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Review Articles

Magnusiomyces Capitatus Breakthrough Infection in Allogeneic Hematopoietic Cell Transplant Recipients Receiving Echinocandin Prophylaxis: Clinical Features, Management, and Structured Review of the Literature

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Abstract. *Magnusiomyces* spp. infections are an uncommon but highly lethal emerging mycosis in immunocompromised patients, particularly those with hematologic malignancies and profound neutropenia. Data in the setting of allogeneic hematopoietic cell transplantation (allo-HCT) remain scarce. These infections typically occur early after transplantation as breakthrough events under antifungal prophylaxis and are associated with high mortality despite appropriate therapy. In this study, we report two concurrent cases from two Spanish transplant centers illustrating complementary clinical patterns, fulminant septic shock and progressive disseminated infection, both arising under echinocandin prophylaxis and both resulting in fatal outcomes, and provide a structured literature review derived from published individual cases to characterize this rare infection. Thirteen cases of *Magnusiomyces* infection in allo-HCT recipients (11 previously reported and 2 from the present study) were depicted, predominantly affecting adult male patients with hematologic malignancies. Infection occurred during profound neutropenia and most commonly as fungemia with frequent hematogenous dissemination to multiple organs. Despite heterogeneous antifungal prophylaxis, treatment outcomes were poor, with high early mortality (69%, 9/13). These findings highlight the aggressive nature of *Magnusiomyces* spp infections in allo-HCT and underscore the need for improved monitoring, preventive strategies, and more effective therapeutic approaches in this high-risk population.

Keywords: *Magnusiomyces* spp, Allogeneic stem cell transplantation, Breakthrough fungal infection, Antifungal prophylaxis.

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Introduction. Invasive fungal disease (IFD) due to non-*Candida* yeast is an increasing problem in patients with hematological malignancies (HM) and in recipients of allogeneic hematopoietic stem cell transplantation (allo-HCT). Antifungal prophylaxis has reduced IFD incidence from 9,4% to less than 2,5%,[1] but in recent years there has been a progressive increase in breakthrough IFD caused by rare and often antifungal-resistant fungi.[2-4] This shift is of particular importance given the limited prophylactic and therapeutic options as well as the difficulties in diagnosing these uncommon pathogens. Among these emerging fungi, *Magnusiomyces capitatus,* historically reported under several taxonomic synonyms including *Saprochaete capitata, Geotrichum capitatum, and Blastoschizomyces capitatus*, is an emerging opportunistic yeast-like fungus causing IFD predominantly in severely immunocompromised patients, such as inpatients with HM experiencing prolonged and profound neutropenia.[5] *Magnusiomyces* spp. is part of the normal microbiota of the respiratory and gastrointestinal tracts,[6] and infection is thought to occur through inhalation or gastrointestinal translocation in immunocompromised hosts.[7]

The information about *Magnusiomyces* spp. infections in the allo-HCT setting remains limited and is largely restricted to isolated case reports and small case series. We report two cases of *Magnusiomyces capitatus* fungemia from 2 Spanish transplant institutions in allo-HCT recipients who developed IFD early after transplant. We also conducted a structured review of the literature to identify reported cases of Magnusiomyces spp. infection in allo-HCT recipients. By integrating our cases with previously published data, we aim to characterize the clinical features, diagnostic challenges, therapeutic approaches, and outcomes associated with this rare but life-threatening infection.

Methods – Structured literature review. We conducted a structured literature review of published cases of invasive *Magnusiomyces spp.* infection in recipients of allo-HCT. The review followed a predefined search strategy and eligibility criteria.

A comprehensive search was performed in PubMed/MEDLINE from database inception to January 2026 using combinations of the following terms: *"Magnusiomyces capitatus", "Magnusiomyces clavatus", "Magnusiomyces spp.", "Saprochaete capitata", "Saprochaete clavata", "Saprochaete spp.", "Geotrichum capitatum", "Geotrichum clavatum", "Geotrichum spp.", "Blastoschizomyces capitatus", "Blastoschizomyces spp.*", "hematopoietic stem cell transplantation", "haematopoietic stem cell transplantation", "bone marrow transplantation", "allogeneic transplantation", "fungemia" and "invasive fungal infection", combined using Boolean operators (AND/OR). To maximize case ascertainment, a complementary search was performed using Google Scholar, and the reference lists of all eligible publications were manually screened to identify additional reports not retrieved through the electronic search.

Eligible publications included case reports, case series, and observational studies describing proven or probable invasive *Magnusiomyces spp*. infection in allo-HCT recipients, provided that individual patient-level data were available. Publications reporting colonization only, non-invasive infections, animal or laboratory studies, review articles without original cases, duplicate publications, or studies lacking sufficient transplant-specific information were excluded. Titles and abstracts were independently screened by two reviewers (J.L.P. and C.G.), followed by full-text assessment of potentially eligible articles. Potential duplicate reports were identified through manual cross-checking of demographic characteristics, transplant variables, timing of infection, fungal species, clinical presentation, and outcomes. When duplicate reporting was suspected, only the publication providing the most comprehensive patient-level information was retained.

Whenever sufficient information was available, cases were classified according to contemporary consensus definitions of IFD (e.g., EORTC/MSGERC criteria)[8]. Demographic characteristics, underlying hematologic disease, transplant-related variables, risk factors, clinical presentation, microbiological findings, antifungal treatment, and outcomes were extracted using a standardized data collection form. Owing to the rarity of this infection and the predominance of isolated case reports, results were synthesized descriptively. The review was intended to provide a comprehensive structured summary of all published allo-HCT cases rather than to perform a formal systematic review or quantitative meta-analysis.

According to the requirements of the local Ethics Committee, formal ethics approval and specific informed consent for publication were not required for these anonymized case reports, as no patient-identifiable information was included.

Case 1. A 57-year-old Caucasian male (CMV seropositive) with no relevant past medical history was diagnosed with acute myeloid leukemia (AML) harboring a TP53 gene mutation, refractory to first-line induction with CPX-351 and salvage therapy with idarubicin, fludarabine, and cytarabine-based therapy. He was referred for urgent allo-HCT. The best available donor was a haploidentical related donor (son, 28 years old, CMV seropositive). He underwent myeloablative conditioning with thiotepa, busulfan, and fludarabine (TBF). Graft-vs-host disease (GVHD) prophylaxis consisted of post-transplant cyclophosphamide (50 mg/Kg on days +3 and +4), followed by cyclosporine and mycophenolate mofetil (MMF) from day +5.

Antimicrobial prophylaxis included letermovir (480 mg orally from day 0, reduced to 240 mg from day +6), acyclovir (800 mg orally twice daily from day –5), and micafungin (50 mg IV daily from day 0). No quinolone prophylaxis was administered. Weekly surveillance cultures were negative for multidrug-resistant bacterial colonization. The patient received 6×10^6 $CD34^+$ cells/kg from fresh peripheral blood stem cells.

On day +7, the patient developed grade IV mucositis with severe oral ulcerations and grade 3 CTCAE diarrhea requiring total parenteral nutrition. Letermovir was discontinued on day +5 due to intolerance. CMV DNAemia was first detected on day +7 (181 IU/mL, log 2.26), with a rapid doubling time (2.15 days) and peak viral load of log 3.08 on day +14. Anti-CMV therapy was started.

Febrile neutropenia occurred on day +7 and was treated empirically with piperacillin–tazobactam and teicoplanin, with no microbiological documentation. On day +11, the patient developed acute kidney injury (peak creatinine 4.5 mg/dL), attributed to drug-related nephrotoxicity, accompanied by a skin rash considered secondary to treatment toxicity. Acyclovir and cyclosporine were discontinued on day +12, and methylprednisolone (2 mg/kg/day) was initiated.

On day +16, he developed a refractory hypertensive crisis with hemodynamic instability requiring urgent hemodialysis and ICU admission. At that time, he remained profoundly pancytopenic (hemoglobin 9.1 g/dL, platelets 9×10^9/L, absolute neutrophil count 0×10^9/L). Daily granulocyte-colony stimulating factor (G-CSF) was administered since day +13. Notably, he had persistent grade IV mucositis, ongoing CMV infection, acute renal failure, and recent high-dose corticosteroid exposure.

On day +18, he developed septic shock with hypotension and respiratory failure requiring vasopressor support and invasive mechanical ventilation. The central venous catheter was removed and sent to culture. Empirical antimicrobial therapy was escalated to meropenem plus daptomycin, later that day switched to ceftazidime–avibactam plus linezolid. On day +18, antifungal prophylaxis was changed from micafungin to prophylactic anidulafungin to preserve liver function.

Blood cultures drawn at the onset of shock, on day +18, yielded yeast on day +21, subsequently identified as *Magnusiomyces capitatus* on day +22 by MALDI-TOF-mass spectrometry (MALDI-TOF-MS). Targeted antifungal therapy with liposomal amphotericin B (3 mg/kg/day) plus posaconazole (300 mg twice daily as loading dose, followed by 300 mg/day) was initiated on day +21, immediately after yeasts were detected in blood cultures, and the new central venous catheters were again removed. On day +23, following identification of M. capitatus, posaconazole was switched to isavuconazole (200 mg every 8 h as loading dose). Antifungal susceptibility testing was unavailable because the patient died before results could be obtained. Despite antifungal escalation, the patient remained in refractory septic shock with the appearance of disseminated skin lesions consistent with hematogenous fungal dissemination. He progressed to multiorgan failure and died on day +24, without neutrophil recovery (ANC 0.25×10^9/L at last assessment). Weekly galactomannan monitoring during neutropenia was persistently negative. Granulocyte transfusions were not considered because of limited availability and the rapidly progressive multiorgan failure.

Case 2. A 67-year-old male with primary myelofibrosis (MPL-mutated) and marked splenomegaly (20 cm below costal margin) underwent allo-HCT from a 10/10 HLA-matched unrelated donor. The conditioning regimen consisted of reduced-intensity TBF. GVHD prophylaxis included a reduced dose of post-transplant cyclophosphamide (30 mg/kg on days +3 and +4), followed by sirolimus and MMF from day +5. Antimicrobial prophylaxis consisted of micafungin (50 mg/day from day +1 until neutrophil recovery), acyclovir (from day –5), and letermovir 480 mg/d (from day +7). A total of 8.7×10^6 $CD34^+$ cells/kg from fresh peripheral blood stem cells were infused on day 0. G-CSF was administered from day +15 until death. During the early neutropenic phase (ANC $< 0.50\times10^9$/L), the patient developed an upper respiratory tract infection caused by human metapneumovirus (hMPV) on day +7, treated with oral ribavirin for 7 days (until day +14) with complete clinical resolution. On day +14, he developed febrile neutropenia, with negative blood and urine cultures, absence of radiological findings, and no evidence of multidrug-resistant bacterial colonization (screening at days –6, 0, and +7). Empirical piperacillin–tazobactam was initiated. On day +21, a marked increase in serum (1→3)-β-D-glucan levels (>300 pg/mL) was detected (**Figure 1**), followed by the appearance of two cutaneous lesions on the left lower limb on day +22. Weekly galactomannan monitoring remained negative. At the time of positive (1→3)-β-D-glucan test along with skin lesions, antifungal therapy was escalated from micafungin prophylaxis to liposomal amphotericin B (3 mg/kg/day) plus anidulafungin. A diagnostic work-up including skin biopsy (non-diagnostic), bronchoscopy (negative except for persistent hMPV), and total-body CT scan revealed multiple hepatosplenic microabscesses and small pulmonary nodules (**Figure 2**), raising suspicion for IFD. Blood cultures became positive after 16 h for *Magnusiomyces* spp. on day +23 (**Figure 3**). Antifungal susceptibility testing was performed using the EUCAST methodology. The isolate showed the expected lack of in vitro activity against echinocandins, consistent with the intrinsic lack of activity of this antifungal class against Magnusiomyces spp., whereas in

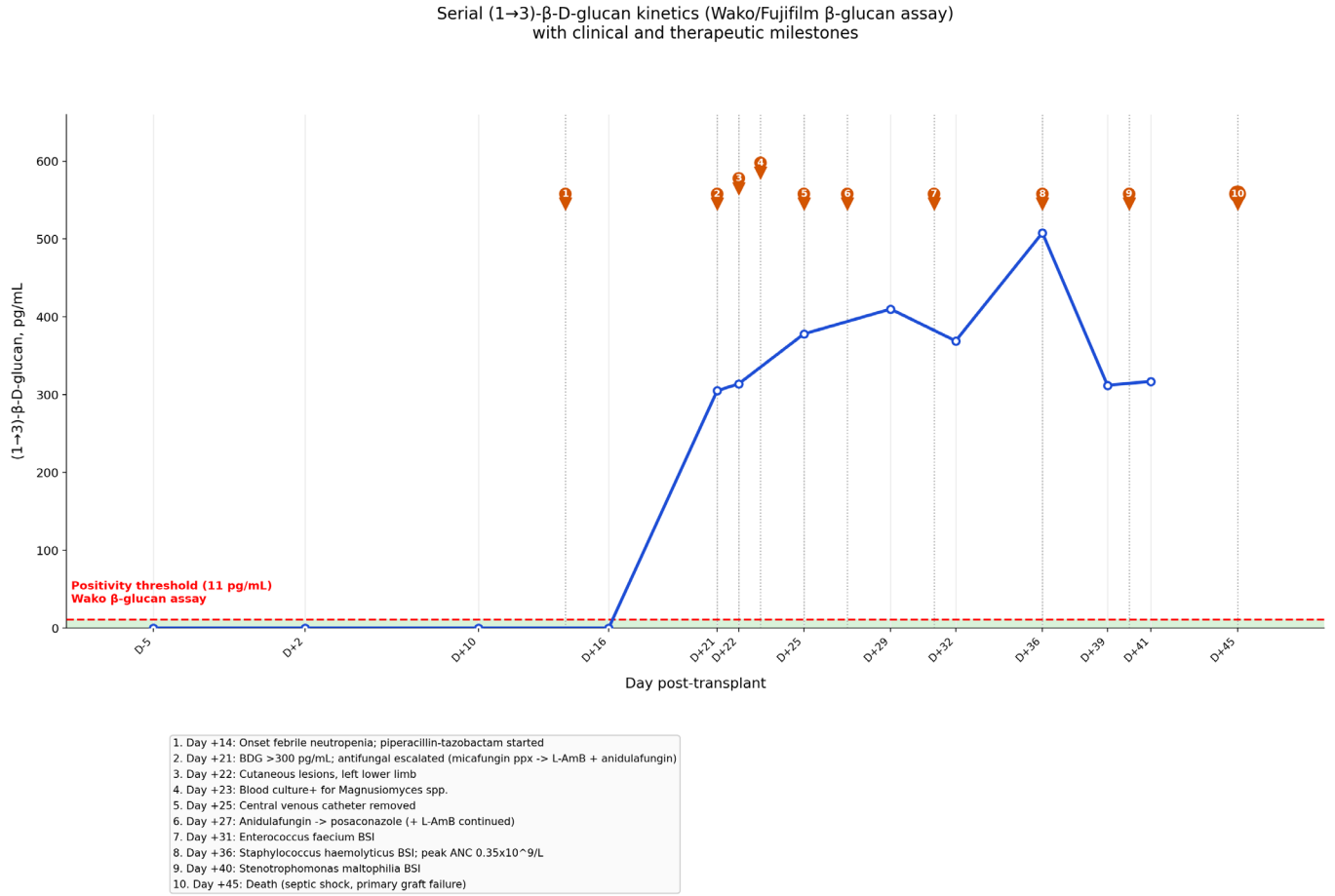

Figure 1: Evolution of (1→3)-β-D-glucan kinetics (Wako/Fujifilm ß-glucan assay) with clinical and therapeutic milestones.

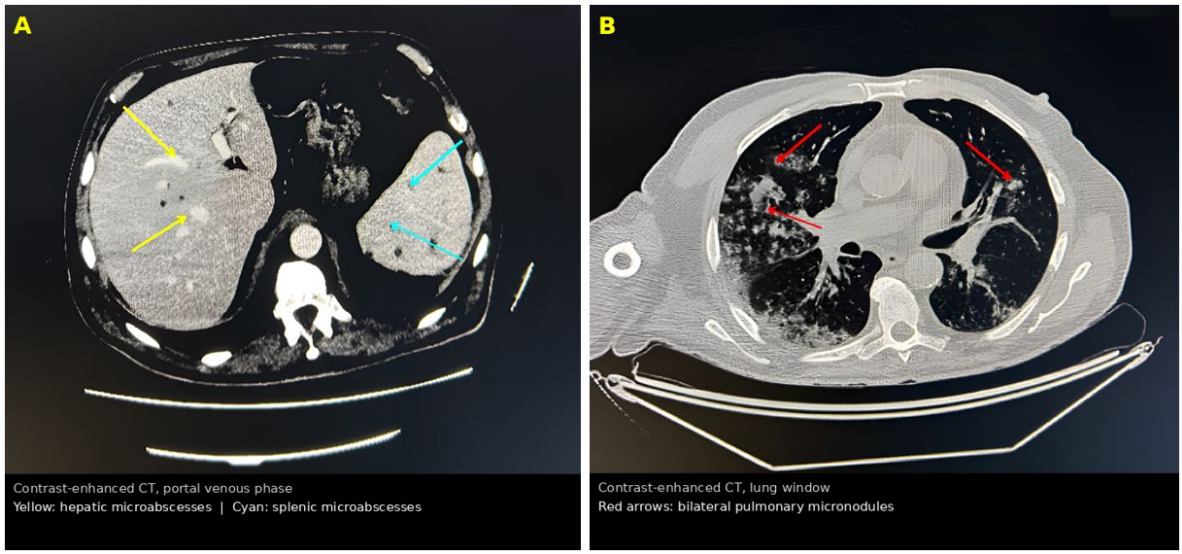

Figure 2.A. Contrast-enhanced CT, portal venous phase. Yellow arrows: hepatic microabscesses. Cyan arrows; splenic microabscesses.
Figure 2.B. Contrast- enhanced CT, lung window. Red arrows: bilateral small pulmonary nodules.

vitro activity was observed for amphotericin B and itraconazole. Consequently, anidulafungin was discontinued and switched to posaconazole on day +27, maintaining combination therapy with amphotericin B. The central venous catheter was removed on day +25, following isolation of *Magnusiomyces spp.* from blood culture identified by MALDI-TOF-MS. Catheter reinsertion was deferred given persistent bloodstream positivity for *Magnusiomyces spp.,* documented on blood cultures obtained approximately every 48 hours and coinciding with febrile episodes. Granulocyte transfusions were not considered in this patient.

Despite combined antifungal therapy, the patient showed persistent fungemia (four consecutive positive blood cultures) and sustained elevation of (1→3)-β-D-glucan levels, in the context of prolonged and profound

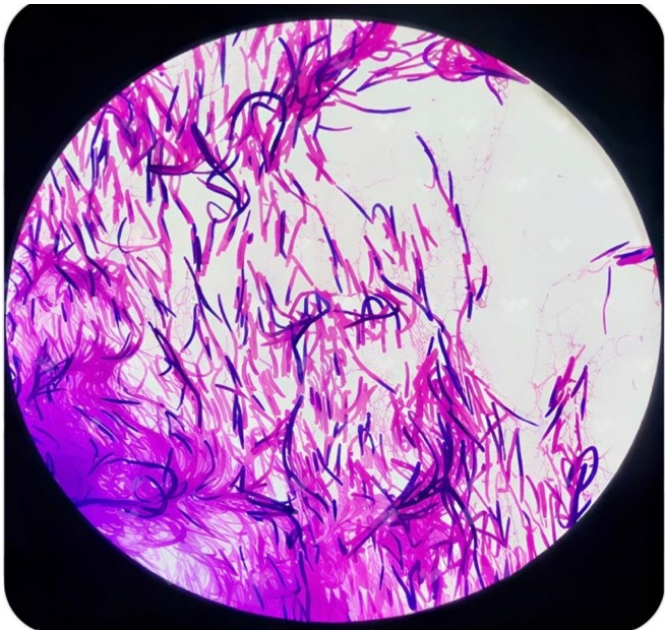

Figure 3. Microscopic morphology of Magnusiomyces spp. Gram-stained smear from a positive blood culture examined under oil immersion (×100 objective; ×1000 total magnification), showing abundant elongated and fragmented hyphal elements consistent with Magnusiomyces spp.

neutropenia without effective hematologic recovery. Although a transient increase in neutrophil count was observed (maximum 0.35×10⁹/L on day +36), this was followed by progressive decline, consistent with primary graft failure. The clinical course was further complicated by sequential bloodstream infections, including *Enterococcus faecium* (day +31), *Staphylococcus haemolyticus* (day +36), and *Stenotrophomonas maltophilia* (day +40). The patient progressively deteriorated with recurrent febrile episodes and ultimately died on day +45 due to septic shock in the setting of polymicrobial infection and primary graft failure.

Systematic overview of reported *Magnusiomyces* spp. infections in allo-HCT. In addition to our two cases, a total of eleven well-documented cases of *Magnusiomyces* infection in allo-HCT recipients have been reported to date,[9-19] predominantly in Europe (8/13, 62%). A summary of most relevant characteristics is provided in **Table 1**. All the following reported numbers and characteristics are based on the eleven previously reported cases together with the two additional cases described in the present study (n = 13). The majority of patients were male (92%, 12/13), adult (≥18 years old: 77%, 10/13), and had a malignant hematologic disease as the underlying disease (77%, 10/13). In all cases with neutrophil data (data available in 9/13, 69% of cases), infection occurred during profound neutropenia (ANC ≈ 0×10⁹/L) (100%, 9/9). Neutropenic fever was the most common clinical presentation (92%, 12/13), and fungemia was documented in most patients, with blood cultures being the primary diagnostic source (92%, 12/13). Less frequently, localized infection (skin/soft-tissue involvement) was reported (8%, 1/13). Deep organ involvement was frequent, including lungs, liver, spleen, kidneys, central nervous system, and skin (85%, 11/13), indicating a strong propensity for hematogenous dissemination.

Among the eleven previously published cases, antifungal prophylaxis was heterogeneous: fluconazole (18%, 2/11), posaconazole (36%, 4/11), micafungin or caspofungin (27%, 3/11), amphotericin B (9%, 1/11), and not reported (9%, 1/11). Galactomannan test monitoring was consistently negative when reported (100%, 3/3; tested in 23%, 3/13 of the full cohort). In contrast, (1→3)-β-D-glucan, when checked, was positive (100%, 3/3; tested in 23%, 3/13).

Treatment strategies varied, but most patients received amphotericin B-based regimens (77%, 10/13), frequently in combination with triazoles such as voriconazole, posaconazole, or isavuconazole (62%, 8/13; representing 80%, 8/10 of those treated with amphotericin B). Despite antifungal therapy, outcomes remained poor, with an overall mortality of 69% (9/13), typically occurring early after infection diagnosis (median day 25) and commonly associated with septic shock or multiorgan failure.

Discussion. *Magnusiomyces capitatus* is an emerging opportunistic pathogen increasingly reported in patients with hematologic malignancies and allo-HCT recipients. Its intrinsic resistance to echinocandins and reduced susceptibility to fluconazole represent a major therapeutic challenge and may contribute to breakthrough infections under antifungal prophylaxis.[3,4,20] In line with this, both of our breakthrough cases occurred under echinocandin exposure, highlighting the clinical need for antifungal prophylaxis strategies with reliable activity against *Magnusiomyces spp* in these profoundly immunocompromised hosts.

A literature review by *Girmenia et al*. identified 35 cases of systemic *M. capitatus* infection between 1983 and 2002, predominantly in HM patients (91.7%), most commonly acute myeloid leukaemia (75%) during induction chemotherapy (85%). Notably, severe neutropenia (< 0.1×10⁹/L) was present in 95% of cases, highlighting its role as a key risk factor for IFD[21]. In the specific setting of allo-HCT, *Magnusiomyces* spp. infections remain rare but increasingly recognized. In our literature review (n = 11), acute leukaemia was the most common underlying condition (55%, 6/11), followed by aplastic anemia (27%, 3/11). A variety of donor types were represented, with a similar proportion of matched unrelated donors (9/10 or 10/10) (33%, 3/9), haploidentical donors (33%, 3/9), and matched related donors (22%, 2/9); donor type was not reported in 18%

Table 1A. Baseline demographic and transplant characteristics of the 13 patients with invasive *Magnusiomyces* infection after allo-HCT (11 previously reported cases and the 2 present cases).

Variable≠	1	2	3	4	5	6	7	8	9	10	11	12*	13*
Reference (author, year)	Rodrigo Martino et al., 2004 [8]	González-Abad et al., 2012 [9]	S.K. Devadas et al., 2015 [10]	Dominika Tanuskova et al., 2017 [11]	Shuki Oya et al., 2018 [12]	Massimiliano Leoni et al., 2019 [13]	Giuliana Lo Cascio et al., 2020 [14]	Julio Maquera-Afaray et al., 2022 [15]	Rinaldi A et al., 2022 [16]	Rochelle Johnstone et al., 2022 [17]	Rahmah S. Alzahrani et al., 2025 [18]	Present study, Case 1, 2025	Present study, Case 2, 2025
Country	Spain	Spain	India	Slovakia	Japan	Italy	Italy	Peru	Italy	Canada	Canada	Spain	Spain
Age / sex	37 y / M	9 y / M	33 y / M	19 y / F	68 y / M	6 y / M	60 y / M	5 y / M	61 y / M	39 y / M	69 y / M	57 y / M	67 y / M
Underlying hematologic disease	ALL	AA	AML	MDS	ALL	AA	AML	AA	AML	AML	PMF	AML	PMF
Donor type (HLA match)	NR	MUD (10/10)	MRD (10/10)	MUD (9/10)	UCB donor (4/6)	Haploidentical	NR	Haploidentical	MUD (10/10)	Haploidentical	MRD (10/10)	Haploidentical	MUD (10/10)
Conditioning regimen	NR	NR	MAC	MAC	RIC	RIC	NR	RIC	RIC	NR	RIC	MAC	RIC
GVHD prophylaxis	NR	NR	CsA + MTX	ATG + CsA + MTX	TAC + MTX	NR	NR	NR	ATG + CsA + MTX	NR	TAC + MMF	SIR + MMF + PTCy	SIR + MMF + PTCy
Stem cell source	PB	BM	NR	PB	UCB	PB	NR	BM	PB	NR	PB	PB	PB
Antifungal prophylaxis	FLC	NR	POS	MCFG	MCFG	L-AmB	POS	POS	POS	CAS	FLC	MCFG	MCFG

Abbreviations: AA, aplastic anemia; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; ATG, antithymocyte globulin; BM, bone marrow; CAS, caspofungin; CsA, cyclosporine A; F, female; FLC, fluconazole; GVHD, graft-versus-host disease; HLA, human leukocyte antigen; HSCT, hematopoietic stem cell transplantation; L-AmB, liposomal amphotericin B; M, male; MAC, myeloablative conditioning; MCFG, micafungin; MDS, myelodysplastic syndrome; MMF, mycophenolate mofetil; MRD, matched related donor; MTX, methotrexate; MUD, matched unrelated donor; NR, not reported; PB, peripheral blood; PMF, primary myelofibrosis; POS, posaconazole; PTCy, post-transplant cyclophosphamide; RIC, reduced-intensity conditioning; SIR, sirolimus; TAC, tacrolimus; UCB, umbilical cord blood. * Present study (Case 1, Hospital Universitario La Princesa, Madrid; Case 2, Hospital Clínico Universitario de Valencia), both 2025; shaded columns. NR: not reported in the source publication. ≠Full case-level detail (ANC values, neutrophil engraftment day, granulocyte transfusion timing, catheter removal, and biomarker assays) is provided in Supplementary Table S1.

Table 1B. Infection characteristics, treatment, and outcome of the same 13 patients.

Variable≠	1	2	3	4	5	6	7	8	9	10	11	12*	13*
Clinical presentation	FN	FN	Skin/soft-tissue nodules	FN	FN	FN	FN	FN	FN	FN	FN	FN	FN
Deep-organ involvement	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
ANC at infection onset	0 ×10⁹/L	NR	NR	0 ×10⁹/L	0 ×10⁹/L	0 ×10⁹/L	NR	0 ×10⁹/L	0 ×10⁹/L	NR	0 ×10⁹/L	0 ×10⁹/L	0 ×10⁹/L
Site of isolation	Blood culture	Blood culture	Skin/soft-tissue biopsy	Blood culture	Blood culture	Blood culture	Blood culture	Blood culture	Blood culture + CSF	Blood culture	Blood culture	Blood culture	Blood culture
Day of infection post-HSCT	NR	NR	>Day +180 (>6 mo)	Day +3	Day +11	Day +2	Day +5	Day +147	NR	Day +5	Day +13	Day +21	Day +23
Antifungal treatment	L-AmB	L-AmB + POS	VRC	MCFG + VRC	L-AmB + FLC	L-AmB + VRC	L-AmB	CAS	L-AmB + ISA	VRC + L-AmB	VRC + L-AmB	L-AmB + POS → ISA	L-AmB + anidulafungin→ POS + L-AmB
Outcome (day post-HCT)	Alive	Death (+90 d)	Alive	Death (+71 d)	Death (+25 d)	Alive	Alive	Death (+150 d)	Death (+17 d)	Death (+13 d)	Death (+22 d)	Death (+24 d)	Death (+45 d)
Cause of death	–	Septic shock	–	Multiorgan failure	Respiratory failure	–	–	Septic shock	Central nervous system IFD	Intracerebral hemorrhage	Septic shock	Multiorgan failure	Septic shock

Abbreviations: ANC, absolute neutrophil count; CSF, cerebrospinal fluid; FN, febrile neutropenia; HSCT, hematopoietic stem cell transplantation; ISA, isavuconazole; L-AmB, liposomal amphotericin B; MCFG, micafungin; POS, posaconazole; VRC, voriconazole. * Present study (Case 1, Hospital Universitario La Princesa, Madrid; Case 2, Hospital Clínico Universitario de Valencia), both 2025; shaded columns. NR: not reported in the source publication. ≠Full case-level detail (ANC values, neutrophil engraftment day, granulocyte transfusion timing, catheter removal, and biomarker assays) is provided in **Supplementary Table S1**.

(2/11). More recently, Del Principe et al. reported the largest multicentre series of *Magnusiomyces* infections, including 90 patients with hematologic diseases, of whom 29 (32%) had undergone HCT.[22] Interestingly, no significant differences in treatment outcomes were observed between transplanted and non-transplanted patients, suggesting that the poor prognosis is mainly driven by the profound underlying immunosuppression rather than transplantation itself. However, because transplant-specific clinical characteristics and individual patient-level data were not fully available, detailed analyses of allo-HCT recipients remain limited. The failure of neutrophil recovery has been described as a risk factor for mortality in infections by *Magnusiomyces* and granulocyte transfusions have shown benefit in selected case reports.[23] Nevertheless, the mortality of *Magnusiomyces* infections is very high, similar or even higher than in candidemia.[24]

Geographical distribution also appears relevant, as most cases have been reported in Europe (55%, 6/11), particularly in Mediterranean countries (45%, 5/11), with fewer cases described in North and South America and Asia.[13,18] This may reflect an endemic epidemiology, although we cannot rule out a reporting bias.

Clinically, *Magnusiomyces capitatus* infection closely resembles disseminated candidiasis, often presenting as persistent neutropenic fever with frequent progression to fungemia. Blood cultures remain the cornerstone of diagnosis, with positivity rates reported up to 70%, higher than those observed for *Candida* and *Aspergillus* infections.[7,24,25] In fact, *Magnusiomyces* spp. fungemia mainly occurs in HM patients.[26] The organism grows on standard fungal media within 24–48 hours, although prolonged incubation may be required, and is characterized microscopically by hyphae, pseudohyphae, and arthroconidia.[2,27] Deep organ involvement occurs in 60–80% of cases, with a predilection for lungs, liver, spleen, kidneys, central nervous system, and skin.[24,25] Our review of allo-HCT recipients confirms these findings. Most patients presented with fungemia (92%, 12/13), and diagnosis was predominantly established through positive blood cultures. Deep organ involvement was documented in 85% (11/13) of cases, most frequently affecting lungs, central nervous system, skin, and kidneys. Localized presentations were uncommon (8%, 1/13), with only isolated cases diagnosed through spinal or subcutaneous cultures.

Currently, no validated culture-independent diagnostic tools, such as PCR assays or specific circulating biomarkers, are available for the early diagnosis of *Magnusiomyces* spp. However, once fungal growth is obtained, MALDI-TOF mass spectrometry has become the first-line method for rapid species identification and may substantially shorten the time to microbiological diagnosis and appropriate antifungal management. Nevertheless, diagnosis still depends on fungal isolation, and additional non-culture-based diagnostic strategies are lacking. Although galactomannan testing is consistently negative, (1→3)-β-D-glucan may be elevated, as demonstrated in vitro and in clinical samples, suggesting a potential role as a non-specific marker of breakthrough infection and for guiding response to therapy[26] in the appropriate clinical context, which is in contrast to current ESCMID recommendations that suggest galactomannan monitoring for this fungal agent.[2] Nevertheless, data remain scarce, and its diagnostic utility in this setting is not well established, requiring further research.

Regarding the therapeutic approach, management of *Magnusiomyces* infections remains challenging due to the lack of robust evidence and standardized guidelines.[2] The organism exhibits intrinsic resistance to echinocandins, related to naturally occurring mutations in the FKS1 gene encoding β-1,3-D-glucan synthase,[28] and high rates of resistance to fluconazole have also been reported.[2,15] Current global guidance indicates that echinocandins lack clinically relevant activity against this organism, whereas voriconazole and amphotericin B formulations are the treatment options most commonly recommended; antifungal susceptibility testing is advisable given inter-strain variability, source control is an important adjunct, and restoration of host immunity, particularly neutrophil recovery, remains central to outcome. Evidence supporting combination antifungal therapy remains of very low quality, derived mainly from case reports and small case series rather than comparative studies.[2,29] However, despite amphotericin B therapy (77%, 10/13) in combination with triazoles (80%, 8/10 of amphotericin-B–treated cases), treatment failure was high (69%, 9/13), highlighting the clinical need for new antifungals in this scenario.

Susceptibility testing is strongly recommended to guide therapy,[2,30] given the variability in azole activity. In cases of fungemia, removal of central venous catheters is generally recommended. However, data from the SEIFEM and FungiScope registries did not demonstrate a clear survival benefit associated with G-CSF administration or catheter removal for these infections.[22] In our review, central venous catheter removal was performed in 8/13 (62%) of cases (not reported in 5/13, 38%); among those with data, removal was performed in 75% (6/8), and in all 8 of those cases catheter cultures were negative, suggesting bloodstream infection may originate from gastrointestinal translocation rather than catheter-related sources. In both presented cases, severe mucositis and diarrhea were likely the relevant predisposing factors.

Breakthrough infections account for up to 40% of *Magnusiomyces* cases in registry data.[22] In this allo-HCT series, 38% (5/13) of infections occurred under echinocandin prophylaxis, while 31% was on posaconazole prophylaxis (4/13), 15% on fluconazole

(2/13), 8% (1/13) was on amphotericin B, and 8% (1/13) had no prophylaxis data reported. Despite early initiation of combination antifungal therapy, outcomes remained poor, with high mortality[15,31]. Importantly, survival was mainly observed in patients achieving neutrophil recovery.[15,22]

Some limitations of this case series and structured literature review should be acknowledged. This review is based on 13 heterogeneous, retrospectively collected case reports/series with substantial missing data and probable publication bias favouring reported (often fatal or unusual) cases; as such, it can describe recurring clinical associations but cannot establish comparative efficacy of prophylaxis or treatment strategies, nor the relative contribution of host- versus transplant-related risk factors. Current evidence supports early treatment schedules based on amphotericin B plus azole therapy, particularly in breakthrough infections arising under echinocandin prophylaxis. However, high mortality rates still make it a clinical challenge for which further evidence is needed. Finally, we acknowledge as a study limitation that MALDI-TOF database version and molecular confirmation by sequencing were not systematically available because microbiological testing was performed as part of routine clinical care rather than a standardized research protocol.

Conclusions. *Magnusiomyces capitatus* infection represents a rare but highly lethal IFD in allo-HCT recipients, typically occurring as a breakthrough infection in the setting of profound neutropenia regardless of antifungal prophylaxis. Mortality remains high despite antifungal therapy, particularly in the absence of neutrophil recovery. Our two cases illustrate complementary clinical presentations, fulminant septic shock and progressive disseminated infection, both occurring under echinocandin prophylaxis and both resulting in fatal outcomes despite combination therapy with amphotericin B and triazoles. These findings are consistent with previously reported cases and underscore the need for early suspicion, rapid initiation of appropriate antifungal therapy, and, critically, restoration of host immunity particularly neutrophil recovery. Given the limited and heterogeneous evidence available, the optimal antifungal treatment for invasive Magnusiomyces spp. infection in allo-HCT recipients remains uncertain. Although amphotericin B-based regimens, frequently combined with an azole, have been commonly used, their efficacy cannot be established from the available case-based evidence, highlighting the need for larger multicenter studies to define therapeutic strategies better.

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