Transcript

I have a weakened immune system, am I at risk for blastomycosis?

JM: Hello and welcome to Think Blasto! I am Dr. Joe McBride, an infectious diseases specialist at the University of Wisconsin.

GG: Yes, welcome to Think Blasto! I am Dr. Greg Gauthier, I am also an infectious diseases specialist at the University of Wisconsin. This podcast series is designed to describe and outline a disease that is more common in Wisconsin than in most parts of the world: an infection called blastomycosis.

JM: The title of today's podcast is "I have a weakened immune system, am I at risk for blastomycosis?"

GG: Thus, we will be talking about blastomycosis in patients who are immunocompromised.

JM: Greg, you used the word "immunocompromised", what does it mean?

GG: Immunocompromise refers to an immune system that is weakened so it harder for the body to fight against infections. People with weakened immune systems can be more susceptible to infections caused by bacteria, viruses, and fungi. However, not all weakened immune systems are the same. The type of infection that immunocompromised patients are susceptible to depends on how the immune system is weakened

JM: How so?

GG: The immune system is complex and made up of many different types cells. Some cells produce antibodies to protect us from infection, other cells are like the video game character Pac Man in which the cells eat up and kill invading microbes, and some cells act like military generals in which they coordinate how the immune cells attack bacteria, viruses or fungi. Thus, each type of cell in the immune system has a specific job to do to in attacking and killing invading organisms.

For example, if cells cannot make antibodies or make antibodies that work normally, it can place a person at risk for certain types of bacterial infections. Another example would be if specific type of white blood cell known as a Natural Killer cell does not work properly, it can increase the risk for certain viral infections. As a final example, if the type of white blood cell known as T lymphocyte is in low numbers or does not work properly, it can result in increased susceptibility to certain types of fungi. To make things easier, we will refer to the T-lymphocyte as a T cell. For the audience, a T-cell is a capitol letter "T" with the word "cell" (c-e-l-l) after it.

JM: So Greg, what does a T-cell do?

GG: A T cell is like a military general that helps coordinate how the immune system attacks. In other words, T-cells tell other immune cells where to go and how to attack the invading organism. It is these T cells that are very important for defending the body against fungal infection.

JM: How do these immune cells become weakened?

GG: There are many ways in which immune cells can be weakened. Most commonly, it occurs when we treat certain diseases with medications. Examples include 1) medications to prevent rejection in people with organ transplants, 2) chemotherapy to treat cancer, 3) medications such as TNF-alpha inhibitors used to treat diseases such as rheumatoid arthritis, lupus, Crohn's disease and ulcerative colitis, 4) and finally, patients on high-dose steroids. An example of high-dose steroid would be prednisone dosed at 20 mg or higher for 4 weeks or longer.

JM: You mentioned that persons who receive a solid organ transplant have a weakened immune system from medications they receive to prevent rejection. Are they at higher risk for blastomycosis.

GG: Yes, a recent study from the University of Wisconsin indicated that the incidence of blastomycosis was increased in SOT recipients. During a 12-year period, 16 out of approximately 5,900 SOT recipients developed blastomycosis. This is about 0.27% of SOT recipients. This sounds like a small number and it is, but it is 18-times higher than the general population of Wisconsin.

JM: Is there any particular time after transplantation in which blastomycosis develops.

GG: No, it can occur at any time after transplantation.

JM: What about people with cancer?

GG: Overall, Blastomycosis is not common in persons receiving chemotherapy, but it can occur. There is no particular type of cancer that is associated with blastomycosis. It can occur with any type of cancer and that includes persons with lymphoma, breast cancer, colon cancer, melanoma, and other types of cancer.

JM: Many persons with auto-immune diseases such rheumatoid arthritis or Crohn's disease are treated with a type of immune suppression medication called TNF-alpha inhibitors. TNF alpha inhibitors include the medications Enbrel, Remicade, Cimzia, Humira, or Simponi. Do those on TNF-alpha inhibitors increase the risk for blastomycosis?

GG: Yes they do. In 2008, the Food and Drug Administration, also known as the FDA, put out a warning about increased risk for fungal infections when people are on these medications. This includes blastomycosis and histoplasmosis as well as coccidioidomycosis, which is also known as Valley Fever. However, fungal infections are not just limited to these fungi, other fungal infections include Cryptococcus, Pneumocystis, and Candida.

In addition to fungal infections, persons on TNF-alpha inhibitors are also at risk for certain types of bacterial infections and viral infections.

JM: What about people swith HIV or AIDS?

GG: Although persons with HIV that has progressed to AIDS are at risk for many types of invasive fungal infections, surprisingly, blastomycosis is not particularly common or frequent. Nevertheless, it can occur. Persons with advanced AIDS are at particularly high risk for

blastomycosis spreading from the lungs to the brain, which can result in brain abscess or meningitis.

JM: Some people are born with immune system that don't work well. In medical terms, this is known as a primary immunodeficiency. Most patients with primary immunodeficiency are diagnosed in childhood. Are these patients at risk for blastomycosis?

GG: As far as we know, they do not appear to be at substantially elevated risk for blastomycosis. Currently, only a few patients with blastomycosis and underlying primary immunodeficiency have been reported in the medical literature.

JM: Some people have been told they have a weakened immune system because they do not have a spleen, their spleen does not work well, or they don't make antibodies. Are these patients at risk for blastomycosis?

GG: No they are not at risk for blastomycosis or other types fungal infections They are, however, are at risk for certain types of bacterial infections.

JM: Greg, we have covered a lot of information. To summarize, conditions that weaken immune cells increase the risk for developing fungal infections. This includes persons who have received solid organ transplants or are on medications that weaken the immune system. Although persons receiving chemotherapy are at risk for fungal infections, blastomycosis does not occur very often in these persons.

Persons who don't have a spleen or don't produce antibodies are not at risk for blastomycosis. Similarly, those born with immune systems that don't work well, do not appear to be at high risk for blastomycosis either.

GG: Joe, could you tell me what symptoms a patient with a weakened immune system would experience with blastomycosis.

JM: Just like in patients with a healthy immune system, persons with weakened immune systems most commonly get a lung infection known as pneumonia. Symptoms of lung infection include fevers, chills, cough, shortness of breath, chest pain, fatigue and decreased appetite. The cough can be dry or productive. A dry cough means that no sputum is coughed up. A productive cough means sputum is produced with coughing. Rarely, blastomycosis can result in coughing up blood. Patients often have symptoms for several weeks that progress.

GG: We learned in a previous podcast that the incubation period of blastomycosis is 3 weeks to 3 months. The incubation period is the time between inhaling spores to symptom onset. Is the incubation period different in patients with weakened immune systems?

JM: It is unknown if the incubation period is different from the 3 weeks to the 3 months that has been reported in patients with healthy immune systems. This would be a really hard question to answer because we usually do not know exactly when people have been exposed to blastomycosis.

GG: Do immunocompromised persons have more severe pneumonia from blastomycosis?

JM: Yes, having a weakened immune system does increase the risk for for more severe infection. A recent study from the University of Wisconsin demonstrated that patients with weakened immune systems present with more severe symptoms and are at higher risk for hospitalization, ICU level care, and even death.

A group of immunocompromised persons who have solid organ transplants appear to be at particular risk for respiratory failure including a severe form of respiratory failure known as acute respiratory distress or ARDS. Respiratory failure and ARDS often requires mechanical ventilation to help the patient breath. Persons with other types of weakened immune systems don't appear to be at as high of risk for respiratory failure and ARDS as persons with solid organ transplants.

GG: Is there anything that can be done to decrease the risk of respiratory failure?

JM: Prompt recognition and diagnosis of blastomycosis, which can result in earlier initiation of treatment with antifungal drugs has the potential to reduce this risk of respiratory failure; however, I do want to point out this has not been formally investigated in a medical study. As we mentioned in a previous podcast, blastomycosis is a great mimicker because it can imitate other diseases such as bacterial pneumonia. Many patients receive 2-3 courses of antibiotics before the diagnosis of blastomycosis is considered. Because blastomycosis is caused by a fungus, antibiotics don't work, antifungals are needed.

GG: Blastomycosis is well known to cause disseminated infection, which means it spreads from the lungs to other organs such as the skin or the bone. Are persons with weakened immune systems at higher risk for disseminated blastomycosis?

JM: Surprisingly, no. The frequency of disseminated blastomycosis is similar between patients with strong and weak immune systems. This makes blastomycosis very different from most other fungal infections in which a weakened immune system is often required for disseminated infection.

GG: Is blastomycosis diagnosed the same way in a person who is immunocompromised as a person who has a healthy immune system?

JM: Yes, the approach to diagnosis is the same. We will be discussing diagnosis of blastomycosis in another podcast

GG: What about treatment?

JM: Because patients who are immunocompromised tend to have more severe disease and are at higher risk for more rapid progression of infection, a powerful antifungal called liposomal amphotericin B is recommended as initial therapy. Liposomal amphotericin B is an antifungal that is given intravenously and helps kill the fungus. This initial knockout punch,

generally lasts for 1-2 weeks. Afterwards therapy is transitioned to treatment by mouth with a different antifungal medication, usually itraconazole, and is prescribed for approximately 12 months.

GG: Wow, 12 months of therapy, is long time to be on antifungal medications. Once treatment is stopped, is it common for the infection to relapse in patients with weakened immune systems?

JM: Fortunately, no. After completion of 12 months of antifungal therapy, relapse is uncommon. Thus, lifelong antifungal therapy is not needed in the vast majority of immunocompromised patients.

GG: Although there is ongoing work to develop a vaccine for humans against blastomycosis, it is not yet available. Is there anything that can be done to prevent an immunocompromised person from developing blastomycosis?

JM: Great question. There have been no studies that have focused on preventing blastomycosis, in part that is because it is a relatively uncommon fungal infection. In addition, exposure to the specific soil habitat in which *Blastomyces* likes to grow does not always result in infection – it is unpredictable. Thus, the main focus is on early recognition of blastomycosis which can result in earlier treatment. Some clues that could suggest blastomycosis is: 1) a history of soil or water exposure, 2) a pneumonia does not get better while on antibiotics, or 3) pneumonia with new onset skin lesions such as ulcers or painful nodules. Also, anyone with severe pneumonia of an unknown cause that requires care in the intensive care unit should undergo fungal diagnostic testing.

GG: Some persons with weakened immune systems live in or visit summer cabins in areas in which there are high rates of blastomycosis. Should these persons move from their home or not visit their cabin?

JM: In general, we do <u>not</u> recommend that persons with weakened immune systems move from their home or stop visiting their cabin to avoid getting blastomycosis. In these situations, there are some precautionary measures that can be taken. This includes not being in the home or visiting the cabin when there is landscaping or home remodeling going on. Similarly, avoiding being around when a well is being dug would also be a good idea. These activities result in disruption of dirt, which can release *Blastomyces* spores into the air that can breathed into the lungs to cause infection.

Greg, earlier in the podcast, you mentioned that persons with weakened immune systems can be at risk for invasive fungal infections of the lungs and the skin that are not blastomycosis. These fungal infections are often from the dirt and go by names such as Histoplasmosis, Coccidioidomycosis, Aspergillosis and Cryptococcus. Is there any advice you can give to avoid these types of infection?

GG: The recommendations are similar to what we discussed before. This includes not being present when there is landscaping, major home renovations or well digging. In addition, people should also avoid going into barns, exploring caves, cleaning chicken coops, turning compost piles, or raking leaves. When gardening, wearing gloves and a mask can also help reduce the risk of developing a fungal infection.

JM: So for patients, families, and nature lovers lets summarize what we have learned today.

GG: When immune cells such as T cells are weakened this can increase the risk for fungal infections

JM: Solid organ transplant recipients have an 18-fold higher incidence of blastomycosis than the general population of Wisconsin

GG: Blastomycosis is uncommon in persons on TNF-alpha inhibitors, are on cancer chemotherapy, or have HIV, but it still can occur.

JM: Blastomycosis in persons with weakened immune systems most often causes pneumonia, which can be severe and lead to respiratory failure that requires mechanical ventilation.

GG: Disseminated blastomycosis occurs at the same frequency in persons with healthy immune systems as those with weakened immune systems. This is very different from most other types of fungal infections.

JM: Preventing blastomycosis is difficult. The best way to avoid blastomycosis developing into a severe infection that causes respiratory failure is to diagnose it early so that way treatment can be started sooner rather than later.

GG: Some clues that could suggest blastomycosis is: 1) a history of soil or water exposure, 2) a pneumonia does not get better while on antibiotics, 3) pneumonia with new onset skin lesions such as ulcers or painful nodules. In addition, anyone with severe pneumonia of unknown cause that requires care in the intensive care unit or ICU should undergo fungal diagnostic testing.

JM: To avoid fungal infections in general, not just blastomycosis, persons with weakened immune systems should not be present when there is landscaping, major home renovations or well digging.

GG: Immunocompromised persons should also avoid going into barns, exploring caves, cleaning chicken coops, turning compost piles, or raking leaves.

JM: When gardening, wearing gloves and a mask can help reduce the risk of fungal infection as well.

GG: to our audience thank you very much for your time and interest. Joe, I look forward to discussing more aspects of blastomycosis with you in the future.
JM: And until next time, Think Blasto!