Diagnosis of deep cutaneous fungal infections: Correlation between skin tissue culture and histopathology

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Background: Deep cutaneous fungal infections (DCFIs) are responsible for significant morbidity and mortality, particularly in immunocompromised patients. Although a direct correlation between histopathologic examination and culture is expected, discordant findings may be seen, presenting a unique diagnostic and therapeutic challenge.

Objectives: We sought to determine the correlation between skin tissue cultures and histopathologic examination in patients with DCFI.

Methods: This is a 10-year retrospective review (2003-2012) of patients with a diagnosis of DCFI seen at a single tertiary care institution. Tissue cultures and histopathologic findings were reviewed.

Results: In 8 of 33 cases, fungal elements were seen on routine histopathologic sections but skin cultures were negative. Three of 8 of the discordant cases had concurrent positive non–skin tissue cultures that correlated with the pathology interpretation, and 3 of 8 patients in the discordant group died of systemic fungal infection.

Limitations: This was a retrospective study design and a single tertiary care institution experience.

Conclusions: The histopathologic interpretation of skin tissue specimens is critical for rapid and accurate diagnosis of DCFI. Despite the identification of fungal organisms on histopathologic assessment of skin tissue specimens, skin tissue culture may fail to show fungal growth. A diagnosis of a DCFI and initiation of appropriate treatment should always be considered in spite of discordant results. (J Am Acad Dermatol 2014;71:293-301.)

Deep cutaneous fungal infections (DCFIs) are associated with significant morbidity and mortality, especially in immunocompromised patients. Mortality rates range from 4% to 10% in localized infections and can be as high as 83% to 94% in disseminated disease.[1] The clinical presentation of DCFI is variable and dependent on host-related factors, the type of fungal organism, and the mode of transmission.[2,3] Because of the nonspecificity of presenting clinical symptoms, cutaneous lesions may be misdiagnosed as cutaneous neoplasms or necrotizing lesions caused by coagulation disorders. In addition, initial presentations in the skin may herald the onset of a life-threatening systemic mycosis.[4,5] Therefore, the rapid diagnosis and characterization of the offending fungus is

Abbreviations used:

BAL:	bronchoalveolar lavage
CSF:	cerebrospinal fluid
DCFI:	deep cutaneous fungal infection
GMS:	Grocott methenamine silver
MPA:	microscopic polyangiitis
PAS:	periodic acid–Schiff
PBSCT:	peripheral blood stem cell transplant
SLE:	systemic lupus erythematosus

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essential for appropriate treatment, which carries significant prognostic implications.

Routine histopathologic examination of lesional skin tissue remains the primary method of confirming a DCFI. It permits fast, presumptive identification of fungi and can also provide some insight into the diagnostic implication of some culture isolates. Because of the variable and longer turnaround time on tissue culture results relative to routine histopathology, the latter is often relied on for the rapid diagnosis of DCFI. Although direct correlation between these 2 diagnostic tests is expected, discrepancies between histopathology and culture results are sometimes seen,[6] with resultant treatment delays, morbidity, and mortality. Few studies have investigated the correlation between the results of histopathologic examination of skin tissue specimens and tissue cultures. The aim of this review is to describe the clinical, histopathologic, and microbiologic findings in a series of patients with a diagnosis of DCFI and characterize features predictive of discordance between the lesional histopathology and skin tissue culture.

CAPSULE SUMMARY

- Deep cutaneous fungal infections are responsible for significant morbidity and mortality.
- Discordant findings between histopathology and culture results are often seen and present a diagnostic and therapeutic challenge.
- Increased awareness about these diagnostic pitfalls may prevent adverse consequences associated with delays in diagnosis and treatment, especially in immunosuppressed patients.

METHODS

We performed a 10-year retrospective review of all histopathologic specimens diagnosed as DCFIs and their corresponding skin culture results in the Department of Dermatology, Mayo Clinic, Rochester, Minnesota between 2003 and 2012. Forty-six DCFI cases were identified by a search of our CoPath (pathology information system) database. Thirteen cases of DCFI without concurrent skin tissue culture for fungi were excluded from analysis. Thirty-three patients with a diagnosis of DCFI were included. The electronic medical record for included cases was reviewed and the following data were abstracted: patient age, sex, location of the sampled skin lesion, underlying medical comorbidities, histopathologic interpretation, histochemical stains, skin microbiology results, and antifungal therapy. The subset of cases with discordance between the pathology diagnosis and tissue culture results (discordant cases) were identified, and review of the lesional skin pathology was performed by a board-certified dermatopathologist (N.C.). Discordant cases were defined as those with fungal organisms identified on histopathology and without growth of fungal organisms in skin tissue culture. The discordant group was defined this way given the differences in turnaround time, with return of histopathology results preceding tissue culture results.

RESULTS

Patient characteristics

Twenty-six of 33 patients were in an immunosuppressed state. Thirteen of 26 immunosuppressed patients were also transplant patients (9/13 with a history of solid organ transplant and 4/13 with bone marrow/stem cell transplant). Five patients had an underlying lymphoproliferative disorder without a history of transplantation. The remaining immunosuppressed patients had an underlying malignancy (10/22). Three patients had a history of autoimmune disorders managed with long-term systemic corticosteroids, including 1 case each of microscopic polyangiitis (MPA), psoriasis, and systemic lupus erythematosus (SLE). Other identified comorbid conditions included HIV, sarcoidosis, diabetes, and occupational exposure (in a patient who worked at a turkey processing plant). Seven of 33 patients were otherwise healthy. Healthy individuals were immunocompetent and had no identifiable underlying systemic predisposition for opportunistic infections. Twenty-one of 33 patients had a primary cutaneous mycosis, while 12 of 33 patients had a systemic mycosis with secondary cutaneous involvement (Tables I-III).

Clinical findings

Areas of involvement included the upper extremities (15/33), lower extremities (10/33), trunk (3/33), multiple sites of skin involvement (3/33), and the head and neck region (2/33). Clinical presentations encompassed nodules (22/33), ulcerated nodules (4/33), plaques (4/33), ulcers (2/33), and erythematous macules in 1 patient. Nine of 33 patients presented with clinical evidence of tissue necrosis (Part *A* of Figs 1 to 3).

Histopathologic findings

In all cases (33/33), fungal elements were identified on routine hematoxylin–eosin (H&E) stained