Episodes 31 & 32

Presentation
A 50-year-old man with decompensated alcoholic cirrhosis and a recent episode of alcoholic hepatitis treated with steroids presents with acute fever, confusion, and dyspnea.

Course
The patient was found to be febrile with a significant leukocytosis. He had high-SAAG ascites without evidence of spontaneous bacterial peritonitis and was treated empirically with broad-spectrum antibiotics without a clear source. He was later found to have multifocal pulmonary nodules concerning for a fungal infection.

Case resolution
Serum beta-D glucan and galactomannan were elevated. A bronchoalveolar lavage culture grew *Aspergillus* spp. Taken together, the risk factors (steroid use), clinical features (prolonged fever without resolution with antibiotics), radiographic features (multifocal pulmonary nodules) and microbiology were diagnostic of invasive pulmonary aspergillosis.

Teaching points

- Different forms of immunosuppression predispose patients to infections from distinct types of pathogens. Cirrhosis[1] leads to an increased risk of, primarily, **bacterial infections** through impairment of both the innate and adaptive immune system, intestinal barrier dysfunction, and alterations to the gut microbiome. Additionally, patients with cirrhosis have higher incidence of infections with multidrug resistant bacteria than the general population.
- *Coccidioides*[2] spp are dimorphic fungi endemic to California and Arizona, with more than 95% of cases occurring in those two states. Clinical manifestations range from asymptomatic/minimally symptomatic pulmonary infections to widely disseminated disease. Conventional approaches to diagnosing **coccidioidomycosis** involve detection of specific anticoccidioidal antibodies (**immunodiffusion** [ID] and **complement fixation** [CF]) and/or identification/recovery of *Coccidioides* from clinical specimens.
    - ID provides a *qualitative* assessment of anti-coccidioidal IgM and IgG antibodies, while *quantitative* CF titers measure the concentration of IgG and can be used to monitor disease activity.
- Aspergillus[3] is a ubiquitous fungal pathogen whose clinical manifestations range from hypersensitivity reactions to severe life-threatening angioinvasive disease, depending largely on the host's immune status. Invasive aspergillosis (i.e., fungal hyphae invading tissues) has been most studied in neutropenic patients, especially those undergoing hematopoietic stem cell transplantation.
    - In non-neutropenic hosts, **corticosteroids** have been identified as the most common risk factor for invasive disease.

Clinical Reasoning Pearl

Clinical reasoning is, in part, the dynamic assessment of probabilities. Occasionally, competing contextual factors may elevate, but not distinguish between, multiple clinical entities. As Dr. Winston points out, real-life practice involves narrowing the range of diagnostic possibilities and then testing for the few most likely in parallel.

For example:
Dr. Winston noted that this patient had strong risk factors for Coccidioidomycosis and Aspergillosis. In real life, she would have pursued testing for both.

References

1. Jalan R, et al. Bacterial infections in cirrhosis: a position statement based on the EASL Special Conference 2013. J Hepatol. 2014 Jun;60(6):1310-24.
2. Saubolle MA, McKellar PP, Sussland D. Epidemiologic, clinical, and diagnostic aspects of coccidioidomycosis. J Clin Microbiol. 2007 Jan;45(1):26-30.
3. Kosmidis C, Denning DW. The clinical spectrum of pulmonary aspergillosis.Thorax. 2015 Mar;70(3):270-7.