, has been confirmed to refer to the same fungus (Lo Cascio *et al*., 2020).

DISCUSSION

IFIs can be caused by various fungi, including *Candida*, *Cryptococcus*, and *Aspergillus*. These infections are commonly observed in patients with conditions such as leukaemia (Sezgin Evim *et al*., 2022), human immunodeficiency virus infections (Mihon *et al*., 2013), undergoing chemotherapy (Mishra *et al*., 2020), organ transplants (Leitheiser *et al.*, 2020; Kennedy *et al*., 2021), and prolonged usage of antibiotics and steroids (Hou *et al*., 2023; Boretti *et al*., 2022). IFIs can disrupt the body's normal microbial community, creating an opportunity for fungi to colonize and cause infection. In the case of this patient, infectious shock occurred following surgery for an abdominal rebar collision injury, compromising the immune system's ability to defend against fungal pathogens. Additionally, due to multiple bacterial infections, the patient received restricted-grade antibiotics such as biapenem, tigecycline, and vancomycin. The combination of postoperative immunocompromise after severe trauma and exposure to restricted antibiotics contributed to the onset of IFI.

Saprochaete clavata was initially described in 1809 (Styczynski *et al*., 2023). Infections caused by *Saprochaete clavata* are rare in mainland China. In 2018, *Saprochaete clavata* caused an IFI in a 10-year-old child with acute lymphoblastic leukaemia, leading to its classification as *Geotrichum clavatum* (Liu *et al*., 2019). Interestingly, both the aforementioned child and the present patient experienced gastrointestinal perforations and underwent ileal repair. However, the timing of the fungal bloodstream infection differed. The child developed a fungal bloodstream infection concurrently with gastrointestinal disorders, whereas the present patient, who was previously healthy, suffered major trauma resulting in perforated intestine, along with subsequent gastrointestinal disease, and ultimately developed a bloodstream infection with this fungus.

Saprochaete clavata can lead to small-scale disseminations, single-centre outbreaks, or multicentre out-

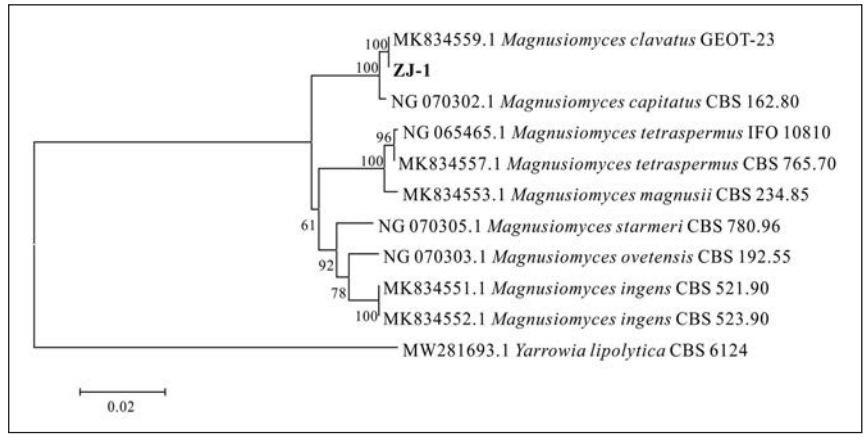

Figure 4 - *Phylogenetic tree of ZJ-1 strains. Yarrowia lipolytica is an outgroup strain, and other strains named using accession numbers were downloaded from the NCBI database.*

breaks. Sophie Vaux *et al.* reported several cases of rapidly fatal infections caused by *Saprochaete clavata* occurring in three French healthcare facilities within a short timeframe. Whole-genome sequencing analysis of 30 isolates was conducted to identify the source of the infections. It was suggested that *Saprochaete clavata* might be transmitted via contaminated medical equipment, and localized outbreaks were observed in haematology wards (Vaux *et al*., 2014). Certain strains of *Saprochaete clavata* have been isolated from human sputum, faeces, and skin microflora. Camus et al. documented a case of *Saprochaete clavata*-induced sepsis in a French patient with acute myeloid leukaemia. As a member of the intestinal flora, this fungus caused peritonitis, subsequently leading to sepsis, liver dysfunction, and multi-organ failure (Camus *et al*., 2014). Furthermore, Menu Estelle *et al.* reported *Saprochaete clavata* infections in nine patients at a cancer centre in Marseille, France. The source of contamination was identified as a dishwasher with a faulty heating system (Menu *et al*., 2020). We hypothesized that the patient in the present study might have an endogenous infection. If *Saprochaete clavata* is isolated from the patient's respiratory or gastrointestinal flora, particularly when cultured from drainage fluid in cases of peritonitis, heightened vigilance is required to address the risk of invasive infections caused by this fungus. Timely administration of antifungal therapy can be instrumental in saving lives.

The treatment of *Saprochaete clavata* infections poses challenges due to the lack of clinically effective therapeutic strategies and a standardized criterion for determining the fold point of antifungal drugs. Therefore, the determination of minimum inhibitory concentration (MIC) *in vitro* in the laboratory was crucial for the clinical use of drugs. In our laboratory, the isolate in the present study showed high MIC values for 5-fluorocytosine and fluconazole, whereas it showed low MIC values for amphotericin B, itraconazole, and voriconazole. A study has suggested that Saprochaete clavata usually exhibits *in vitro* resistance to echinocandins and fluconazole; thus, amphotericin B with or without flucytosine is the recommended first-line treatment against the fungal infection, and source control and immune system recovery are key to successful treatment (El Zein *et al*., 2020). Massimiliano Leoni *et al.* have reported that a combination of amphotericin B and voriconazole appears to be more effective in restricting infection without causing organ toxicity in patients (Leoni *et al*., 2018). However, in this case, the patient had acute kidney injury with markedly elevated urea levels, which could potentially lead to renal failure. Therefore, the application of amphotericin B was deemed inappropriate. After three days of initial treatment with voriconazole, the patient's condition remained critical. Subsequently, combination therapy with caspofungin was added, leading to infection control. The combination of voriconazole and caspofungin has shown efficacy in treating *Candida* infections and coccidioidomycosis (Yang *et al*., 2022; Levy *et al*., 2013). Many national and international studies have recommended not to use echinocandin, caspofungin, a member of the echinocandin class, because the fungus exhibits resistance to this drug *in vitro* and *in vivo* (El Zein *et al*., 2020), and its action mode depends on the inhibition of β-1,3-glucan synthase, a necessary enzyme for synthesizing β-1,3-glucan (Wagener, J., 2017), the main carbohydrate of the fungal cell wall, and 1-3-β-D-glucan, a constituent of most fungal cell walls, except for *Spliceolates* and *Cryptococcus spp*. (Skubic, J., 2020). Herein, some studies have argued that the addition of caspofungin probably exerted an additive or synergistic effect owing to the presence of voriconazole (Keene, S., 2019). Additionally, the patient in the present study suffered from a closed blunt trauma injury, acute renal insufficiency, a non-healing postoperative incision infection, and a bloodstream *S. clavata* infection, which was successfully treated using the combination of voriconazole and caspofungin in clinical settings. Thus, whether the voriconazole and caspofungin combination can be used as a therapeutic strategy for patients who are intolerant to amphotericin B or poor treatment with voriconazole alone needs further investigation.

Early identification of *Saprochaete clavata* infections is crucial for rapid diagnosis and treatment. Clinical microbiology laboratories can achieve more accurate identification by using mass spectrometry. Regular updating of mass spectrometry databases is essential for detecting this fungus. Additionally, sequencing of the internal transcribed spacer region allows differentiation at the species level (El Zein *et al*., 2020; Kangül *et al*., 2020). Monitoring serologically relevant infection surveillance indicators is important. The galactomannan test is recommended as an early indicator for suspected diagnosis and efficacy evaluation (Liu *et al*., 2019). A positive galactomannan test for invasive candidiasis, along with a typical clinical course, should raise suspicion of a potential *Saprochaete clavata* infection (Styczynski *et al*., 2023). Infections caused by rare fungi such as *Saprochaete clavata* have a poor prognosis. Despite appropriate antifungal treatment, there is a high mortality rate. In this report, the patient was treated in the ICU for 42 days and then transferred to the general gastrointestinal surgery department to continue with treatment. Overall the patient was hospitalized for 88 days and was successfully treated. His entire treatment course was challenging. Therefore, early identification and prompt intervention in cases involving rare and specific pathogens are crucial for saving patients' lives.

Author contributions

X.Z. designed the study. W.J., W.X.L. and G.C. conducted the study, collected the data and prepared the article. J.M. and X.Z. provided valuable advice and edited the article. All authors have read and agreed to the published version of the manuscript.

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Acknowledgements

We thank Bullet Edits Limited for the linguistic editing and proofreading of the manuscript.

References

Boretti A. (2022). Steroids Induced Black Fungus Infection in India During the May 2021 COVID-19 Outbreak. Indian journal of otolaryngology and head and neck surgery: official publication of the Association of Otolaryngologists of India. **74** (Suppl. 2), 3216-3219.

Buchta V., Bolehovská R., Hovorková E., Cornely O.A., Seidel D., et al. (2019). Saprochaete clavata Invasive Infections-A New Threat to Hematological- Oncological Patients. *Frontiers in microbiology*. **10**, 2196.

Camus V., Thibault M.L., David M., Gargala G., Compagnon P., et al. (2014). Invasive Geotrichum clavatum fungal infection in an acute myeloid leukaemia patient: a case report and review. *Mycopathologia*. **177** (5-6), 319-324.

Del Principe M.I., Sarmati L., Cefalo M., Fontana C., De Santis G., et al. (2016). A cluster of Geotrichum clavatum (Saprochaete clavata) infection in haematological patients: a first Italian report and review of literature. *Mycoses*. **59** (9), 594-601.

El Zein S., Hindy J.R., Kanj S.S. (2020). Invasive Saprochaete Infections: An Emerging Threat to Immunocompromised Patients. *Pathogens* (Basel, Switzerland). **9** (11), 922.

Hou S., Wang X., Yu Y., Ji H., Dong X., et al. (2023). Invasive fungal infection is associated with antibiotic exposure in preterm infants: a multi-centre prospective case-control study. *The Journal of hospital infection*. **134**, 43-49.

Kangül H., Özcan N., Uzuner N., Mete M., Mert Erginer U. (2020). Saprochaete clavata (Geotrichum clavatum) septicemia in a patient with multiple myeloma; An emerging case from Southeastern Turkey. *Current medical mycology*. **6** (4), 66-69.

Keene S., Sarao M.S., McDonald P.J., Veltman J. (2019). Cutaneous geotrichosis due to Geotrichum candidum in a burn patient. *Access microbiology*. **1** (1), e000001.

Kennedy C.C., Pennington K.M., Beam E., Razonable R.R. (2021). Fungal Infection in Lung Transplantation. Seminars in respiratory and critical care medicine. **42** (3), 471-482.

Leitheiser S., Harner A., Waller J.L., Turrentine J., Baer S., et al. (2020). Risk Factors Associated With Invasive Fungal Infections in Kidney Transplant Patients. *The American journal of the medical sciences*. **359** (2), 108-116.

Leoni M., Riccardi N., Rotulo G.A., Godano E., Faraci M., et al. (2018). Magnusiomyces clavatus infection in a child after allogeneic hematotopoetic stem cell transplantation: Diagnostic and therapeutic implications. *Medical mycology case reports*. **23**, 65-67.

Levy E.R., McCarty J.M., Shane A.L., Weintrub P.S. (2013). Treatment of pediatric refractory coccidioidomycosis with combination voriconazole and caspofungin: a retrospective case series. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. **56** (11), 1573-1578.

Liu X., Zhou W., Jiang Y., Kuang L. (2019). Invasive Fungal Infection Caused by Geotrichum clavatum in a Child with Acute Leukemia: First Documented Case from Mainland China. *Japanese journal of infectious diseases*. **72** (2), 130-132.

Lo Cascio G., Vincenzi M., Soldani F., De Carolis E., Maccacaro L., et al. (2020). Outbreak of Saprochaete clavata Sepsis in Hematology Patients: Combined Use of MALDI-TOF and Sequencing Strategy to Identify and Correlate the Episodes. *Frontiers in microbiology*. **11**, 84.

Menu E., Criscuolo A., Desnos-Ollivier M., Cassagne C., D'Incan E., et al. (2020). Saprochaete clavata Outbreak Infecting Cancer Center through Dishwasher. *Emerging infectious diseases*. **26** (9), 2031-2038.

Mihon C., Alexandre T., Pereira A. (2013). Clinical experience in invasive fungal infections: multiple fungal infection as the first presentation of HIV. *Clinical drug investigation*. **33** (Suppl. 1), S37-S40.

Mishra P., Agrawal N., Bhurani D., Agarwal N.B. (2020). Invasive Fungal Infections in Patients with Acute Myeloid Leukemia Undergoing Intensive Chemotherapy. Indian journal of hematology & blood transfusion: an official journal of Indian Society of Hematology and Blood Transfusion. **36** (1), 64-70.

Sezgin Evim M., Tüfekçi Ö., Baytan B., Ören H., Çelebi S., et al. (2022). Invasive Fungal Infections in Children with Leukemia: Clinical Features and Prognosis. Turkish journal of haematology: official journal of Turkish Society of Haematology. **39** (2), 94-102.

Skubic J., Taghavi S., Castillo-Angeles M., Ramsis R., Salim A., et al. (2020). Detecting Invasive Fungal Disease in Surgical Patients: Utility of the (13)-β-d-Glucan Assay. *Surgical infections*. **21** (5), 461-464.

Stanzani M., Cricca M., Sassi C., Sutto E., De Cicco G., et al. (2019). Saprochaete clavata infections in patients undergoing treatment for haematological malignancies: A report of a monocentric outbreak and review of the literature. *Mycoses*. **62** (12), 1100-1107.

Styczynski T., Sadlok J., Richert-Przygonska M., Debski R., Zalas-Wiecek P., et al. (2023). Infection With Saprochaete Clavata in Children After Hematopoietic Cell Transplantation. *Journal of pediatric hematology/oncology*. **10**. 1097/MPH.0000000000002686.

Vaux S., Criscuolo A., Desnos-Ollivier M., Diancourt L., Tarnaud C., et al. (2014). Multicenter outbreak of infections by Saprochaete clavata, an unrecognized opportunistic fungal pathogen. *mBio*. **5** (6), e02309-14.

Wagener J., Loiko V. (2017). Recent Insights into the Paradoxical Effect of Echinocandins. *Journal of fungi* (Basel, Switzerland). **4** (1), 5.

Yang Q., Liu Z., Wang Y., Xie J., Zhang K., et al. (2022). In vitro synergistic antifungal activities of caspofungin in combination with fluconazole or voriconazole against Candida species determined by the Etest method. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases. **122**, 982-990.