Infection and Drug Resistance

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

Successful Treatment of Lomentospora Prolificans Infection Following Allogeneic Hematopoietic Stem Cell Transplantation: A Case Report and Literature Review

Yi-Han Yang[1,*], Chun Di[2,*], Hao Zheng[1], Ya Luo[1], Ao-Ran Zhang[1], Tong Su[1], Xiao-Dong Mo[1], Yu-Qian Sun[1], Yu Wang[1], Meng Lv[1,3]

[1]Peking University People's Hospital, Peking University Institute of Hematology, National Clinical Research Center for Hematologic Disease, Beijing Key Laboratory of Cell and Gene Therapy for Hematologic Malignancies, Beijing, People's Republic of China; [2]Department of Clinical Laboratory, Peking University People's Hospital, Beijing, People's Republic of China; [3]Clinical Trial Institution and Clinical Research Ward, Peking University People's Hospital, Beijing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Meng Lv, Clinical Trial Institution and Clinical Research Ward, Peking University People's Hospital, No. 11 Xizhimen South, Beijing, 100044, People's Republic of China, Tel +86-10-88324637, Email drlvmeng@bjmu.edu.cn

Abstract: Lomentospora prolificans is an opportunistic fungal pathogen known for its intrinsic multidrug resistance. This pathogen poses a significant challenge in immunocompromised individuals, particularly patients with hematologic malignancies. We present a case of a 27-year-old male diagnosed with adverse-risk acute myeloid leukemia (AML) who developed pulmonary Lomentospora prolificans infection following therapy for positive measurable residual disease (MRD) and severe chronic graft-versus-host disease (cGVHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Despite the pathogen's multidrug resistance and the typically poor prognosis associated with invasive infections in immunocompromised hosts, the patient achieved sustained remission and favorable outcome. This study systematically reviews Lomentospora prolificans infections following HSCT by analyzing 37 reported cases from 24 studies identified through a PubMed search. The majority of cases had acute myeloid leukemia as the most common underlying disease. Disseminated infections were predominant (83.8%), with frequent pulmonary and central nervous system involvement. Antifungal treatment strategies largely involved combination therapy, yet outcomes remained poor, with an overall survival rate of only 13.5%. These findings highlight the critical need for novel therapeutic approaches and early intervention strategies to improve patient outcomes.

Keywords: hematopoietic stem cell transplantation, Lomentospora prolificans, terbinafine, voriconazole

Introduction

Due to neutropenia, immunosuppressive treatments, and suboptimal reconstruction of immunity, allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients are vulnerable to invasive fungal infections (IFIs), which represent a leading cause of non-relapse mortality and prolonged hospitalization in this population.[1–3] IFIs are predominantly caused by *Candida spp., Aspergillus spp*. or *Mucorales*.[4] However, as an emerging opportunistic fungal pathogen with a high mortality rate, Lomentospora prolificans has been increasingly reported in immunocompromised individuals over the past three decades. Cases have been documented in the United States, Australia, and several European countries, particularly Spain.[5–8] Lomentospora prolificans can cause disseminated infections involving multiple organs with fungemia, as well as localized infections such as pulmonary or cerebral invasive mycosis and osteoarticular infections.[6] Previous studies have demonstrated that Lomentospora prolificans exhibits intrinsic resistance to most conventional antifungal agents, including triazoles and amphotericin B.[9] Moreover, breakthrough infections have been observed even in patients receiving antifungal prophylaxis,

Received: 28 March 2025
Accepted: 16 July 2025
Published: 23 July 2025

often with poor clinical outcomes.[10,11] Therefore, identifying optimal therapeutic strategies for Lomentospora prolificans infections is of critical importance. Current consensus guidelines recommend voriconazole as the first-line treatment,[12,13] and a retrospective study by Jenks et al has highlighted the efficacy of voriconazole-terbinafine combination therapy.[14] Here, we report the first successfully treated case of post-HSCT Lomentospora prolificans infection in China using a combination of voriconazole and terbinafine. To our knowledge, this represents the longest survival reported among all documented cases of Lomentospora prolificans infection, which contributes valuable clinical data and insights into the diagnosis and management of Lomentospora prolificans infections.

Case Report

A 27-year-old male was admitted to the hospital in October 2019 with a persistent fever. Subsequent bone marrow analysis confirmed a diagnosis of acute myelomonocytic leukemia (AML-M4). On June 15, 2020, the patient underwent matched sibling donor (MSD) allo-HSCT due to poor response to chemotherapy and recurrent relapses. The patient had an ECOG performance status of grade 2 and a Karnofsky Performance Status (KPS) score of 80 prior to HSCT, with a Hematopoietic Cell Transplantation–Comorbidity Index (HCT-CI) of 2. Neutrophils and platelets successfully engrafted on day +12 (day+12 means the twelfth day after the day of stem cell infusion). After HSCT, He received Cyclosporine A(CsA) for GVHD prevention while CsA was tapered and discontinued by day+90. Due to persistent MRD positivity, a prophylactic donor lymphocyte infusion (DLI) was administered on day+30 and a preemptive treatment with interferon-α was administered on day +128 to prevent relapse.[15,16] By day +144, he developed severe cGVHD and methylprednisolone was used as first-line therapy, followed by second-line ruxolitinib and CsA. It is worth noting that the patient received posaconazole oral suspension for antifungal prophylaxis starting on day −9 (the first day of the conditioning regimen). Therapeutic drug monitoring (TDM) confirmed that posaconazole plasma concentrations were consistently maintained above the effective threshold (≥1.0 μg/mL).

He developed fever and cough with yellow-green sputum on day+151 (Figure 1). Chest computed tomography (CT) revealed mild inflammation in the bilateral lower lung bodes (Figure 2A). Multiple sputum bacterial cultures obtained between days +151 and +183 identified Klebsiella pneumoniae producing extended-spectrum beta-lactamases (ESBLs). Cefoperazone-Sulbactam and subsequently Imipenem were administered. By day +161, CT showed improvement

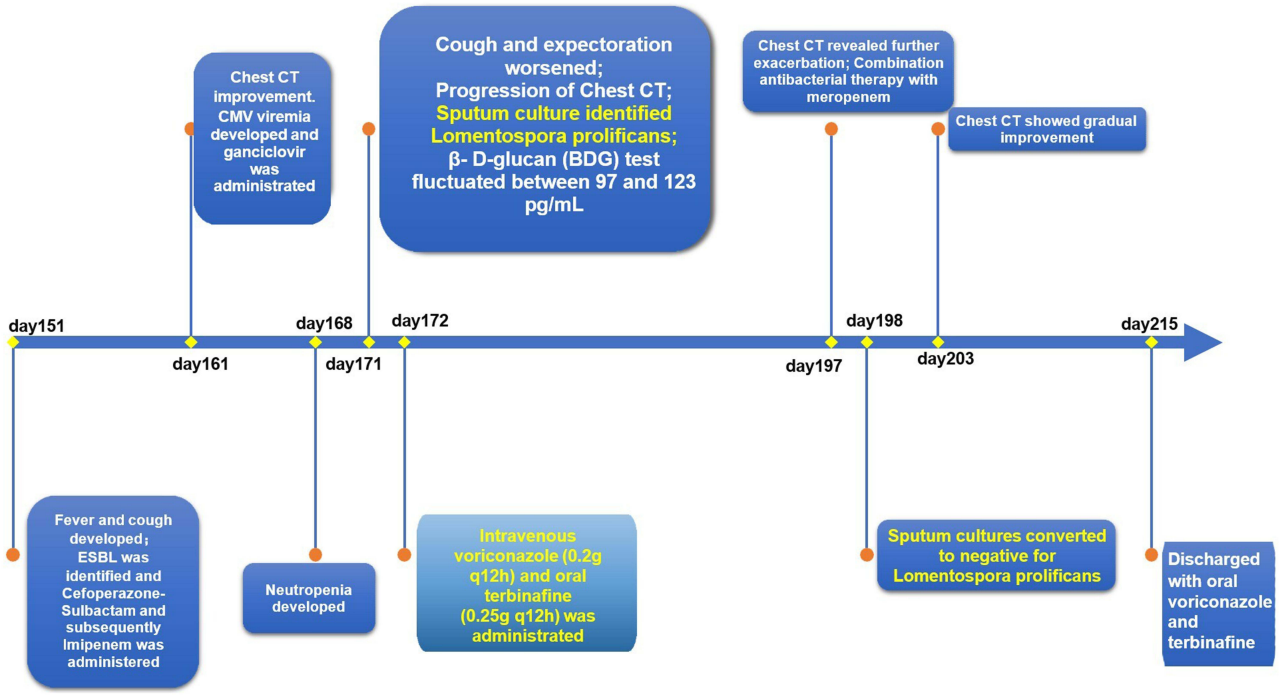

Figure 1 Timeline of the episodes of Lomentospora prolificans infection involving therapeutic interventions and diagnostic hallmarks.

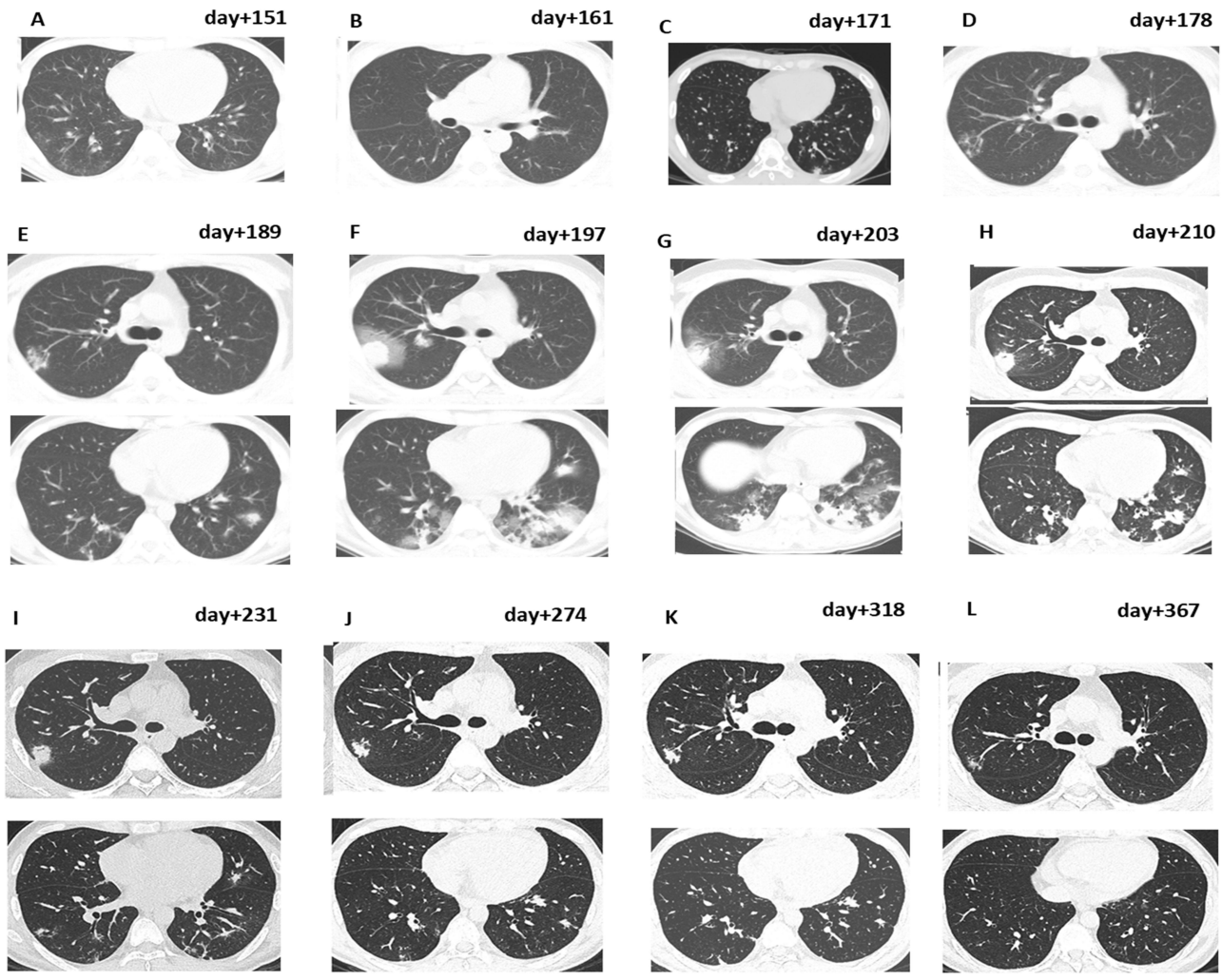

Figure 2 Representative CT scans of the patient's lungs at different time points post-HSCT. (**A**) Day +151; (**B**) Day +161; (**C**) Day +171, first sputum culture identified as Lomentospora prolificans; (**D**) Day +178; (**E**) Day +189; (**F**) Day +197, (**G**) Day +203, last sputum culture identified as Lomentospora prolificans; (**H**) Day +210, (**I**) Day +231, (**J**) Day +274, outpatient, (**K**) Day +318, (**L**) Day +367.

(Figure 2B). Then he developed cytomegalovirus viremia and subsequent ganciclovir treatment was administrated. The patient then developed neutropenia on day +168. On day +171, his symptoms, including cough and expectoration, worsened, and chest CT revealed multiple infections in both lungs, showing progression compared to previous scans (Figure 2C).

The first sputum culture identified Lomentospora prolificans, with subsequent cultures consistently detecting the same pathogen from day +171 to day +197. Incubated at 28°C for 5–7 days, colonies on SCDA medium appeared flat, spreading, black, and velvety (Figure 3A). On SDA medium, colonies were flat, spreading, olive-gray, and suede-like in texture (Figure 3B). Lactophenol cotton blue staining followed by observation under a fluorescence microscope at 400× magnification reveals the characteristic morphological features of the fungus. Lomentospora prolificans produces conidia through annellidic conidiogenesis, distinguished by annellations on the conidiogenous cells. The conidia are single-celled, hyaline to light brown, ovoid to pyriform in shape, with a thin, smooth cell wall. They are arranged in small clusters in an acropetal fashion on flask-shaped conidiogenous cells, which exhibit basal swelling where they connect to the hyphae (Figure 3C and D). Antifungal susceptibility testing was performed using the E-test method (bioMérieux, France) in adherence to the manufacturer's protocol and Aspergillus flavus ATCC® 204304 was employed as the quality control (QC) strain to monitor the reliability of the antifungal susceptibility testing. The result indicated that Amphotericin B, Itraconazole, Caspofungin, and Voriconazole all had a minimum inhibitory concentration (MIC) exceeding 32 μg/mL, suggesting high-level resistance.

https://doi.org/10.2147/IDR.S529984

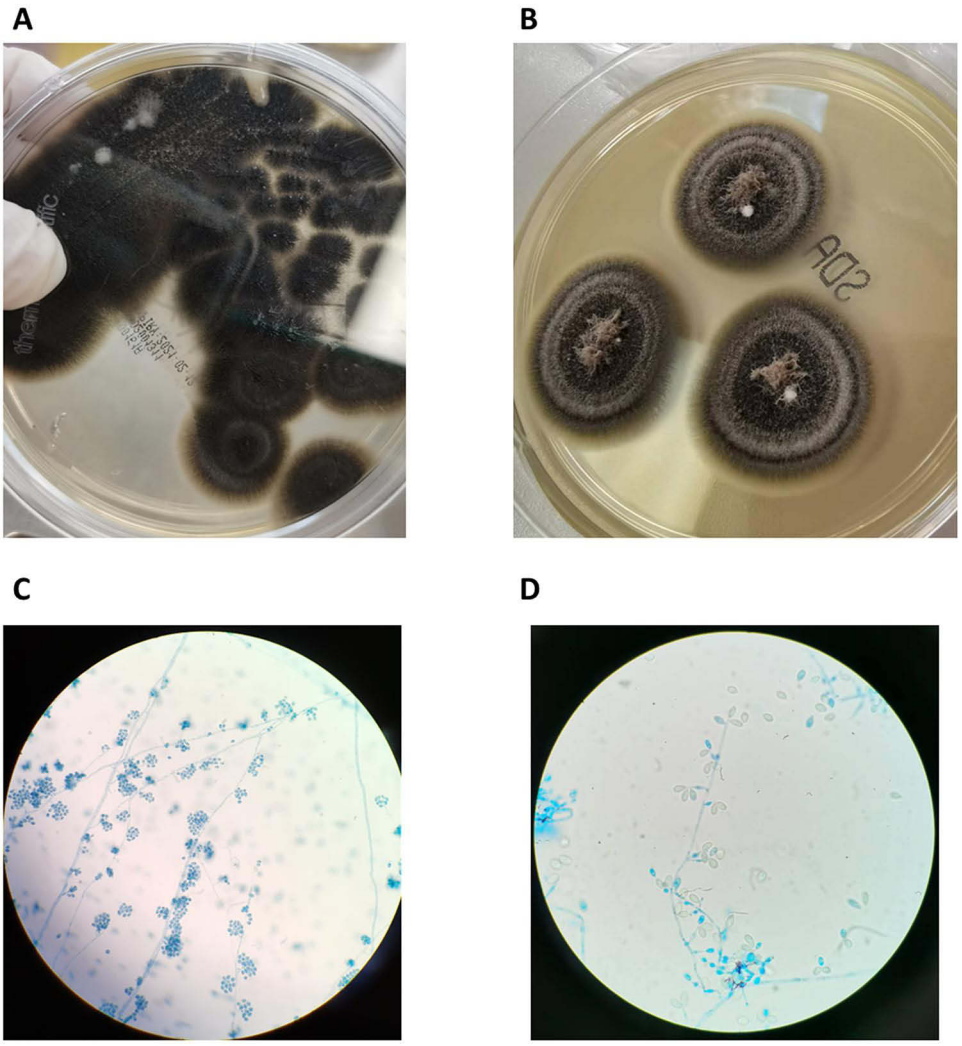

Figure 3 Morphological characteristics of Lomentospora prolificans. (**A**) colonies on SCDA medium; (**B**) On SDA medium; (**C** and **D**) Lactophenol cotton blue staining.

On day +172, He was administered with voriconazole (0.2g q12h) and oral terbinafine (0.25g q12h) for Lomentospora prolificans eradication. During day +177 to day +197, the β-D-glucan (BDG) test fluctuated between 97 and 123 pg/mL and voriconazole plasma concentration was maintained around 2.0 μg/mL. On day +197, he developed high fever and dyspnea. A CT scan revealed further exacerbation of the lung infection, characterized by an increased number of infectious lesions and an expanded affected area (Figure 2C–F). Then he received combination antibacterial therapy with meropenem for five days, after which his body temperature returned to normal. Sputum cultures converted to negative for Lomentospora prolificans from day +198. Additionally, chest CT showed gradual improvement starting from day +203. After being discharged on day +215, he continued oral voriconazole and terbinafine. Pulmonary CT continued to show sustained improvement up to one-year post-transplant, and at the last follow-up, he remained alive at 58 months post-allo-HSCT (Figure 2G–L).

Literature Review

Methods

We conducted a PubMed keyword-based search search using the term "((((Scedosporium prolificans) OR (Lomentospora prolificans)) OR (Scedosporium inflatum)) AND (infection)) AND (transplant)", including articles published up to March 2025. Case reports or articles concerning Lomentospora prolificans infection in HSCT recipients were included, while studies that

concerning Lomentospora prolificans infection in solid organ transplantation was excluded. After screening and data extraction, 24 studies were selected, encompassing a total of 37 reported cases of Lomentospora prolificans infection after HSCT (Table 1).

Baseline Data

The 37 reported cases came from nine countries, with Australia (11 cases, 29.7%) and Spain (10 cases, 27%) having the most. Among the patients, 19 (51.4%) were male, and the mean age was 43 years (±16; range: 3–67).

The most common underlying disease was acute myeloid leukemia (AML; 11 cases, 29.7%), followed by chronic myeloid leukemia (CML; 7 cases), multiple myeloma (MM; 5 cases), and lymphoma (5 cases: 4 non-Hodgkin lymphoma [NHL], 1 Hodgkin lymphoma [HL]). Other diseases included acute lymphoblastic leukemia (ALL; 2 cases), aplastic anemia (1 case), myelofibrosis (1 case), myelodysplastic syndrome (1 case), breast cancer (1 case), neuroblastoma (1 case), and X-linked chronic granulomatous disease (1 case). Underlying diseases were unreported in two cases.

Risk or Predisposing Factors

All 37 patients underwent HSCT, with 24 (64.7%) receiving allo-HSCT and 7 (18.9%) undergoing auto-HSCT. Post-HSCT immunosuppressants were used for GVHD prophylaxis or treatment.

Among 30 patients with available risk factor data (81.1%), neutropenia was most common (19 patients, 63.3%). Acute GVHD (aGVHD) occurred in 6 patients (20%), chronic GVHD (cGVHD) in 7 (35%), and immunosuppressants were recorded in 13 (43.3%).

Origin of the Isolate and Location of Infection

Lomentospora prolificans infection was diagnosed via culture from blood (25/37, 67.6%), bronchoalveolar lavage (10/37, 27.0%), sputum (8/37, 21.6%), skin (5/37, 13.5%), and urine (8/37, 21.6%). Four cases (10.8%) were diagnosed postmortem by autopsy.

Disseminated infection was most common (31/37, 83.8%). Lung was most frequently affected (18/37, 48.6%), followed by the central nervous system (CNS; 8 cases, 21.6%, including 3 meningitis cases). Ocular involvement occurred in 7 cases (18.9%, with 4 endophthalmitis cases). Other sites included skin (3/37, 8.1%), bone and joints (4/37, 10.8%), and one endocarditis case, with Lomentospora prolificans cultured from endocardial vegetation.

Antifungal Treatment

Treatment records were available for 33 patients, with 26 (78.8%) receiving combination antifungal therapy and 7 (21.2%) receiving monotherapy. The most common combination was amphotericin B (AMB) plus a triazole (13/26), especially AMB + itraconazole (8/13). Voriconazole (VZ) combined with terbinafine (TBF) was used in 8 patients. Monotherapy consisted of either AMB or a triazole.

Lomentospora prolificans was tested for antifungal susceptibility in 9 studies (Table 2). According to CLSI guidelines, MIC was used for triazoles and AMB, while minimum effective concentration (MEC) was used for echinocandins. For geometric mean calculations of MIC, MEC, and FICI, out-of-range values were adjusted to the next highest concentration.

Geometric mean MIC values were: voriconazole (5.04 μg/mL), itraconazole (24.66 μg/mL), posaconazole (21.11 μg/mL), isavuconazole (22.63 μg/mL), amphotericin B (14.67 μg/mL), and terbinafine (2.83 μg/mL). For echinocandins, geometric mean MEC values were 5.66 μg/mL for micafungin and 4.00 μg/mL for caspofungin.

Synergy testing was performed in four studies (Table 3), with three showing synergistic effects of VZ + TBF combination. Synergy was defined as FICI ≤ 0.5, no interaction as $0.5 < \text{FICI} \leq 4.0$, and antagonism as FICI > 4.0.[40]

Clinical Outcome of Patients

Among the 37 patients, only 5 (13.5%) survived, resulting in an overall mortality rate of 86.5%. Four survivors received combination antifungal therapy, while only one survived with monotherapy. Survival rates were 12.5% for AMB + triazoles and 23.1% for VZ + TBF. Of the five survivors, two had localized infections, one underwent debridement surgery, and one had breast cancer. Three received Granulocyte Colony-Stimulating Factor (G-CSF) during the neutropenic phase.

https://doi.org/10.2147/IDR.S529984

Table 1 Characteristics of Reported Cases of Post-HSCT Lomentospora Prolificans Infections

First Author	Year of Publication	Age	Gender	Country	Underlying Disease	Clinical Manifestation	Origin of Isolates	VZ +TBF	Outcome	Risk Factors	Mono/ Combination Therapy	Antifungal Agents
Salesa[17]	1993	56	F	Spain	AML	Fungemia	Blood	N	Death	NTP	N	AMB
Tapia[18]	1994	45	M	Spain	MM	Fungemia, meningism, pneumonia	Blood culture	N	Death	NTP	NA	NA
Spielberger[19]	1995	32	F	US	AML	Fungemia, lung, sepsis	Blood, sputum	N	Death	NTP, IS	Y	AMB+ITR
Maertens[20]	2000	3.2	M	Australia	Neuroblastoma	Fungemia, lung, liver and spleen	Blood, urine, skin, feces	N	Death	NA	N	AMB
Barbaric[21]	2001	14	F	Australia	CML	Respiratory distress	BAL, Lung biopsy	N	Death	aGVHD, IS	Y	AMB+ITR
Idigoras[9]	2001	55	F	Spain	Breast cancer	Fungemia	Blood culture	N	Survival	NTP	N	ITR
Carreter de Granda[22]	2001	52	F	Spain	MM	Fungemia, endocarditis, endophthalmitis, brain mycotic aneurysm	Blood, Aortic valve	N	Death	NA	Y	AMB+ITR
Oliveira[23]	2002	42	M	Brazil	CML	Granulomatous, skin lesion	Skin biopsy	N	Survival	IS, aGVHD, cGVHD	Y	AMB+ITR
Howden[24]	2003	53	F	Australia	MM	Fungemia, discitis, osteomyelitis	Tissue specimens, Ethmoid sinus, Intervertebral disc, Fungal aneurysm	Y	Survival	NTP, IS	Y	VZ+TBF
Marco de Lucas[25]	2006	37	M	Spain	AML	Fungemia, Orbit cellulitis, multiple brain lesions, pneumonia	Autopsy	N	Death	NTP	Y	AMB+ITR/ FLU
Marco de Lucas[25]	2006	36	M	Spain	AML	Fungemia, multiple brain lesions, pneumonia	Autopsy	N	Death	NTP	Y	AMB+ITR/ FLU
Marco de Lucas[25]	2006	45	M	Spain	AML	Fungemia, arterial brain thrombosis, pneumonia	Autopsy Blood culture	N	Death	NTP	Y	AMB+ITR/ FLU
Marco de Lucas[25]	2006	18	F	Spain	MDS	Fungemia, pansinusitis, orbital cellulitis, multiple brain lesions, pneumonia	Autopsy	N	Death	NTP	Y	AMB+ITR/ FLU
Cooley[26]	2007	NA	NA	Australia	ALL	Fungemia, joint effusion	Blood, synovium, joint, prostate	Y	Death	NTP, cGVHD	Y	VZ/ITR +TBF
Cooley[26]	2007	NA	NA	Australia	AML	Fungemia, pneumonia	Blood, sputum, BALF	Y	Death	cGVHD	Y	VZ/ITR +TBF
Cooley[26]	2007	NA	NA	Australia	NHL	Fungemia, sepsis	Blood	N	Death	NTP	NA	NA
Cooley[26]	2007	NA	NA	Australia	AML	Fungemia, sepsis	Blood, sputum, BALF, lungs, skin	N	Death	NTP	NA	NA
Cooley[26]	2007	NA	NA	Australia	MM	Fungemia, pneumonia, sepsis	Sputum	Y	Death	NTP, cGVHD	Y	VZ/ITR +TBF
Tong[27]	2007	61	M	Australia	AML	Fungemia, endophthalmitis	Blood culture	Y	Death	aGVHD, IS	Y	VZ+TBF
Pellón Dabén[28]	2008	34	F	Spain	CML	Fungemia, lung	Sputum	N	Death	aGVHD, IS	N	AMB
Tintelnot[29]	2009	44	F	Germany	CML	Fungemia, pneumonia, sepsis	BAL, urine, CVC, blood	N	Death	NA	Y	FLU+CAS
Tintelnot[29]	2009	NA	M	Germany	NA	Fungemia, sepsis, endophthalmitis	Blood	N	Death	NA	N	POS

Tintelnot[29]	2009	60	M	Germany	MF	Fungemia, sepsis, endophthalmitis	BAL, blood	N	Death	NA	Y	AMB+VZ, AMB+CAP
Grenouillet[30]	2009	44	M	France	CML	Fungemia, gingival abscess	Gingival abscess, blood, urine, trachea culture	Y	Death	cGVHD, IS	N	VZ
Grenouillet[30]	2009	67	M	France	NHL	Fungemia, pneumonia	Blood, urine, BAL culture	N	Death	cGVHD, IS	Y	VZ+CAS
Grenouillet[30]	2009	41	M	France	HL	Pneumonia	Sputum, BAL	N	Survival	IS	Y	POS+AMB +TBF
Kubisiak-Rzepczyk[31]	2013	21	F	Poland	ALL	Fungemia	Blood culture	N	Death	NTP	N	VZ
Rolfe[32]	2014	47	M	US	CML	Lung	Sputum culture	N	Death	NA	Y	VZ+CAS
Rolfe[32]	2014	44	M	US	AML	Fungemia, lung, blood, skin	BAL, blood, skin culture	N	Death	NTP	Y	AMB+VZ
Tamaki[33]	2016	62	M	Japan	AML	Fungemia, fungal meningitis	CSF, blood	N	Death	NTP, IS	Y	AMB+VZ
Cobo[34]	2017	53	M	Spain	AA	NA	Sputum	N	Survival	cGVHD IS	Y	AMB+VZ
Elizondo-Zertuche[35]	2017	48	F	Mexico	CML	Fungemia	BAL, urine, blood culture	N	Death	NA	Y	ITR+CAS
Penteado[36]	2018	17	M	Brazil	X-linked chronic granulomatous disease	Fungemia, pneumonia	Blood, urine culture	N	Death	aGVHD, IS	NA	NA
Boglione-Kerrien[37]	2019	61	NA	France	MM	Fungemia, meningitis, brain abscess, ophthalmitis, pyelonephritis	Blood, urethral stones	Y	Death	NTP,	Y	VZ+TBF +MTF
Boan[38]	2020	53	M	Australia	NHL	Skin necrosis, osteomyelitis	Skin tissue	Y	Death	aGVHD, IS	Y	VZ+TBF
Boan[38]	2020	25	F	Australia	AML	Fungemia	Blood, joint, urine	Y	Death	NTP	Y	VZ+TBF
Gow-Lee[39]	2021	63	M	US	NHL	Fungemia, pneumonia, bacteremia, septic arthritis	BALF, blood, synovial fluid	Y	Death	NTP	Y	VZ+MIC

Abbreviations: AMB, amphotericin B; VZ, voriconazole; FLU, fluconazole; CAS, caspofungin; POS, posaconazole; ITR, itraconazole; TBF, terbinafine; MIC, micafungin; MTF, miltefosine; AML, acute myeloid leukemia; AA, aplastic anemia; ALL, acute lymphoblastic leukemia; CML, chronic myeloid leukemia; HL, Hodgkin lymphoma; MF, myelofibrosis; NHL, non-Hodgkin lymphoma; MM, multiple myeloma; MDS, myelodysplastic syndrome; CVC, central venous catheter; aGVHD, acute graft versus host disease; cGVHD, chronic graft versus host disease; IS, immunosuppressant; NTP, neutropenia; BAL, bronchoalveolar lavage fluid; Y, yes; N, no; M, male; F, female; NA, not available.

https://doi.org/10.2147/IDR.S529984

Table 2 Susceptibility Testing of Lomentospora Prolificans

First Author	MIC (μg/mL)						MEC (μg/mL)	
	Voriconazole	Amphotericin B	Terbinafine	Posaconazole	Itraconazole	Isaconazole	Micafungin	Caspofungin
Tamaki[33]	8	>16	NA	NA	>8	NA	>16	NA
Cooley[26]	2	>16	1	NA	>8	NA	NA	NA
Howden[24]	2	8	4	NA	>16	NA	NA	NA
Boan[38]	2	8	NA	8	>16	NA	1	1
Boan[38]	8	4	NA	>8	>16	NA	2	4
Christelle[37]	8	NA	NA	>32	NA	>32	NA	NA
Gow-Lee[39]	8	>8	>2	>16	>16	>4	>8	>8
Tong[27]	4	16	4	NA	>16	NA	NA	NA
Mariana[35]	16	>16	NA	16	NA	NA	NA	NA
Idigoras[9]	NA	>16	NA	NA	>8	NA	NA	NA
Geometric mean	5.04	14.67	2.83	21.11	24.66	22.63	5.66	4.00

Abbreviation: NA, not available.

Table 3 Synergistic Test of Voriconazole and Terbinafine Combination Therapy

First Author	Monotherapy (μg/mL)		Combination Therapy (μg/mL)		FICI
	TBF	VZ	TBF	VZ	
Howden[24]	4	2	0.5	0.008	0.129
Tong[27]	4	4	0.5	0.006	0.141
Gow-Lee[39]	>2	>16	2	4	0.625
Cooley[26]	Totally tested 7 L.prolificans isolates, and terbinafine+voriconazole were synergistic for 5 of 7 isolates				

Abbreviations: FICI, fractional inhibitory concentration index; TBF, terbinafine; VZ, voriconazole.

Discussion

Our case is characterized by a patient with relapsed acute myeloid leukemia (AML) who underwent allo-HSCT while in a minimal residual disease (MRD)-positive state. Post-transplant, the recurrence of MRD further exposed him to the risk of cGVHD. During both first-line and second-line treatment for cGVHD, he received posaconazole prophylaxis according to guideline recommendations, with therapeutic drug monitoring confirming effective plasma concentrations. However, this prophylaxis proved ineffective against Lomentospora prolificans. Upon diagnosis, we promptly adjusted antifungal therapy to a combination of voriconazole and terbinafine, ultimately achieving successful clearance of the Lomentospora prolificans infection. Remarkably, the patient maintained MRD-negative remission for nearly five years post-transplant. To the best of our knowledge, this represents the longest survival reported among all documented cases of Lomentospora prolificans infection.

Among malignancies, leukemia and lymphoma are the primary contributing risk factors for Lomentospora prolificans infection.[5,6,41] For patients with hematological malignancies who had HSCT, neutropenia and immunosuppressive therapy were also unavoidable. Seidel et al also demonstrated that allo-HSCT is an independent risk factor associated with poor outcomes in patients infected with Lomentospora prolificans.[42] Husain et al demonstrated that Lomentospora prolificans infection was more prevalent in HSCT patients than in solid organ transplantation (SOT) patients (39.1% vs 16.9%, $P = 0.045$). Moreover, HSCT patients were more frequently affected by fungemia,[43] and Lomentospora prolificans infection was frequently disseminated and significantly associated with higher rate of 1-month mortality (HR = 6.87, $P < 0.001$).[44] According to Konsoula et al, although Lomentospora prolificans infection is rare in immunocompromised patients, the overall mortality rate is relatively high, reaching 87.3% in cases of disseminated infection. In our review, the overall mortality rate of Lomentospora prolificans infection in HSCT patients was 86.5%, markedly higher than the reported mortality rates of post-HSCT invasive fungal infections, which range from 13.7% to 47%.[45–48]

Currently, many antifungal agents are largely ineffective in eradicating Lomentospora prolificans infections. In our case, the isolated strain exhibited resistance to amphotericin B, itraconazole, caspofungin, and voriconazole, with all agents demonstrating a minimum inhibitory concentration (MIC) of ≥32 μg/mL. However, many studies have found that combination therapy can possibly improve treatment outcomes. Terbinafine and triazoles target different stages of fungal ergosterol biosynthesis, suggesting potential synergy. Terbinafine (an allylamine) inhibits squalene epoxidase, causing squalene accumulation and defective ergosterol production. Triazoles inhibit 14α-demethylase, blocking lanosterol methylation, a key step in ergosterol synthesis. This complementary action may enhance antifungal efficacy and improve outcomes.[49] Several in vitro studies have demonstrated the efficacy of voriconazole plus terbinafine combination therapy. In 2000, Meletiadis et al reported that itraconazole plus terbinafine showed in vitro synergy against nearly all Lomentospora prolificans isolates after 48 and 72 hours.[50,51] Subsequently, they applied a modified MIC analysis method and a novel statistical model, which further demonstrated that voriconazole also exhibited significant in vitro synergistic effects when combined with terbinafine.[52] In 2003, Howden et al successfully treated disseminated Lomentospora prolificans infection with voriconazole and terbinafine.[24] In 2020, Jenks et al conducted a retrospective study of 41 cases of invasive Lomentospora prolificans infections, revealing that the voriconazole plus terbinafine combination therapy was associated with significantly improved overall survival.[14]

Apart from the synergistic antifungal effects of voriconazole and terbinafine, several other factors may have contributed to the successful control of Lomentospora prolificans infection. Including the recovery of innate and adaptive immunity following the rapid cessation of immunosuppressive agents, resolution of prolonged neutropenia through the administration of G-CSF, and the potential benefit of adjunctive debridement surgery in reducing fungal burden.[24,44,45] These supportive interventions likely played a crucial role in improving treatment outcomes in patients with Lomentospora prolificans infection.

Finally, it is worth mentioning that our case represents a single patient experience, and factors such as the patient's relatively young age, specific immune reconstitution profile, or the early initiation of combination therapy may not be generalizable to all immunocompromised hosts with Lomentospora prolificans infection. Future multi-center prospective registries, collaborative studies, better therapies and rapid diagnostic tools are pressingly needed.

Conclusions

This case highlights the importance of early recognition and prompt initiation of synergistic antifungal therapy (voriconazole-terbinafine) for Lomentospora prolificans infection in immunocompromised patients. The sustained remission achieved in this patient underscores the importance of combination antifungal strategies. However, the persistently high mortality rate (86.5% in HSCT recipients) emphasizes the critical need for novel antifungals and improved diagnostic tools for Lomentospora prolificans infection.

Data Sharing Statement

The dataset supporting the conclusions of this article is available in the clinical data repository of each participating hospital. Individual participant data were not shared. For the original data, please contact drlvmeng@bjmu.edu.cn.

Ethics Approval and Patient Consent

Written informed consent was obtained from the patient for the publication of the case details. The publication of anonymized case data and images was specifically approved by the Ethics Committee of Peking University People's Hospital (ethical approval no. 2022PHB242-001).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the National key research and development plan of China (2021YFA1100902), Beijing Nova Program of Science and Technology (No. 20230484446), Peking University People's Hospital (RZ2024-01), Joint Research Project of the Shijiazhuang-Peking University Cooperation Program.

Disclosure

The author(s) report no conflicts of interest in this work.

References

1. Busca A, Cinatti N, Gill J, et al. Management of invasive fungal infections in patients undergoing allogeneic hematopoietic stem cell transplantation: the Turin experience. *Front Cell Infect Microbiol*. 2021;11:805514. doi:10.3389/fcimb.2021.805514
2. Gavriilaki E, Evangelidis P, Kotsiou N, et al. Antifungal prescription and stewardship in hematology and hematopoietic stem cell transplantation units worldwide: an international survey of EHA-SWG Infections in Hematology. *Bone Marrow Transplant*. 2025;60(5):729–732. doi:10.1038/s41409-025-02545-x
3. Gavriilaki E, Dolgyras P, Dimou-Mpesikli S, et al. Risk factors, prevalence, and outcomes of invasive fungal disease post hematopoietic cell transplantation and cellular therapies: a retrospective monocenter real-life analysis. *Cancers*. 2023;15(13):3529. doi:10.3390/cancers15133529

4. Li C, Zhu DP, Chen J, et al. Invasive fungal disease in patients undergoing allogeneic hematopoietic stem cell transplantation in China: a multicenter epidemiological study (CAESAR 2.0). *Clin Infect Dis*. 2025;80(4):807–816. doi:10.1093/cid/ciae612
5. Seidel D, Meißner A, Lackner M, et al. Prognostic factors in 264 adults with invasive *Scedosporium* spp. and *Lomentospora prolificans* infection reported in the literature and FungiScope®. *Crit Rev Microbiol*. 2019;45(1):1–21. doi:10.1080/1040841x.2018.1514366
6. Rodriguez-Tudela JL, Berenguer J, Guarro J, et al. Epidemiology and outcome of Scedosporium prolificans infection, a review of 162 cases. *Med Mycol*. 2009;47(4):359–370. doi:10.1080/13693780802524506
7. Neoh CF, Chen SC, Lanternier F, et al. Scedosporiosis and lomentosporiosis: modern perspectives on these difficult-to-treat rare mold infections. *Clin Microbiol Rev*. 2024;37(2):e0000423. doi:10.1128/cmr.00004-23
8. Konsoula A, Tsioutis C, Markaki I, Papadakis M, Agouridis AP, Spernovasilis N. Lomentospora prolificans: an emerging opportunistic fungal pathogen. *Microorganisms*. 2022;10(7):1317. doi:10.3390/microorganisms10071317
9. Idigoras P, Perez-Trallero E, Pineiro L, et al. Disseminated infection and colonization by Scedosporium prolificans: a review of 18 cases, 1990-1999. *Clin Infect Dis*. 2001;32(11):E158–65. doi:10.1086/320521
10. Alvarez-Uria A, Guinea JV, Escribano P, et al. Invasive scedosporium and lomentosora infections in the era of antifungal prophylaxis: a 20-year experience from a single centre in Spain. *Mycoses*. 2020;63(11):1195–1202. doi:10.1111/myc.13154
11. Ananda-Rajah MR, Grigg A, Slavin MA. Breakthrough disseminated scedosporium prolificans infection in a patient with relapsed leukaemia on prolonged voriconazole followed by posaconazole prophylaxis. *Mycopathologia*. 2008;166(2):83–86. doi:10.1007/s11046-008-9131-2
12. Blyth CC, Gilroy NM, Guy SD, et al. Consensus guidelines for the treatment of invasive mould infections in haematological malignancy and haemopoietic stem cell transplantation, 2014. *Intern Med J*. 2014;44(12b):1333–1349. doi:10.1111/imj.12598
13. Tortorano AM, Richardson M, Roilides E, et al. ESCMID and ECMM joint guidelines on diagnosis and management of hyalohyphomycosis: fusarium spp. Scedosporium spp. and others. *Clin Microbiol Infect*. 2014;20 Suppl 3:27–46. doi:10.1111/1469-0691.12465
14. Jenks JD, Seidel D, Cornely OA, et al. Voriconazole plus terbinafine combination antifungal therapy for invasive Lomentospora prolificans infections: analysis of 41 patients from the FungiScope(R) registry 2008-2019. *Clin Microbiol Infect*. 2020;26(6):784e1–784e5. doi:10.1016/j.cmi.2020.01.012
15. Wang Y, Chang YJ, Chen J, et al. Consensus on the monitoring, treatment, and prevention of leukaemia relapse after allogeneic haematopoietic stem cell transplantation in China: 2024 update. *Cancer Lett*. 2024;605:217264. doi:10.1016/j.canlet.2024.217264
16. Shen MZ, Zhang XH, Xu LP, et al. Preemptive interferon-α therapy could protect against relapse and improve survival of acute myeloid leukemia patients after allogeneic hematopoietic stem cell transplantation: long-term results of two registry studies. *Front Immunol*. 2022;13:757002. doi:10.3389/fimmu.2022.757002
17. Salesa R, Burgos A, Ondiviela R, Richard C, Quindos G, Ponton J. Fatal disseminated infection by Scedosporium inflatum after bone marrow transplantation. *Scand J Infect Dis*. 1993;25(3):389–393. doi:10.3109/00365549309008516
18. Tapia M, Richard C, Baro J, et al. Scedosporium inflatum infection in immunocompromised haematological patients. *Br J Haematol*. 1994;87(1):212–214. doi:10.1111/j.1365-2141.1994.tb04897.x
19. Spielberger RT, Tegtmeier BR, O'Donnell MR, Ito JI. Fatal Scedosporium prolificans (S. inflatum) fungemia following allogeneic bone marrow transplantation: report of a case in the United States. *Clin Infect Dis*. 1995;21(4):1067. doi:10.1093/clinids/21.4.1067
20. Maertens J, Lagrou K, Deweerdt H, et al. Disseminated infection by Scedosporium prolificans: an emerging fatality among haematology patients. Case report and review. *Ann Hematol*. 2000;79(6):340–344. doi:10.1007/s002779900137
21. Barbaric D, Shaw PJ. Scedosporium infection in immunocompromised patients: successful use of liposomal amphotericin B and itraconazole. *Med Pediatr Oncol*. 2001;37(2):122–125. doi:10.1002/mpo.1180
22. Carreter de Granda ME, Richard C, Conde E, et al. Endocarditis caused by Scedosporium prolificans after autologous peripheral blood stem cell transplantation. *Eur J Clin Microbiol Infect Dis*. 2001;20(3):215–217. doi:10.1007/pl00011256
23. Oliveira JS, Kerbauy FR, Colombo AL, et al. Fungal infections in marrow transplant recipients under antifungal prophylaxis with fluconazole. *Braz J Med Biol Res*. 2002;35(7):789–798. doi:10.1590/s0100-879x2002000700005
24. Howden BP, Slavin MA, Schwarer AP, Mijch AM. Successful control of disseminated Scedosporium prolificans infection with a combination of voriconazole and terbinafine. *Eur J Clin Microbiol Infect Dis*. 2003;22(2):111–113. doi:10.1007/s10096-002-0877-z
25. Marco de Lucas E, Sadaba P, Lastra Garcia-Baron P, et al. Cerebral scedosporiosis: an emerging fungal infection in severe neutropenic patients: CT features and CT pathologic correlation. *Eur Radiol*. 2006;16(2):496–502. doi:10.1007/s00330-005-2869-8
26. Cooley L, Spelman D, Thursky K, Slavin M. Infection with scedosporium apiospermum and S. prolificans, Australia. *Emerg Infect Dis*. 2007;13(8):1170–1177. doi:10.3201/eid1308.060576
27. Tong SY, Peleg AY, Yoong J, Handke R, Szer J, Slavin M. Breakthrough scedosporium prolificans infection while receiving voriconazole prophylaxis in an allogeneic stem cell transplant recipient. *Transpl Infect Dis*. 2007;9(3):241–243. doi:10.1111/j.1399-3062.2007.00203.x
28. Pellón Dabén R, Marco de Lucas E, Martín Cuesta L, et al. Imaging findings of pulmonary infection caused by Scedosporium prolificans in a deep immunocompromised patient. *Emerg Radiol*. 2008;15(1):47–49. doi:10.1007/s10140-007-0634-9
29. Tintelnot K, Just-Nübling G, Horré R, et al. A review of German scedosporium prolificans cases from 1993 to 2007. *Med Mycol*. 2009;47(4):351–358. doi:10.1080/13693780802627440
30. Grenouillet F, Botterel F, Crouzet J, et al. Scedosporium prolificans: an emerging pathogen in France? *Med Mycol*. 2009;47(4):343–350. doi:10.1080/13693780802454761
31. Kubisiak-Rzepczyk H, Gil L, Zawirska A, et al. Scedosporium prolificans fungaemia in a patient with acute lymphoblastic leukaemia. *J Mycol Med*. 2013;23(4):261–264. doi:10.1016/j.mycmed.2013.08.003
32. Rolfe NE, Sandin RL, Greene JN. Scedosporium infections at a cancer center over a 10-year period (2001–2010). *Infectious Dis Clin Pract*. 2014;22(2):71–74. doi:10.1097/IPC.0b013e318297d5bf
33. Tamaki M, Nozaki K, Onishi M, Yamamoto K, Ujiie H, Sugahara H. Fungal meningitis caused by Lomentospora prolificans after allogeneic hematopoietic stem cell transplantation. *Transpl Infect Dis*. 2016;18(4):601–605. doi:10.1111/tid.12563
34. Cobo F, Lara-Oya A, Rodríguez-Granger J, Sampedro A, Aliaga-Martínez L, Navarro-Marí JM. Infections caused by scedosporium/lomentospora species: clinical and microbiological findings in 21 cases. *Med Mycol*. 2018;56(8):917–925. doi:10.1093/mmy/myx147
35. Elizondo-Zertuche M, Montoya AM, Robledo-Leal E, et al. Comparative pathogenicity of lomentospora prolificans (Scedosporium prolificans) Isolates from Mexican patients. *Mycopathologia*. 2017;182(7–8):681–689. doi:10.1007/s11046-017-0137-5

36. Penteado FD, Litvinov N, Sztajnbok J, et al. Lomentospora prolificans fungemia in hematopoietic stem cell transplant patients: first report in South America and literature review. *Transpl Infect Dis*. 2018;20(4):e12908. doi:10.1111/tid.12908
37. Boglione-Kerrien C, Verdier MC, Gautier-Veyret E, et al. Using unusual drug-drug interactions to maximize voriconazole treatment efficacy. *Med Mal Infect*. 2019;49(7):555–557. doi:10.1016/j.medmal.2019.05.004
38. Boan P, Pang S, Gardam DJ, Darragh H, Wright M, Coombs GW. Investigation of a lomentospora prolificans case cluster with whole genome sequencing. *Med Mycol Case Rep*. 2020;29:1–4. doi:10.1016/j.mmcr.2020.05.003
39. Gow-Lee VJ, Moyers JT, Rogstad DK. Fatal recurrent disseminated lomentospora prolificans infection during autologous hematopoietic stem cell transplantation: a case report and review, and discussion on the importance of prolonged neutropenia. *Transpl Infect Dis*. 2021;23(6):e13701. doi:10.1111/tid.13701
40. Odds FC. Synergy, antagonism, and what the chequerboard puts between them. *J Antimicrob Chemother*. 2003;52(1):1. doi:10.1093/jac/dkg301
41. Czech MM, Cuellar-Rodriguez J, Kwon-Chung KJ, et al. Clinical significance and antifungal susceptibility profile of 103 clinical isolates of scedosporium species complex and lomentospora prolificans obtained from NIH patients. *J Clin Microbiol*. 2025;63(4):e0155024. doi:10.1128/jcm.01550-24
42. Seidel D, Hassler A, Salmanton-Garcia J, et al. Invasive Scedosporium spp. and lomentospora prolificans infections in pediatric patients: analysis of 55 cases from FungiScope(R) and the literature. *Int J Infect Dis*. 2020;92:114–122. doi:10.1016/j.ijid.2019.12.017
43. Husain S, Muñoz P, Forrest G, et al. Infections due to scedosporium apiospermum and scedosporium prolificans in transplant recipients: clinical characteristics and impact of antifungal agent therapy on outcome. *Clin Infect Dis*. 2005;40(1):89–99. doi:10.1086/426445
44. Neoh CF, Chen SCA, Crowe A, et al. Invasive scedosporium and lomentospora prolificans infections in Australia: a multicenter retrospective cohort study. *Open Forum Infect Dis*. 2023;10(2):ofad059. doi:10.1093/ofid/ofad059
45. Konsoula A, Agouridis AP, Markaki L, Tsioutis C, Spernovasilis N. Lomentospora prolificans disseminated infections: a systematic review of reported cases. *Pathogens*. 2022;12(1):67. doi:10.3390/pathogens12010067
46. Neofytos D, Horn D, Anaissie E, et al. Epidemiology and outcome of invasive fungal infection in adult hematopoietic stem cell transplant recipients: analysis of multicenter prospective antifungal therapy (PATH) alliance registry. *Clin Infect Dis*. 2009;48(3):265–273. doi:10.1086/595846
47. Sun Y, Meng F, Han M, et al. Epidemiology, management, and outcome of invasive fungal disease in patients undergoing hematopoietic stem cell transplantation in China: a multicenter prospective observational study. *Biol Blood Marrow Transplant*. 2015;21(6):1117–1126. doi:10.1016/j.bbmt.2015.03.018
48. Puerta-Alcalde P, Monzó-Gallo P, Aguilar-Guisado M, et al. Breakthrough invasive fungal infection among patients with haematologic malignancies: a national, prospective, and multicentre study. *J Infect*. 2023;87(1):46–53. doi:10.1016/j.jinf.2023.05.005
49. Ghannoum MA, Rice LB. Antifungal agents: mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance. *Clin Microbiol Rev*. 1999;12(4):501–517. doi:10.1128/cmr.12.4.501
50. Meletiadis J, Mouton JW, Meis JF, Verweij PE. Combination chemotherapy for the treatment of invasive infections by scedosporium prolificans. *Clin Microbiol Infect*. 2000;6(6):336–337. doi:10.1046/j.1469-0691.2000.00089.x
51. Meletiadis J, Mouton JW, Rodriguez-Tudela JL, Meis JF, Verweij PE. In vitro interaction of terbinafine with itraconazole against clinical isolates of scedosporium prolificans. *Antimicrob Agents Chemother*. 2000;44(2):470–472. doi:10.1128/AAC.44.2.470-472.2000
52. Meletiadis J, Mouton JW, Meis JF, Verweij PE. In vitro drug interaction modeling of combinations of azoles with terbinafine against clinical scedosporium prolificans isolates. *Antimicrob Agents Chemother*. 2003;47(1):106–117. doi:10.1128/AAC.47.1.106-117.2003