Fatal Invasive Mold Infections after Transplantation of Organs Recovered from Drowned Donors, United States, 2011–2021

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Karen Wu, an epidemiologist at CDC in Atlanta. We'll be discussing fatal mold infections after organ transplants from drowned donors.

Welcome back to our show, Dr. Wu.

[Karen Wu] It's a pleasure to be here.

[Sarah Gregory] What are fungal infections and why can they be so bad? And which ones are the worst? It seems like there's so many different kinds.

[Karen Wu] You are completely correct. There are many types of fungal infections that can range from more superficial skin infections such as ringworm to severe systemic infections such as candidemia. Some fungal infections can become disseminated, affecting multiple body systems, and these are usually the most severe. Examples of fungal infections that can cause disseminated disease include blastomycosis, an environmental fungi commonly associated with moist soils that can cause disease when spores are inhaled, and sporotrichosis, an implantation mycosis commonly known as Rose Gardener's Disease.

[Sarah Gregory] Your study is about fatal fungal infections in recipients who got organs from people who drowned from 2011 to 2021. How many drowned donors were there and how many organs were transplanted?

[Karen Wu] So our report describes three donors who died of drowning, and a total of nine organs, including kidneys, liver, pancreas, and heart were transplanted from those three donors.

[Sarah Gregory] And why did you choose that time period for your study?

[Karen Wu] So we described cases that we investigated from 2011 to 2021. Only in 2011 did CDC start formally investigating potential donor-derived infections that were deemed of public health interest, and that includes fungal infections. So we only had records from this time period.

[Sarah Gregory] I see. So you pretty much looked at everything that was actually available.

[Karen Wu] Yes, at the time.

[Sarah Gregory] So what kinds of fungus could a drowning person acquire?

[Karen Wu] So when a person drowns, water from the environment enters their lungs, and this water can have bacteria or fungi that can then cause pneumonia (a lung infection). Although rare, scedosporiosis, caused by *Scedosporium apiospermum*, or aspergillosis, caused by *Aspergillus* species, are usually the most common mold infections associated with drowning.

[Sarah Gregory] Are organ transplant recipients more vulnerable to infections and, if so, why is that?

[Karen Wu] So organ transplant recipients are at increased risk of infections because they need to take immunosuppressive medications to prevent organ rejection. In addition, as transplant candidates, they also have underlying conditions that may suppress their immune system. And immunosuppression is a very common risk factor for fungal diseases.

[Sarah Gregory] You mentioned CDC data started in 2011, so transplant-transmitted infections are tracked in some way. How is this done?

[Karen Wu] So organizations that are involved with transplants are required to report unexpected but suspected transplant-transmitted infections to the Organ Procurement and Transplantation Network, also known as OPTN. The Disease Transmission Advisory Committee, of which the CDC is a member, then turns around and investigates these reports.

[Sarah Gregory] So what exactly is it that CDC does with this tracking?

[Karen Wu] We investigated these reports of potential donor-derived infections to decide whether they occurred through transplantation and to provide recommendations to prevent further transmission. Through our investigation, we also provide additional laboratory testing as needed, which is pretty common when it comes to fungal diseases.

[Sarah Gregory] Is there any way to test for fungus before the organ is used? I know the organs are very time sensitive, but how is this done?

[Karen Wu] So there are many ways to test for different fungi, but it can be quite difficult to test for invasive mold infections or IMI's, which we describe in this report. The tests can be invasive, time consuming, and difficult to interpret. For example, a fungal culture can take days or weeks to result, and a positive result can mean the patient is colonized (meaning the mold is not creating disease) or the patient can have invasive disease. Also, exposed donors may not have developed detectable pulmonary disease even in the presence of mold, so clinicians may not even order any testing. Average incubation periods for invasive mold infections in drowning victims are, for the most part, longer than the time between drowning and organ procurement because, as you said, organs are very time sensitive.

[Sarah Gregory] So how long did it take from the detection once it was implanted?

[Karen Wu] So the four recipients diagnosed with an invasive mold infection tested positive for fungi a median of seven days after transplant. The range was sort of three to 26 days. These patients all had severe disease and were detected relatively early post-transplant.

[Sarah Gregory] Tell us what happens when an infected organ is introduced into a recipient. How does this lead to death and how does the fungus spread?

[Karen Wu] If an infected organ is transplanted, the fungi can spread throughout the recipient's body via the bloodstream. The mold infections described in our study are considered angioinvasive, meaning that they tend to invade blood vessels. Because the recipient is immunosuppressed, the body is unable to fight the mold, and the extensive mold infection can lead to thrombosis (or clotting), tissue necrosis (or tissue death), and subsequent organ failure.

[Sarah Gregory] Do we know what kinds of water the donors drowned in and does that potentially make a difference in infection possibility? And is the type of water or should the type of water be considered when assessing whether to use an organ or not?

[Karen Wu] Unfortunately for this study, we were limited to the information provided in the medical records, so we have very limited information on the type of water and situation the donors drowned in. We do suspect that the type of water can make a difference in the possibility of acquiring an invasive mold infection, but these infections are very rare and so they are currently still being described.

[Sarah Gregory] You want to tell us briefly a little bit about the patients and the donors in your study and what happened to each of them?

[Karen Wu] Of course. So the first donor was a male that was found unconscious in a pool and unfortunately passed, and his kidneys and liver were donated. The bilateral kidney recipient lost blood flow to the kidneys about eight days post-transplant and the transplanted kidneys were removed; he died two days later. Mucormycotic fungal emboli and necrosis were identified by histopathology in the removed kidneys and also in the abdominal and pelvic cavities. The liver recipient had a similar story; she also lost blood flow to her transplanted liver and the transplanted liver was removed three days post-transplant. She died a day later. The histopathology of this removed liver revealed similar findings of thrombosis, fungal elements, and necrosis.

The second donor was a man who had a cardiac arrest while swimming. His liver, left kidney, and right kidney were donated. The liver recipient's liver and kidney function declined, and the doctors found decreased blood flow to the liver with necrosis. Mucormycetes were identified in the liver on autopsy, and the left and right kidney recipients fortunately did not develop clinical signs consistent with an invasive mold infection.

For our last donor, he was a man who fell into a lake after having a seizure and upon arrival at the hospital, he was found to have black particulate matter in the lungs, but no organisms were able to be identified. His liver and right kidney, pancreas, heart, and left kidney were all donated. The liver and right kidney were both donated to one recipient who was diagnosed with scedosporiosis approximately one month after the transplant and unfortunately developed brain lesions. He sadly died eight weeks after transplantation. The other three recipients were started on antifungal prophylaxis, and none developed scedosporiosis.

[Sarah Gregory] Embedded in all of that, you sort of mention the time frame for death for each of those. But do you want to give us the average time frame for all of them between receiving the organ and dying?

[Karen Wu] The transplant recipients died a median of eight days after their transplant, with a range of four to 55 days.

[Sarah Gregory] Why does it take that amount of time and what should clinicians be alert to so that they can recognize what's happening maybe sooner?

[Karen Wu] Illnesses in the index patients were primarily identified by closely monitoring their transplanted organ function. In the cases diagnosed with mucormycosis, failure of the transplanted organ was one of the first signs that there was a potential infection. If an organ originated from a drowned donor, and there are signs of transplanted organ failure with thrombosis and necrosis, empiric antifungal treatment should be considered.

[Sarah Gregory] You mentioned that some of the recipients received prophylaxis when they got the organs and they survived. So why isn't this done routinely with a drowned donor?

[Karen Wu] So unfortunately, the effectiveness of antifungal prophylaxis for invasive mold infections is not well established in the literature. Different molds can have different sensitivities to different antifungals, and also antifungal medications such as amphotericin B, which is the standard therapy for mucormycosis, can have severe side effects that can heavily impact already immunocompromised and sick recipients.

[Sarah Gregory] I see. So what protocols or steps should be instituted or followed to make these outcomes better?

[Karen Wu] For these invasive mold infections, early diagnosis and timely treatment are extremely important. In these recipients who received organs from donors who drowned, there should be prompt communication among transplant centers to facilitate early prophylaxis, diagnosis, and treatment of other recipients when indicated.

[Sarah Gregory] It's my understanding that the reporting system is a passive one. Should that be changed to a mandatory system in your opinion?

[Karen Wu] That is completely correct. The organ procurement organizations and transplant centers are required to report any test results or information that indicate a possible and unexpected donor-derived disease to the OPTN. The Disease Transmission Advisory Committee investigates select donor IMIs, but not all, to determine whether transmission occurred through transplantation. However, this process depends on the OPO (organ procurement organization) or transplant center staff to suspect a donor-derived infection. Unfortunately, mold can also be found in the environment, and immunocompromised transplant recipients are at increased risk for non-transplant-associated invasive mold infections, so it can be really difficult to determine whether the infection is donor-derived.

[Sarah Gregory] Dr. Wu, why did you do this study?

[Karen Wu] So the occurrence of invasive mold infections after drowning is well-documented in the literature. However, donor-derived infections are relatively rare, so we aimed to describe the limited number of cases that we investigated. In addition, the cases described in this study had an onset of disease that was faster and more severe than other published literature on donor-derived IMIs. We really felt the need to highlight our observations given the rarity of these infections and the severity of these cases.

[Sarah Gregory] Were there challenges that you encountered looking into this?

[Karen Wu] Definitely. Donor-derived invasive mold infections are difficult to investigate as many of these pathogens are found in the environment. Molds, such as Mucorales or *Aspergillus*, can be found throughout the environment, so it's difficult to determine with certainty that these infections came from the donor. However, these infections were so severe and had such a rapid onset that it really supported a donor-derived source for these infections.

[Sarah Gregory] What would you like to see done differently with surveillance of pathogens in transplant organs?

[Karen Wu] So I mentioned before, the reporting of invasive mold infections by organ procurement organizations or transplant centers is dependent on the clinicians suspecting a donor-derived infection. Since many fungal infections are opportunistic and tend to affect immunocompromised patients, I would love to see ongoing surveillance in transplant recipients

to identify additional infections to be able to better compare potential donor-derived infections versus community-acquired infections.

[Sarah Gregory] What area of CDC were you working in when you did this study? And I believe you've moved to another program. What are you doing now?

[Karen Wu] I was previously an Epidemic Intelligence Service Officer with the Mycotic Diseases Branch, where I worked with fungal diseases such as mucormycosis and scedosporiosis. I am now an epidemiologist with the Division of Healthcare Quality and Promotion in the International Infection Control Program. I work to prevent the spread of infectious diseases in healthcare settings by improving infection prevention and control practices and surveillance systems in resource-limited settings.

[Sarah Gregory] Tell us what mycotic diseases are.

[Karen Wu] They are fungal diseases of all sorts. It is an entire kingdom of life that can cause disease in people, although most of them are harmless to us.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Wu.

[Karen Wu] Thank you so much for having me. It has been a pleasure.

[Sarah Gregory] And thanks for joining me out there. You can read the July 2023 article, Fatal Invasive Mold Infections after Transplantation of Organs Recovered from Drowned Donors, United States, 2011–2021, online at cdc.gov/eid.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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