EDUCATIONAL COMMENTARY - ASPERGILLUS SPECIES

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Learning Outcomes:
Upon completion of this exercise, the participant will be able to:

- Discuss the epidemiology of infections caused by Aspergillus species.
- Discuss laboratory findings that help differentiate whether an Aspergillus species isolated in the laboratory is a contaminant or the cause of infection.
- Discuss laboratory methods currently used to diagnose invasive aspergillosis.

Members of the genus Aspergillus occur widely in nature as saprophytic fungi, meaning that they live on decaying organic matter such as soil and plants. Of the more than 180 species that belong to the genus Aspergillus, approximately 40 have been linked to human disease (16 of these only once). The species most commonly isolated from human specimens are Aspergillus fumigatus, Aspergillus flavus, Aspergillus niger, and Aspergillus terreus.

Aspergillus species can cause infections of the lungs, ears, skin, nails, sinuses, endocardium, and central nervous system. Persons most at risk for developing invasive aspergillosis include those with leukemia, lymphoma, pulmonary diseases, or advanced AIDS. People who have received bone marrow or organ transplants and those who have been treated with glucocorticosteroid or cytotoxic drugs are also at increased risk.

Laboratory Evaluation
Because Aspergillus species occur widely in nature, they often appear as contaminants in cultures of respiratory, skin, and other specimens. In fact, Aspergillus is second only to Candida in its frequency of isolation in the laboratory. However, infections caused by Aspergillus are associated with high morbidity and mortality, especially in invasive disease. For this reason, it is critically important for laboratories to determine whether an Aspergillus isolate is a harmless contaminant or the cause of infection.

Evidence suggesting that an Aspergillus isolate is the cause of infection includes the following:

- Presence in the specimen of hyphae that are morphologically compatible with the isolated colony.
- Isolation of several colonies from a single specimen or isolation from repeat specimens.
- Confirmation that growth occurs on the area of the slant or plate where the specimen was placed.
Aspergillus isolated from body fluids or deep body tissue should always be considered a potential invasive pathogen, but a definitive diagnosis of invasive aspergillosis can be very difficult to make due to the limitations of the laboratory tests that are available. At present, high-resolution computed tomography and tests to detect Aspergillus antigens are used to help make this diagnosis.

Antigen detection tests include radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA), biotin-avidin-linked immunosorbent assay (BALISA), latex agglutination, or immunoblotting methods. However, only a few of these tests are commercially available, and the latex agglutination test lacks sensitivity. These drawbacks limit their use in most clinical laboratories.

One antigen detection method that has shown promise is an ELISA test that detects Aspergillus galactomannin, a polysaccharide found in the cell wall. Studies have shown that this method can detect the antigen before clinical signs and symptoms appear. These studies evaluated patients with blood malignancies, and therefore, more studies are needed to evaluate this method in other high-risk groups.

Tests to detect Aspergillus antibodies can help diagnose aspergilloma (a mass or “fungus ball” caused by fungal infection) and allergic bronchopulmonary aspergillosis. However, they are of limited use in diagnosing invasive aspergillosis for three reasons: (1) Patients with poorly functioning immune systems may not produce antibodies, which can cause false-negative results. (2) Many people have high background antibody titers due to the widespread distribution of Aspergillus in the environment, which can cause false-positive results. (3) Standardized antigens are not widely available, which contributes to discrepancies in interlaboratory results. Finally, Aspergillus isolates that are determined to be the cause of infection must be identified to the species level, because species differ in their susceptibility to antifungal drugs. Identification of Aspergillus species requires a high level of expertise. Many laboratories send fungal cultures or isolates to reference laboratories for identification and susceptibility studies.

Conclusion
The difficulty of determining whether an Aspergillus isolate is a contaminate or the cause of infection, the time needed to culture and identify the mold, and the limitations of currently available rapid tests make a quick diagnosis of invasive aspergillosis difficult. Researchers are working to improve existing methods and introduce new tests, but at present the diagnosis is made based on a combination of laboratory and clinical findings. For this reason, effective communication between the microbiologist and clinician is essential to ensure good patient care.
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