Best Practices in Management of Blastomycosis: Primary Care Perspective

Introduction: Thank you for participating in this course, *Best Practices in the Management of Fungal Pneumonias: Primary Care and Emergency Medicine Perspectives*. In this section, we talk with Dr James Montana, a primary care provider from Ely Minnesota, about the management of blastomycosis.

Q: Please tell us about your background in primary care.

Dr Montana: I trained in family medicine, internal medicine, and critical care medicine a long time ago and have been practicing in northeast Minnesota for 23 years. I've been primarily practicing outpatient internal medicine as well as some inpatient internal medicine, at both small and larger hospitals. It's a broad-spectrum practice with bread-and-butter internal medicine, acute care, and a little bit of acute-care family medicine as well.

Q: How did you become interested in blastomycosis management?

Dr Montana: In my residency training and fellowship, I saw cases of blastomycosis. Those were hospitalized individuals who were quite sick. So, I learned that blastomycosis is a fungal infection in northeast Minnesota that presents with varying severity—from a rather mild nagging pneumonia that can be treated in the outpatient setting with oral antifungal medication to severe infections that require ventilator support and even extracorporeal membrane oxygenation (ECMO) as we saw in a young man earlier this year. The fact that it is prevalent in northeast Minnesota was interesting. I'm also friends with local veterinarians who see blastomycosis a lot more often than we do in human medicine.

Q: So, it sounds like you've had some full-spectrum experience with blastomycosis. Tell us about how you've learned about fungal pneumonia in general. Has your experience been mostly with blastomycosis, or have you seen other types of fungal pneumonias?

Dr Montana: I had just a little bit of experience in training. When I was in the Twin Cities at a tertiary care hospital, I can think of one person who got very sick with histoplasmosis after they were given steroids for a presumed inflammatory lung condition, which turned out to be smoldering histoplasmosis. That got a lot worse with steroids. I learned about fungal infections since I did medical school and training in Minnesota, including histoplasmosis and blastomycosis. And then of course, all students learn about coccidioidomycosis in the southwestern United States. But I don't think I have ever diagnosed a case of coccidioidomycosis.

Q: When you were doing critical care, did you have to deal with aspergillosis or any of the other molds?

Dr Montana: Those are more opportunistic infections in immunocompromised hosts. I think of coccidioidomycosis, histoplasmosis, and blastomycosis as pathogenic fungi that can infect otherwise healthy people, very healthy people in my experience. Whereas *Aspergillus* is more of an opportunistic fungus. I can't think of a case where I've seen it. I know we've always discussed it as a differential, but I can't think of a case where I've participated in treating aspergillosis.

Q: So, in your view, why is it important to take a proactive approach to managing these infections?

Dr Montana: Well, I think if you can make the diagnosis of blastomycosis early, you can hopefully prevent those severe disease progressions that require ventilator support or, as I mentioned earlier, ECMO as we saw in a young man earlier this year. He was from Ely but was treated with ECMO for 3 weeks at a tertiary care center. In any case, if you can make the diagnosis of blastomycosis at an early stage, you can treat it quite easily with itraconazole. You need to advise the patients about the proper way to take itraconazole and monitor the drug levels. With appropriate treatment, you can prevent a severe illness that requires hospitalization.

And the classic story of making the diagnosis of blastomycosis, and I would also assume histoplasmosis, is the person comes in with a pneumonia, you give them the typical community-acquired pneumonia (CAP) antibacterial medication, and they come back a week or two later and say they're no better. At our clinic, that usually makes us think: *Did we miss blastomycosis from the start?* And we can easily perform a urine *Blastomyces* antigen test and get the diagnosis. I think the turnaround time for that test in our clinic is 2 days. Sometimes, if I have someone who's coughing up sputum, I've had them cough up sputum and I've spun it down, and I've had one case where I could see the broad-base budding yeast on a Gram stain and made the diagnosis that way instead of having to wait for the urine antigen. That approach obviously depends on them being able to cough up a reasonable sputum sample. So, I guess in summary, I think if you can make the diagnosis early and get them on oral itraconazole (or some other azole if they can't tolerate itraconazole), you can avoid hospitalization and a more life-threatening pneumonia.

Q: You've talked a little bit about your diagnostic process. How closely do you follow the CDC testing algorithm for blastomycosis? Can you provide more detail?

Dr Montana: Well, I can tell you, I've looked at those algorithms in our clinic. We're actually even more aggressive in our testing. If we have a suspicion, if a person is working in construction tearing up soil and comes in with a pneumonia, I think that will prompt us to maybe screen for blastomycosis right away. I don't think that we would necessarily start the itraconazole on day number one in that person—we'd wait for the urine *Blastomyces* results. And our urine test is a combo *Blastomyces*/*Histoplasma* antigen test. It's not strictly *Blastomyces*, but I think up here, if that test comes back positive, you can be very confident that it's blastomycosis.

So, we'll do that. If someone is more ill or they have a lung nodule and the person's older and you're thinking about malignancy as well, those folks will often be referred to the pulmonologists for an urgent-ish bronchoscopy. The sensitivity of the urine *Blastomyces* antigen test is very high; if the test were to come back negative and you still had a suspicion, then sputum culture and/or bronchoscopy would be the next test. The *Blastomyces* antibody can be helpful in the right clinical scenario, although the sensitivity of that antibody test is not terrific.

My partners and I, over the 23 years I've been here, we've all stumbled across cases of blastomycosis. As I mentioned previously, it's the classic story is giving antibiotics for CAP that is not getting better and then going down the algorithm of getting urine antigen, or if it's a little bit more concerning, transferring them to a facility where a pulmonologist can do a bronchoscopy. But more often than not, we make the diagnosis in the outpatient setting. And I think up here we were comfortable treating it with itraconazole ourselves and don't always get infectious diseases or pulmonary medicine involved if it's a mild case of blastomycosis.

Q: You are managing many of these cases—when do you think of referring patients?

Dr Montana: If someone is in the hospital hypoxic, in those cases, amphotericin B is probably a better initial antifungal agent to use. Our hospital is probably too small to safely use that drug. And so I'll transfer the patient to a bigger hospital. It's a consideration in the setting of hypoxia. In addition, when people are that ill, sometimes they're getting worse before they get better. And then the other case where I get pulmonary involved is a lung mass or nodule, and the person may not have had typical pneumonia-type symptoms in the last year. I can think of someone who is a smoker for whom I did a low-dose computed tomography (CT) scan of the chest. The scan showed a nodule that, frankly, I was thinking was going to be a cancer. It turned out to be blastomycosis. So that would be the other setting in which I would ask for a pulmonary medicine referral—if I had a mass of unclear etiology without typical pneumonia symptoms.

Q: Have you witnessed any blastomycosis outbreaks? And can you tell us about that experience?

Dr Montana: Not a public health type outbreak. In 1999 in Mountain Iron, Minnesota, there was a construction site, I think a subdivision being built, and there was an outbreak then, but I wasn't practicing. The only thing I can think of similarly is two guys were tearing apart a small shed in the middle of winter, but when they ripped up the floor, they had dry dirt underneath. And one of the gentlemen ended up coming in with the pneumonia and was diagnosed with blastomycosis. And then a week later, his partner, who was working with him, came in with pneumonia. And in his case, we were confident that it was the same fungal pneumonia in his partner. That's the closest to an outbreak that I could see is two people who were doing a demolition project in the middle of winter, but they ended up getting into soil underneath the flooring of the cabin, and that's how they got the infection.

Q: That's really very interesting. We've seen documentation of other types of outbreaks occurring in the Upper Midwest. These infections are often overlooked

and underdiagnosed. What can you tell your fellow primary care providers about breast practices to assure early diagnosis and effective management of these fungal pneumonias? And are there any special clues that you can think of that point to the diagnosis?

Dr Montana: During the summer and fall, if someone comes in with pneumonia, I've learned to get better about asking about exposures. Are they outdoorsy? Have they been doing construction work in which they are tearing up soil or dealing with rotting trees? And if they answer yes to those questions, I will often, even on the initial visit, go ahead and send off a urine *Blastomyces* antigen because it's so easy. The other thing I'll often do, if there's a pneumonia, I'll ask them if there's any skin lesions that have cropped up because *Blastomyces* can disseminate and cause cutaneous lesions. I can't say that I've ever stumbled across that, but I know it's one of the review of systems questions that can be useful. And then the other story, as we've talked about earlier, is the person whom you treat for a CAP and then comes back a week later and is not better or even a little bit worse. You need to think about resistant bacteria or non-bacterial causes in that situation. If they are living in the right area, we definitely start thinking about non-bacterial etiologies, which might be causing the lung infiltrates and a pneumonia-like picture.

Q: You had mentioned that the veterinarians in your area see a lot of blastomycosis. Have you ever seen someone who has a sick dog, and then they get sick because they had a similar exposure?

Dr Montana: I have not run across that story in my clinic, and it’s not a question that I have asked. But presumably, if a patient has a hunting dog or something like that, it could happen. I think it would be a reasonable question to ask someone with pneumonia if they have a dog that has come down with pneumonia—it’s probably a smart question to ask.