Introduction

In the past, filamentous fungal infections have nearly always been ascribed to *Aspergillus* species as they are the principal pathogens responsible for invasive filamentous fungal infections [1,2]. Recently, the incidence of infections caused by non-*Aspergillus* fungi, which are histologically indistinguishable from *Aspergillus* species, has increased [3]. These filamentous fungi may be resistant to conventional antifungal treatment. However, there has been little research on how the results of histologic examinations correlated with those obtained by microbiologic cultures of clinical tissue samples. We evaluated histologic reports to determine how many were concordant with culture results in cases of filamentous fungal infections in an actual clinical practice.

Methods

We reviewed the histologic reports of 2,074 Gomori methenamine silver and Periodic acid-Schiff stained tissue samples prepared between January 2004 and June 2009 at Seoul National University Hospital (SNUH, Republic of Korea). SNUH is a university-affiliated tertiary care hospital with 1,600 beds. We identified 393 patients whose tissue specimens presented fungal hyphae infection on histologic examination. If acute-angle branching, septated hyphae were observed, the result was reported as ‘consistent with aspergillosis’. Obtuse branching hyphae were reported as ‘consistent with mucormycosis’. We cultured portions of the specimens on Sabouraud-dextrose plates with and without chloramphenicol. The plates were incubated in room air at 30°C and examined twice each week to determine the identity of filamentous fungi by standard morphologic criteria [4].

Results

The tissue specimens of 393 patients showed evidence of fungal hyphae infection on histologic examination. The
median age of the 393 patients with fungal positive histology reports was 59 years (range: 18–84 years), of which 169 (43%) were male. Two hundred and thirty-one (58.8%) patients had rhinocerebral infections, 136 (34.6%) had pulmonary infections, and eight (2%) had soft tissue infections. The findings of the histologic examinations of the 393 positive tissue specimens indicated that 367 (93.4%) were consistent with aspergillosis, 8 (2%) were consistent with mucormycosis, and 18 (4.6%) had unidentified mold infections.

Fungal culture studies for microbiologic identification of the etiologic agents were requested for only 122 (31%) of the tissue specimens. Fifty-three (43.4%) of the cultured specimens were positive for filamentous fungi of which 44 (83%) were concordant with the results of histologic examination and 9 (17%) were discordant. Of the 44 concordant cases, 43 were identified as Aspergillus species and one as a Mucor species. We identified the isolates as Aspergillus fumigatus (22 specimens), Aspergillus flavus (three specimens), Aspergillus niger (two specimens), Aspergillus nidulans (one specimen), Aspergillus terreus (one specimen), unidentified Aspergillus species (14 specimens), and Mucor species (one specimen). Of the nine discordant cases, three were identified as Scedosporium species, one as a Fusarium species, one as a Pseudallescheria species, one as Phialophora verrucosa, one as a Trichophyton species, and two as unidentified molds (Table 1).

Discussion

The results of our study suggest that in actual clinical practice there may be marked discrepancies between the results of histologic examinations of tissue samples and those obtained through the culturing of the same specimens. Two decades ago, a study of 19 tissue specimens from suspected fungal infections found no discordance between histologic examination results and those found through culture [2]. However, a recent study found 5 (24%) instances of discordance in 21 specimens [5], similar to our results. Our study differs from previous investigations in that, to our knowledge, our study included the largest number of tissue samples from clinical cases whereas autopsy species were included in prior investigations [2,5,6].

The nine cultures which differed from histologic data involved Scedosporium, Fusarium, Pseudallescheria, Phialophora, and Trichophyton species. Previous investigations suggest that the incidence of filamentous fungal infections caused by Scedosporidium and Fusarium species has increased [7,8]. In our study, about 50% of the discordant aspergillosis cases were caused by non-Aspergillus fumigatus or unidentified Aspergillus species, in line with the results of previous reports [5,9].

Amphotericin B may not be effective in the treatment of Scedosporidium and Fusarium infections. In addition, variable results have been obtained through in vitro susceptibility tests of different Aspergillus species to amphotericin B [10]. Hence, identification of the causative organism is essential for choosing appropriate antifungal therapy. Despite this, our study revealed that about 70% of specimens in which hyphae were found on histologic examinations were not cultured. Anecdotal data suggest that a large proportion of fungal infection specimens are not cultured, but we found no published data to support these assertions.

Discrepancy rates between histology and culture in filamentous fungal infections were 17% in our study. The main factor that may have caused this discrepancy was the characterization of all invasive hyalohyphomycoses as ‘consistent with aspergillosis’, despite the fact that cases caused by other hyaline, septate molds, such as a Fusarium species and Pseudallescheria boydii, may be morphologically indistinguishable from the appearance of aspergillosis in histologic examinations. Therefore, we suggest that ‘hyalohyphomycosis’ or ‘invasive hyaline septate hyphae’ should be used instead of ‘consistent with aspergillosis’ for describing septate hyphal mold infections found with histologic examination.

Our study has some limitations. First, selection bias could have occurred as we included only cases in which organisms were identified histologically. Second, the number of cases that were histologically and microbiologically confirmed was relatively small to allow us to generalize our findings. Third, and finally, all discordant isolates were not identified to the species level.

In summary, despite substantial discordances between histologic reports and culture results for filamentous fungal infections, culture studies involving tissue specimens are not performed often in actual clinical practice. Physicians should consider requesting microbiologic cultures in

<table>
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<tr>
<th>Table 1 Comparison of histologic and culture results for filamentous fungal infections.</th>
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<tr>
<td><strong>Histologic results</strong></td>
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<tr>
<td>------------------------</td>
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<tr>
<td>Aspergillosis (n = 367)</td>
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<tr>
<td>Mucormycosis (n = 8)</td>
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<tr>
<td>Unidentified mold (n = 18)</td>
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<td>Total (n = 393)</td>
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*Nine discordant cases: three Scedosporium species, one Fusarium species, one Pseudallescheria species, one Phialophora verrucosa, one Trichophyton species, and two unidentified molds.*
addition to histologic examination when a fungal infection is suspected.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

**References**


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