

Sarah's Sickness: The Diagnosis and Treatment of an Infectious Disease



by

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Part I – A Rough Start

Sarah is a first-year pharmacy student who is juggling a lot of personal turmoil. Between the pressures of school, monetary concerns, the recent loss of her Amazon grey parrot, and her own health issues, she turns to her roommate, Dana, for support.

“Dana, I just don’t know how much more I can handle right now! Losing Polly has me so upset! My vet wanted to do an autopsy since Polly died of unknown causes but I can’t afford it. She was always so healthy until we moved to this house. Maybe the stress of moving and me spending less time with her because I’m studying all of the time affected her.”

“Don’t be so hard on yourself, Sarah. It was probably just her time to go and it has nothing to do with the move. Besides, think about the great deal we got on this place because it was damaged in the flood a few years ago! It’s so quiet out here in the country and the rent is so cheap. Our student loans are going to be so high when we finish pharmacy school that finding this house was a blessing. Speaking of school, how did you do on the Principles of Drug Action test this morning?”

“Terrible! Since Polly died, I just can’t concentrate. My coughing had me up a lot last night too thanks to my asthma. But I also have some chest pain. I often feel breathless and I’ve lost my appetite too. I’ve been more tired than usual lately too. In fact, I really need to study but I think I’ll take a quick nap.”

Later that week, Sarah’s condition worsens. She has started to wheeze, has a low-grade fever and chills, feels nauseous, and notices some blood tinged mucus when she coughs. She feels fatigued and wonders if she might be experiencing depression. She decides to go to her primary care physician for help.

Questions

1. Besides asthma, what do you think Sarah might have? List at least two disorders, the etiological agent if it is an infectious disease, and your rationale for choosing each one.
2. What diagnostic tests should be performed to determine the likely cause of her illness?

Part II – Tests

Sarah's primary care physician ordered a number of tests. Table 1 shows the results of Sarah's physical exam and lab tests while Table 2 shows the results of the diagnostics tests.

Table 1. Physical Exam and Lab Tests

<i>Physical Exam</i>	Moderate respiratory distress; bloody sputum with cough; bilateral rales; chest pain
<i>Vital Signs</i>	BP 115/65 mmHg; T 39.6°C; P 98/min; R 41/min
<i>Blood</i>	Hematocrit: 25%; serum normal; WBC 8600/uL; differential: eosinophils >500/mm ³ ; blood gases: pO ₂ 72 mmHg
<i>Imaging</i>	Chest X-ray: Lesion in the right lung and bilateral infiltrates CT scan: pulmonary nodules

Table 2. Diagnostic Tests

<i>Direct Microscopy of Sputum</i>	Gram stain and acid-fast stain negative ; Gomori's silver methenamine stain positive, white blood cells present
<i>Blood Cultures</i>	Negative for bacteria
<i>Fungal Cultures</i>	Sputum cultures positive for <i>Aspergillus fumigatus</i>
<i>Serum Antigen and Antibody</i>	Galactomannan antigen assay was positive; elevated IgEs and IgGs; interferon-gamma release assay negative
<i>Skin Test</i>	Positive for <i>Aspergillus</i> allergen

“Sarah, your body is reacting to excess exposure to *Aspergillus fumigatus*, spores which you have probably inhaled due to your living conditions,” explained Dr. Devraj. “Because you also have asthma and are taking an inhaled corticosteroid, your body has had a hard time combatting the effects of these allergens. You’ve probably learned about aspergillosis in your microbiology courses, right?”

“Yes, but I never thought it would affect me! I thought I had my asthma under control,” Sarah exclaimed.

“Well, since you are living in flood-damaged property that is under renovation, your exposure to these allergens has probably been pretty high. I would demand that your landlord put in a HEPA filtration system if you plan on staying at this house to prevent further re-exposure. I’m just glad we caught this when we did. The good news is that you are probably at the early stage of Allergic Bronchopulmonary Aspergillosis so no permanent lung damage has occurred. I’m going to prescribe oral glucocorticoids and a triazole antifungal medication called voriconazole, which you will need to take for several months. It will slow the growth of the fungus.”

“We haven’t started our pharmacotherapeutics courses yet so I am not familiar with triazoles. It looks like I’ll be educated about these antifungals ahead of time! Thanks for your advice, Dr. Devraj.”

A few days later Sarah's coughing starts to subside but she is now experiencing bouts of dizziness, diarrhea and subsequent thirst, plus some loss of appetite. She tries to stay hydrated by drinking plenty of tap water. She wonders if these are side effects of the drug or if something else is plaguing her. She is also starting to doubt if she'll ever make it through the semester.

Questions

1. Describe the life cycle of *Aspergillus fumigatus*. (Note: include the microbiological properties, epidemiology, and pathogenesis.)
2. What is the likelihood that *Aspergillus* was the cause of the parrot Polly's death?
3. Dr. Devraj suspected a bacterial or fungal pathogen. Which tests helped him rule out a bacterial pathogen? What renders the fungal pathogen tests positive?

4. Besides Allergic Bronchopulmonary Aspergillosis (ABPA), what other syndromes are associated with *Aspergillus* infections?
5. What is the mechanism of action for triazoles?
6. What are the most common potential side effects of voriconazole and itraconazole?
7. Do you think that Sarah is experiencing side effects from the drug or that she is suffering from another disorder? Or it is a combination of both? Explain your reasoning.

Part III – Co-Infection

After experiencing a couple more weeks of dysphoria and nausea, as well as hematuria, bloating, and excessive gas, Sarah visits Dr. Devraj again. Based on Sarah's complaints, Dr. Devraj decides to have a stool sample analyzed, orders an ELISA, and performs an entero-test. The results reveal a motile trophozoite in the stool sample. He realizes what pathogen is causing Sarah's additional problems and refers her to an infectious diseases clinic for further evaluation and treatment.

Questions

1. What is an entero-test?
2. With what do you think Sarah has subsequently become infected? What was the likely route of transmission?
3. In response to Sarah's introduction to these two pathogens, her immune system has been "on call" to defend her body against these pathogenic agents. Initially, her innate immune response tried to prevent both infections from occurring. Because of continuous reinfection, her adaptive immune response had to play a role in her immune defense.
 - a. List at least three *innate* immune cells that would respond to Sarah's asthma, *Aspergillus* spores, and her new infective pathogen. Include the action of the cell and any secretory substances. Would some of these be more active against some pathogens or disease states than others?
 - b. List at least three *adaptive* immune cells that would respond to Sarah's asthma, *Aspergillus* spores, and her new infective pathogen. Include the action of the cell and any secretory substances. Would some of these be more active against some pathogens or disease states than others?
4. Explain how MHC and exogenous (endosomal) antigen processing would help Sarah's body recognize and destroy these foreign pathogens.

Upon visiting the infectious diseases clinic, the specialist prescribes metronidazole for Sarah's intestinal disorder. The physician also works with a clinical pharmacist, infectious diseases resident, and pharmacy student on rotation, who are asked to evaluate Sarah's drug therapy and problems. Based on their recommendations, the physician changes voriconazole to itraconazole because of potential side effects, plans to check the antifungal serum concentration, and decreases Sarah's dose of inhaled glucocorticoid (from fluticasone propionate 220mcg to 110mcg twice daily) due to drug interactions.

Questions

5. What are the goal serum concentrations to document absorption and predict efficacy of itraconazole for invasive aspergillosis?
6. What are the side effects of metronidazole and what should Sarah be told to avoid until several days after taking it?



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