Esophageal Aspergillus in Cytologic Brushings: Report of Two Cases Associated With Acute Myelogenous Leukemia

Simon Bergman, M.D.,* and Kim R. Geisinger, M.D.

Aspergillus, which commonly involves the sinonasal region and upper respiratory tract, is reported for the first time in esophageal brushings in two immunocompromised patients with a history of acute myelogenous leukemia (AML). Aspergillus species was identified in both cases in smears as scattered three-dimensional groups of fungi with 45° angle branching. One case had a local esophageal noninvasive form, while the other, in addition to the esophagus, had disseminated to the spleen. Although Aspergillus is an uncommon cause of esophagitis in immunocompromised patients, its presence may be associated with an extremely poor prognosis as both expired shortly after detecting this fungus on esophageal brushings. Diagn. Cytopathol. 2004;30:347–349.

© 2004 Wiley-Liss, Inc.

Key Words: esophageal brushing; Aspergillus; immunocompromised patients; acute myelogenous leukemia

Aspergillus has been implicated along with Mucor, Histoplasma, and Cryptococcus species as a rare cause of esophagitis in immunocompromised patients. To the best of our knowledge, the cytologic diagnosis of Aspergillus has not been reported in peer-reviewed literature in esophageal brushings. Aspergillus diagnosed cytologically in esophageal brushings is reported in two patients with acute myelogenous leukemia (AML).

Materials and Methods

Esophageal brushings were obtained endoscopically. Direct smears were fixed in 95% alcohol and subsequently stained with a standard Papanicolaou stain.

Results

Case 1

A 79-year-old white woman was diagnosed with AML (M2) in August 1998 and subsequently underwent chemotherapy. Her past medical history was complicated by non-Hodgkin’s lymphoma diagnosed in 1988 and follicular carcinoma of the thyroid gland diagnosed in 1984. She subsequently had a relapse of her AML in 1999, underwent a second course of chemotherapy, and did not achieve remission. She presented with esophagitis and endoscopic esophageal brushing cytology revealed fungal organisms morphologically consistent with Aspergillus species. She expired 1 week after induction chemotherapy.

Case 2

A 29-year-old white man was diagnosed with AML (M3) in 1990. The patient had a long and complicated hospital course. The patient underwent chemotherapy with subsequent bone marrow biopsies showing residual leukemia. A computerized tomography scan of the patient’s abdomen revealed a 4 cm cystic lesion of the spleen, which revealed Aspergillus on fine-needle aspiration biopsy. The patient also presented concurrently with esophagitis, and esophageal brushing cytology revealed fungal organisms morphologically consistent with Aspergillus species. The patient’s course deteriorated with the development of gram-negative sepsis and multiorgan failure. He expired 2 weeks later.

Esophageal Brushing Cytology

Both cases had similar findings on esophageal brushings with poorly cellular smears containing scattered benign squamous cells and abundant granular debris. In addition, there were scattered three-dimensional aggregates of fungal hyphae. The fungal hyphae were deeply cyanophilic and composed of moderately thick, uniform, septated structures with 45° acute angle branching (Figs. 1 and 2).
Discussion
Aspergillus has been implicated along with Mucor, Histoplasma, and Cryptococcus species as rare causes of esophagitis. Esophageal brushings provide a sensitive diagnostic test in the more common fungal infections such as Candida, as well as diagnostic material in cases of malignancy. Esophageal cytologic brushings are diagnostically complimentary to endoscopic biopsy in the cases of Candida and malignancy. While Aspergillus species has been isolated to cytologic specimens on sputum, bronchial washings, and FNA, this report represents the first two cases of Aspergillus diagnosed in esophageal brushings.

Aspergillus is a fungal pathogen more commonly seen on the sinonasal passages and upper respiratory tract. This organism can occasionally invade tissue and disseminate via the bloodstream, posing a life-threatening infection especially in an immunocompromised host. More commonly, Aspergillus presents as a noninvasive form of superinfection in immunocompromised patients. This was demonstrated in both cases reported herein with case 1 showing a noninvasive form of Aspergillus on esophageal brushing and case 2 showing an invasive disseminated form, both forms present in severely immunocompromised patients with AML. Additionally, the esophageal brushing was more sensitive than the corresponding biopsy in case 1 as the latter was negative. In both cases, esophageal brushing provided a sensitive means of diagnosis of Aspergillus with septate 45° branching hyphae. Aspergillus should be differentiated from mucor by the uniform thickness and presence of septae. True hyphae with septae of larger size differentiate it from Candida. It is likely that the severe immunocompromised state of both patients led to superinfection in one case and a disseminated form in the second...
Interestingly, Aspergillus was diagnosed in esophageal brushings shortly before each patient expired. In this sense, the finding of Aspergillus on esophageal brushings may indicate a gravely poor prognosis. This may in part explain why Aspergillus has not been previously reported on esophageal brushings due to its appearance extremely late in the terminal stages of AML.

In conclusion, Aspergillus diagnosed cytologically on esophageal brushings in two patients is reported for the first time. Both patients were severely immunocompromised with AML, status postchemotherapy, and died shortly thereafter. In both cases, esophageal brushing cytology provided a sensitive tool in the diagnosis of Aspergillus. The isolation of Aspergillus by esophageal brushings may be associated with a gravely poor prognosis. Perhaps with increased testing with esophageal brushing cytology, Aspergillus will be diagnosed more frequently in the future and hopefully at an earlier stage.

References