Fusarium Infection
Report of 26 Cases and Review of 97 Cases From the Literature

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INTRODUCTION

Fusarium species, Aspergillus species, and Zygomycetes are the most clinically important molds. Fusarium species isolates are universally found in the environment and cause infection in both humans and plants.29,33,94,95,97 In humans, infection starts with the inhalation of Fusarium conidia or direct contact with materials contaminated with Fusarium conidia. Subsequently, conidia germinate and form filaments that invade the surrounding tissue when a suitable environment is offered.

There is a paucity of reports describing the predisposing factors and clinical characteristics of patients with Fusarium infection.77 The clinical presentation of fusariosis depends on the host’s immune status.140 Invasive infections, such as sinusitis, pneumonia, deep cutaneous infections, and disseminated infections, present in immunocompromised patients and most commonly manifest as fever not responding to antimicrobial medications.96 Specifically, neutropenia, deficits in cellular immunity, induction chemotherapy for leukemia, and hematopoietic cell transplantation are considered risk factors for the development of invasive fusariosis.15,96,98 On the other hand, immunocompetent patients present more frequently with superficial infections, such as keratitis and onychomycosis.19,49,50,60

In the current study, we describe the clinical characteristics of 26 patients with proven or probable invasive fusariosis managed at Massachusetts General Hospital (MGH) during a 10-year period and review the literature of cases with fusariosis published since January 2000, focusing on the therapeutic approach and outcome of patients.

PATIENTS AND METHODS

We identified patients with fusariosis treated at MGH from January 2000 to January 2010 by searching the records of the clinical microbiology laboratory at MGH, Boston, MA. We collected data by reviewing the electronic medical records of the patients; we retrieved their baseline characteristics, underlying diseases, treatment modalities, and outcome. We categorized all patients according to the revised definitions of the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/IFICG and NIAID/MSG) into proven and probable cases.

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Abbreviations: COPD = chronic obstructive pulmonary disease, EORTC = European Organization for Research and Treatment of Cancer, FSSC = Fusarium solani species complex, G-CSF = granulocyte colony-stimulating factor, GM-CSF = granulocyte macrophage colony-stimulating factor, HSCT = hematopoietic stem cell transplant, IFICG = Invasive Fungal Infection Cooperative Group, MIC = minimum inhibitory concentration, MSG = Mycoses Study Group, MGH = Massachusetts General Hospital, NIAID = National Institute of Allergy and Infectious Diseases.
## TABLE 1. Characteristics of 26 MGH Patients With Fusarium Infection

| Patient | Age (yr)/Sex | Underlying Disease | Pathogen Source | Reason for Admission | Antifungal Prophylaxis Treatment | Treatment Trial or Empiric Therapy | Reason for Other Fungal Cause | Outcome |
|---------|--------------|--------------------|-----------------|---------------------|----------------------------------|-----------------------------------|---------------------------------|---------|
| 1       | 45/F         | Skin               | Not significant | Excision for planter mass | NA                              | NA                               | NA                             | Recovered |
| 2       | 23/M         | Blood, CSF, urine  | Focal segmental glomerulosclerosis | Nausea and vomiting and headache | NA                              | NA                               | NA                             | Died    |
| 3       | 20/F         | Bronchial washings | Cystic fibrosis (lung transplant 1 yr ago) | NA                             | NA                               | NA                               | NA                             | Liposomal amphotericin B plus caspofungin (for Aspergillus) | Died    |
| 4       | 68/F         | Skin               | Not significant | NA                  | NA                              | NA                               | NA                             | Recovered |
| 5       | 4/M          | Skin               | Burn            | NA                  | Voriconazole                     | NA                               | NA                             | Recovered |
| 6       | 17/F         | Bone               | Burn            | NA                  | Voriconazole                     | NA                               | NA                             | Recovered |
| 7       | 55/M         | Bronchial washings | Alpha-1-antitrypsin deficiency (lung transplant 2 mo ago) | NA                             | NA                               | NA                               | NA                             | Recovered |
| 8       | 59/F         | Bronchial washings | Idiopathic pulmonary fibrosis (lung transplant 1 yr ago) | Motor vehicle accident | Liposomal amphotericin B plus caspofungin | NA | NA | Recovered |
| 9       | 66/F         | Bronchial washings | COPD (lung transplant 15 yr ago) | NA                             | NA                               | NA                               | NA                             | Liposomal amphotericin B plus voriconazole | Recovered |
| 10      | 8/F          | Skin               | Not significant | NA                  | NA                               | NA                               | NA                             | Liposomal amphotericin B plus voriconazole | Recovered |
| 11      | 4/F          | Skin               | Burn            | NA                  | NA                               | NA                               | NA                             | Liposomal amphotericin B plus micafungin | Died    |
| 12      | 59/M         | Skin               | Acute myelogenous leukemia | NA                             | NA                               | NA | NA | Fluconazole | Recovered |
| 13      | 52/M         | Skin               | COPD (lung transplant 2 years ago) | Hospitalization assessment for end-stage liver disease | Fluconazole | NA | NA | Liposomal amphotericin B plus voriconazole | Recovered |
| 14      | 19/F         | Bronchial washings | Cystic fibrosis, (lung transplant 2 years ago) | Fever and shortness of breath | Fluconazole | NA | NA | Vericonazole | Recovered |

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| Patient | Age | Gender | Site | Condition | Symptoms | Treatments | Outcome |
|---------|-----|--------|------|-----------|----------|------------|---------|
| 15      | 36F | Skin   | Burn | Burn      |          | NA         | M RAFV    |
| 16      | 52M | Blood culture | B-cell lymphoma | Abdominal pain and nausea and vomiting | M RAFV | Voriconazole plus (surgical debridement) | NA      |
| 17      | 51M | Bronchial washings | COPD, and TB | Shortness of breath, chest pain, cough, and fever | Liposomal amphotericin B plus voriconazole | NA      | Died    |
| 18      | 63M | Blood | Acute myelogenous leukemia | Anemia, shortness of breath, hyperuricemia | Fluconazole | NA      | Voriconazole | NA      |
| 19      | 42F | Blood and left inguinal nodes | Not significant | Fever due to infection in the groin region after catheterization | NA | Voriconazole | NA      |
| 20      | 44M | Bronchial washings | Idiopathic pulmonary fibrosis (lung transplant 4 mo ago) | Respiratory failure | Liposomal amphotericin B plus voriconazole | NA      | Died    |
| 21      | 15F | Skin | Burn |          |          | Liposomal amphotericin B plus (surgical debridement) | NA      |
| 22      | 39F | Bronchial washings | Hodgkin disease, autologous stem cell transplant 3.5 yr ago | Shortness of breath | Liposomal amphotericin B plus voriconazole | NA      | Died    |
| 23      | 53M | Blood culture | Acute myelogenous leukemia | Chemotherapy | Liposomal amphotericin B plus voriconazole | NA      | Recovered |
| 24      | 7M  | Skin | Asthma | Motor vehicle accident | Voriconazole (extensive debridement) | NA      | Recovered |
| 25      | 56F | Skin | Lung cancer, burn | Burn | Liposomal amphotericin B plus voriconazole (then D/C) and surgical debridement | NA      | NA      |
| 26      | 54F | Sputum | Lung cancer and COPD |          | Itraconazole | NA      | Recovered |

Abbreviations: CSF = cerebrospinal fluid, NA = not applicable, TB = tuberculosis.

* Patients 3, 7, 8, 9, 14, and 20 have previously been reported.
In our literature review, we identified published cases of fusariosis in the English literature by searching the MEDLINE database (National Library of Medicine, Bethesda, MD) using the terms “Fusarium” or “fusariosis.” Non-English language studies, expert commentaries, and abstracts from scientific meetings were excluded. Of note, in order to focus on invasive fusariosis, we also excluded patients with superficial localized infections, such as keratitis and onychomycosis. Finally, we excluded cases with positive cultures for Fusarium species but without histopathologic confirmation, and cases with limited data.

RESULTS

Case Series

We identified 26 patients with proven (n = 20) or probable (n = 6) invasive fusariosis. The mean age was 38 years (range, 4–68 yr). Table 1 represents the baseline patient characteristics. The most common underlying conditions included burns (n = 7), lung transplantation (n = 6, performed 2 mo, 4 mo, 1 yr, 1 yr, 2 yr, and 15 yr before the diagnosis of fusariosis was established) and hematologic malignancies (n = 5), such as acute myeloid leukemia (n = 3), B-cell lymphoma (n = 1), and Hodgkin lymphoma treated with stem cell transplantation 3.5 years before the index hospitalization (n = 1). Less frequent underlying diseases included focal segmental glomerulosclerosis (n = 1), end-stage liver disease (n = 1), chronic obstructive pulmonary disease (COPD) and tuberculosis (n = 1), lung cancer and COPD (n = 1), and asthma (n = 1). Of note, 3 patients had no comorbidities. Twelve patients were receiving immunosuppressive therapy at the time of admission, including cancer chemotherapy (n = 9), calcineurin inhibitors (n = 5), such as tacrolimus or cyclosporine and steroids (n = 2). Six patients developed fusariosis while receiving antifungal agents for prophylaxis, specifically fluconazole (n = 4), micafungin (n = 1), and voriconazole (n = 1).

Skin was the most common site of infection (n = 11; 8 proven and 3 probable), followed by lung (n = 8 proven) and disseminated infection (n = 7; 4 proven and 3 probable). No speciation of Fusarium species was performed by the clinical laboratory of MGH. The minimum inhibitory concentration (MIC) of antifungal agents was determined for 4 isolates. Two were resistant to voriconazole (≥8 µg/mL) and 2 to both voriconazole and amphotericin B (≥8 µg/mL).

The diagnosis of skin fusariosis was established with cultures from the skin growing Fusarium species (n = 11) and skin biopsy (n = 8). Regarding the therapeutic management of skin fusariosis, 4 patients received medical treatment alone; 3 received combination therapy and died (liposomal amphotericin B/voriconazole: n = 2; and liposomal amphotericin B/micafungin: n = 1); and 1 received monotherapy with voriconazole and was cured. Five patients received both surgical and antifungal therapy; 3 received combination therapy (1 liposomal amphotericin B/micafungin and recovered, 1 voriconazole/micafungin and recovered, and 1 liposomal amphotericin B and voriconazole and died) and 2 received monotherapy (1 liposomal amphotericin B lost to follow-up and 1 voriconazole and recovered). Finally, 2 patients were treated surgically only and recovered. We note that 2 patients received granulocyte colony-stimulating factor (G-CSF) and G-CSF combined with granulocyte macrophage colony-stimulating factor (GM-CSF), respectively, for neutropenia (Table 2). Overall, 4 of 6 patients who received combination therapy died (66.7% mortality), and 1 of them had undergone subsequent surgery. On the other hand, none of the patients who received monotherapy, surgical treatment alone, or monotherapy with surgical treatment died.

Patients with pulmonary fusariosis presented with shortness of breath (n = 6), fever (n = 6), cough (n = 3), fatigue (n = 2), and chest pain (n = 1), and Fusarium species were isolated from bronchial washings (n = 7) and sputum (n = 1). Regarding the treatment administered, 4 patients received monotherapy and recovered (voriconazole: n = 3; itraconazole: n = 1), while 4 received combination therapy (2 liposomal amphotericin B/voriconazole and died, 1 liposomal amphotericin B/caspofungin and died, and 1 inhaled amphotericin B and oral voriconazole and recovered). Overall, 3 of 4 patients who were treated with combination therapy died (75% mortality), while none of the patients treated with monotherapy died. Of note, as shown in Tables 1 and 2, 5 of the 8 cases of pulmonary fusariosis have previously been described.17 Patients with disseminated fusariosis presented with various clinical symptoms, including nausea and vomiting (n = 2), shortness of breath (n = 2), and fever (n = 1), and all of them had blood cultures positive for Fusarium species. Three patients were treated with combination therapy (liposomal amphotericin B/voriconazole, 2 died and 1 recovered), 3 patients received monotherapy with voriconazole and recovered, while 1 patient received no therapy and died (fusariosis was diagnosed after death). Overall, 2 of 3 patients who received combination therapy died (66.7% mortality), while none of the patients treated with monotherapy died. Of note, as shown in Tables 1 and 2, 1 case of disseminated fusariosis has previously been reported.17

Literature Review

We identified 97 cases of invasive fusariosis from the literature published since 2000.1

In our literature review, we identified published cases of fusariosis from the English literature by searching the MEDLINE database (National Library of Medicine, Bethesda, MD) using the terms “Fusarium” or “fusariosis.” Non-English language studies, expert commentaries, and abstracts from scientific meetings were excluded. Of note, in order to focus on invasive fusariosis, we also excluded patients with superficial localized infections, such as keratitis and onychomycosis. Finally, we excluded cases with positive cultures for Fusarium species but without histopathologic confirmation, and cases with limited data.
TABLE 2. Treatment and Outcome of 26 MGH Patients

| Skin fusariosis (n = 11)* | Adjunct therapy (n = 8) | Outcome |
|---------------------------|------------------------|---------|
| Medical therapy (n = 9)   | Liposomal amphotericin B/voriconazole (n = 3) | Surgery (n = 1) | Died |
| Combination therapy (n = 6) | Liposomal amphotericin B/micafungin (n = 2) | Surgery (n = 1) | Died |
| Monotherapy (n = 3)       | Voriconazole (n = 1) | Surgery (n = 1) | Died |
| No medical therapy (n = 2) | Liposomal amphotericin B (n = 1) | Surgery and G-CSF (n = 1) | Lost to follow-up |

| Pulmonary fusariosis (n = 8) | Adjunct therapy (n = 0) | Outcome |
|-------------------------------|------------------------|---------|
| Medical therapy (n = 8)       | Liposomal amphotericin B/voriconazole (n = 2) | NA | Died* |
| Combination therapy (n = 4)   | Liposomal amphotericin B/caspofungin (n = 1) | NA | Died† |
| Monotherapy (n = 4)           | Voriconazole (n = 1) | Inhaled amphotericin B/voriconazole (n = 1) | Recovered† |

| Disseminated fusariosis (n = 7) | Adjunct therapy (n = 0) | Outcome |
|---------------------------------|------------------------|---------|
| Medical therapy (n = 6)         | Liposomal amphotericin B/voriconazole (n = 1) | NA | Died† |
| Combination therapy (n = 3)     | Liposomal amphotericin B/voriconazole (n = 2) | NA | Died* |
| Monotherapy (n = 3)             | Voriconazole (n = 3) | Recovered* |
| No medical therapy (n = 1)       | NA | Recovered* |

*New MGH cases.
†Previously published MGH cases.

7 recovered; liposomal amphotericin B/flucytosine: n = 2, 1 recovered; liposomal amphotericin B/flucytosone: n = 1, recovered; liposomal amphotericin B/itraconazole: n = 1, recovered; itraconazole/terbinafine: n = 1, recovered; and liposomal amphotericin B/posaconazole/terbinafine: n = 1, recovered). Two patients had the combination of surgery and antifungal monotherapy and recovered (amphotericin B: n = 1; and voriconazole: n = 1), while 3 underwent only surgery and recovered. We note that 9 patients received G-CSF because of neutropenia, while 1 received granulocytes, and 1 received the combination of G-CSF and granulocytes. Overall, 5 of the 16 patients who received combination therapy died (31.3% mortality), while 2 of the 19 patients who received monotherapy died (12.5% mortality).

DISCUSSION

Herein we present 26 patients with proven or probable invasive fusariosis treated at a general hospital (MGH patients) and review 97 cases reported since 2000. Hematologic malignancies, solid organ transplantation, HSCT, or immunosuppressive therapy were the predominant underlying conditions, and the skin was the predominant site of infection in both MGH and literature cases. The most frequently identified species among literature patients were members of the Fusarium solani complex (49%; 29 of 59 isolates). The clinical presentation varied depending on the infected site; diagnosis was established with biopsy and culture. Blood cultures were positive in 86% of MGH patients and 82% of literature patients with disseminated fusariosis (82% of
TABLE 3. Treatment and Outcome of 97 Patients From the Literature

| Initial Medical Therapy          | Sequential Medical Therapy         | Adjunct Therapy | Outcome |
|----------------------------------|------------------------------------|-----------------|---------|
| **Skin fusariosis (n = 40)**     |                                    |                 |         |
| Combination therapy (n = 18)     | Liposomal amphotericin B/voriconazole (n = 7) | NA (n = 5)      | Died (n = 3) |
| Liposomal amphotericin B/voriconazole (n = 12) | G-CSF (n = 1) | Recovered (n = 2) |
| Liposomal amphotericin B/itraconazole (n = 1) | G-CSF/granulocytes (n = 1) | Died (n = 1) |
| Liposomal amphotericin B (n = 3) |                                    | G-CSF (n = 1)   | Recovered (n = 2) |
| Posaconazole (n = 1)             | Liposomal amphotericin B/flucytosine (n = 2) | NA (n = 1)      | Died (n = 1) |
| Flucytosine (n = 1)              | Liposomal amphotericin B/fluconazole (n = 1) | G-CSF (n = 1)   | Recovered (n = 1) |
| Liposomal amphotericin B/fluconazole (n = 1) | Liposomal amphotericin B/fluconazole (n = 1) | NA (n = 1)      | Recovered (n = 1) |
| Voriconazole (n = 1)             | Liposomal amphotericin B/posaconazole/terbinafine (n = 1) | Granulocytes (n = 1) | Recovered (n = 1) |
| Itraconazole/terbinafine (n = 1) | Itraconazole/terbinafine (n = 1) | NA (n = 1)      | Recovered (n = 1) |
| Monotherapy (n = 19)             | Voriconazole (n = 8)               | NA (n = 3)      | Recovered (n = 7) |
| Liposomal amphotericin B/voriconazole (n = 1) | Voriconazole (n = 1)              | Surgery (n = 1) | Recovered (n = 7) |
| Liposomal amphotericin B (n = 1) |                                    | G-CSF (n = 2)   | Died (n = 1) |
| Liposomal amphotericin B/fluconazole (n = 1) | Liposomal amphotericin B (n = 3) | G-CSF (n = 3)   | Recovered (n = 2) |
| Liposomal amphotericin B/fluconazole (n = 1) | Liposomal amphotericin B (n = 1) | G-CSF (n = 1)   | Died (n = 1) |
| Liposomal amphotericin B/posaconazole/terbinafine (n = 1) | Itraconazole/terbinafine (n = 1) | NA (n = 1)      | Recovered (n = 2) |
| Fluconazole (n = 2)              |                                    | G-CSF (n = 1)   | Recovered (n = 1) |
| Itraconazole (n = 1)             |                                    | NA (n = 4)      | Recovered (n = 2) |
| Itraconazole/terbinafine (n = 1) |                                    | Surgery (n = 1) | Recovered (n = 1) |
| No medical therapy (n = 3)       |                                    |                 | Recovered |

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### Pulmonary fusariosis (n = 3)

| Monotherapy (n = 3) | Voriconazole (n = 1) | Amphotericin B deoxycholate (n = 1) | Posaconazole (n = 1) | Voriconazole (n = 1) | Amphotericin B deoxycholate (n = 1) | Posaconazole (n = 1) | NA (n = 3) | Recovered (n = 3) |
|---------------------|----------------------|--------------------------------------|----------------------|----------------------|--------------------------------------|----------------------|------------|-----------------|

### Disseminated fusariosis (n = 23)

| Combination therapy (n = 7) | Liposomal amphotericin B/fluconazole (n = 2) | Liposomal amphotericin B/fluconazole (n = 2) | G-CSF (n = 2) | Recovered (n = 1) Died (n = 1) |
|-----------------------------|-----------------------------------------------|-----------------------------------------------|---------------|-----------------------------|
|                             | Liposomal amphotericin B (n = 1)              | Liposomal amphotericin B/voriconazole (n = 2) | G-CSF (n = 2) | Recovered (n = 2)           |
|                             | Voriconazole (n = 1)                          | Liposomal amphotericin B/terbinafine (n = 2)  | NA (n = 1)    | Died (n = 1)                |
|                             | Liposomal amphotericin B (n = 1)              | Liposomal amphotericin B/posaconazole (n = 1) | NA (n = 1)    | Died (n = 1)                |
|                             | Caspofungin/voriconazole (n = 1)              | Liposomal amphotericin B/posaconazole (n = 1) | NA (n = 1)    | Died (n = 1)                |
| Monotherapy (n = 16)        | Liposomal amphotericin B (n = 7)              | Liposomal amphotericin B (n = 9)              | NA (n = 4)    | Recovered (n = 3) Died (n = 1) |
|                             | Voriconazole (n = 1)                          | G-CSF (n = 1)                                |               | Recovered (n = 4)           |
|                             | Liposomal amphotericin B/voriconazole (n = 1) | NA (n = 1)                                   |               |                              |
|                             | Voriconazole (n = 1)                          | G-CSF (n = 1)                                |               |                              |
|                             | Liposomal amphotericin B (n = 3)              | Voriconazole (n = 4)                         | NA (n = 3)    | Recovered (n = 2) Died (n = 1) |
|                             | Voriconazole/caspofungin (n = 1)              | G-CSF/granulocytes (n = 1)                   | Recovered (n = 4) |                              |
|                             | Liposomal amphotericin B (n = 1)              | Itraconazole (n = 1)                         | G-CSF (n = 1) |                              |
|                             | Liposomal amphotericin B/voriconazole/        | Posaconazole (n = 1)                         | GM-CSF (n = 1) |                              |
|                             | caspofungin (n = 1)                           |                                               |               |                              |
|                             | Liposomal amphotericin B (n = 1)              | Caspofungin (n = 1)                          | G-CSF (n = 1) |                              |

### Other infected sites (n = 6)

| Nasal cavity (n = 2) | Liposomal amphotericin B (n = 2) | Voriconazole (n = 2) | NA (n = 6) | Recovered (n = 6) |
|----------------------|----------------------------------|----------------------|------------|-----------------|
| Peritonitis (n = 2)  | Liposomal amphotericin B/flucytosine (n = 1) | Liposomal amphotericin B/flucytosine (n = 1) | Liposomal amphotericin B/ketoconazole (n = 1) | Liposomal amphotericin B (n = 1) |
| Sinusitis (n = 1)    | Liposomal amphotericin B (n = 1)  | Liposomal amphotericin B (n = 1)  | Liposomal amphotericin B (n = 1)  | Liposomal amphotericin B (n = 1)  |
| Liver (n = 1)        | Fluconazole (n = 1)              | Liposomal amphotericin B (n = 1)  | Liposomal amphotericin B (n = 1)  | Liposomal amphotericin B (n = 1)  |
all patients with disseminated disease). The most commonly used therapeutic scheme in MGH patients was monotherapy with voriconazole (n = 8, 0% mortality), followed by the combination of amphotericin B/voriconazole (n = 8, 87.5% mortality). On the contrary, literature patients were more frequently treated with monotherapy with amphotericin B (n = 19, 10.5% mortality), followed by the administration of voriconazole as monotherapy (n = 15, 6.7% mortality) and the combination of amphotericin B/voriconazole (n = 14, 35.7% mortality). Overall, the mortality rates of patients receiving combination therapy were higher than those of patients receiving monotherapy in both MGH and literature patients and for all infected sites. Also, patients who underwent surgical intervention exhibited lower mortality rates than patients treated with antifungal agents only.

Fusarium species are ubiquitous in the environment and can be found in soil and water. In humans, Fusarium species cause a wide spectrum of diseases, ranging from superficial infections to locally invasive and disseminated infections. Invasive and disseminated fusariosis occurs mostly in patients with compromised immune systems, and especially neutropenia. In fact, in our study 61.5% of MGH patients and 100% of literature patients were immunocompromised. The most frequent underlying disease in both the MGH and the published cases was hematologic malignancies (53% of patients overall), while other major underlying diseases included solid organ transplantation (15% of patients overall) and HSCT (15% of patients overall). Also, the majority of patients (63% of patients overall) were receiving immunosuppressive regimens at the time of diagnosis of fusariosis, and 31% were neutropenic.

Although the clinical presentation of invasive fusariosis is highly variable, high fever that is not responsive to antifungal agents, respiratory infections also occur frequently, while skin involvement represents either a primary site of infection or metastatic lesions from disseminated disease and manifests as papules, nodules, areas of necrosis, mycetomas, target lesions, or bullae. In the current study, the skin was one of the main sites of infection (54% of patients overall). Since fusariosis leads to fatal outcomes without treatment or when treatment is delayed, skin lesions in immunocompromised patients should be investigated aggressively.

The diagnosis of fusariosis is mainly based on culture of infected sites and histopathology, which require more than 5–7 days. This can cause a delay in treatment and result in fatalities. Moreover, the microscopic characteristics of Fusarium species are not always distinguishable from other molds, especially Aspergillus species, and therefore identification requires significant expertise. In addition, immunocompromised patients often receive prophylaxis with antifungal medications, which turn cultures for Fusarium species negative and render diagnosis more difficult. Thus, non-culture methods such as polymerase chain reaction (PCR) may be superior for detecting Fusarium species.

Since there are not enough data to support a solid evidence-based approach to the treatment of invasive fusariosis, improvement in this domain is mandatory. Medical intervention remains the mainstay of treatment. Amphotericin B monotherapy is considered an effective therapeutic approach in immunocompromised patients, according to previously published studies. Specifically, in a retrospective study, amphotericin B cured or stabilized 15 of 26 patients with invasive fusariosis. Moreover, posaconazole has been reported as a successful salvage treatment for patients with invasive fusariosis. Most clinicians start with either amphotericin B or voriconazole as first-line therapy. In the current study, amphotericin B was used as monotherapy in 1 MGH patient, who recovered, and in 19.6% of literature patients with a mortality rate of 10.5%. Voriconazole was also commonly administered (30.8% of MGH patients and 15.5% of literature cases, with mortality rates of 0% and 6.7%, respectively). Finally, the combination of amphotericin B/voriconazole was used in 30.8% of MGH patients and 14.4% of literature cases with mortality rates of 87.5% and 35.7%, respectively. These results show that monotherapy with voriconazole and monotherapy with amphotericin B are both successful in treating invasive fusariosis, since the difference in mortality is not significant.

Among patients with skin fusariosis, for MGH patients the mortality for those treated with combination therapy was 66.7% compared with 0% mortality for those treated with monotherapy and, for literature patients the mortality was 31.3% for those treated with combination therapy compared with 10.5% for those treated with monotherapy. MGH patients with pulmonary fusariosis had a mortality rate of 75%, while none of the literature patients treated with monotherapy died. Finally, disseminated disease led to a mortality rate of 66.7% in MGH patients treated with combination therapy compared to 0% in those treated with monotherapy, while the mortality rates for literature patients were 42.9% and 12.5%, respectively. The higher mortality rates of patients who received combination therapy may be explained by the fact that more severely ill patients tend to receive more medications and thus are more likely to be treated with combination therapy. Overall, the most effective antifungal therapy should be based on Fusarium species susceptibility testing. Although in the present series, the MIC of antifungal agents was determined for only 6 isolates, the resistance profiles of some of these isolates highlight the emerging resistance of Fusarium species to traditional antifungal regimens.

Finally, surgery was performed in 7 MGH patients with skin fusariosis (14.3% mortality), 5 literature patients with skin fusariosis (0% mortality), and 1 literature patient with disseminated infection (0% mortality). The mortality rates of patients who underwent surgery were lower compared to those who did not have surgery (rates of 75%, 19.4%, and 8.7%, respectively). This finding suggests that the surgical removal of focal lesions may result in better outcomes and thus should be considered for patients with skin or disseminated infections.

Despite medical intervention, invasive fusariosis has been linked to a high mortality rate. In the current report, the mortality rate was 50% among the MGH patients with disseminated fusariosis, 40% among patients with skin fusariosis, and 37.5% among patients with lung fusariosis. On the other hand, the mortality rates of the literature patients with disseminated, skin, and pulmonary fusariosis were 30%, 18%, and 0%, respectively. The higher mortality rates of the MGH patients in the current series may be attributed to their comorbidities, and the lower mortality rates of the literature patients may be due to a “publication bias.” A representative example of more comorbidities among MGH patients is the presence of burns (7.7%, n = 7 MGH patients vs 2.1%, n = 2 literature patients). This difference may lead to the observation of a higher mortality in the MGH patient population and may be explained by the fact that most case reports in the literature present patients with a favorable outcome and thus with fewer comorbidities. We note that 6 of 7 patients with burns had skin fusariosis. However, a true association between burns and skin fusariosis is difficult to establish, because of the small sample size of the MGH cohort.

In conclusion, the results of the current study suggest that monotherapy with voriconazole is equally effective to monotherapy with amphotericin B for the treatment of invasive fusariosis, and that the addition of surgery leads to better outcomes in patients with disseminated fusariosis.
with skin and disseminated fusariosis. More studies with larger sample sizes that will allow for stratification of the outcomes by disease severity are required to investigate the difference in the effectiveness of combination medical therapy versus monotherapy, with the low prevalence of invasive fusariosis being a limiting factor.

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