Transcript Details
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Patient Case: ATTRwt-CM Discovered Decades After Heart Transplant

Announcer:
You're listening to *Heart Matters* on ReachMD. On this episode, we'll hear from Dr. Lily Stern, who's an Assistant Professor of Cardiology at Cedars-Sinai Smidt Heart Institute. She'll be discussing her recent case study on a patient who was diagnosed with wild-type transthyretin amyloid cardiomyopathy, or ATTRwt-CM, after a heart transplant. Let's hear from Dr. Stern now.

Dr. Stern:
This is a fascinating case. Just to provide some background, this patient is an 88-year-old woman who underwent a heart transplant 21 years prior for ischemic cardiomyopathy, and she presented to an outside hospital after a mechanical fall. In the emergency room, she was noted to be in atrial flutter with 2:1 conduction at a ventricular rate of 150 beats per minute, and on echocardiogram, she was found to have a drop in her left ventricular ejection fraction from a baseline of 65 percent down to 40 to 45 percent.

So this is not an unusual scenario for an 88-year-old woman, whether she had a heart transplant or not. But since this patient is a transplant patient, it does shift our differential slightly. The closer the patient is to transplant, the more we are worried about the dreaded post-transplant complication of rejection, which occurs and requires treatment for up to 12–13% of patients within the first year post transplant.

Cellular-mediated rejection is more common up front, and as one gets further from transplant, antibody-mediated rejection is more common. But the overall risk of rejection really lessens as the patient is farther from transplant. And in this case, she is very far from transplant—21 years out. So risk factors for rejection this many years from transplant would be due to missing immunosuppression doses, whether due to forgetfulness from dementia—as may have been the case with her history—or conditions that impair absorption of the immunosuppression medications, such as severe diarrhea or vomiting. If there are drug interactions with other medications, that can increase the metabolism of immunosuppression medications or the removal of medications that inhibit the metabolism of the immunosuppression medications. So a more likely diagnosis for a drop in her ejection fraction and atrial arrhythmias in a patient this far from transplant is the development of cardiac allograft vasculopathy.

To work up this patient, due to the drop in her ejection fraction, she was taken to the cath lab primarily for a coronary angiogram to assess her coronaries for cardiac allograft vasculopathy. But after she was noted to have clean coronaries, they performed a right heart catheterization with endomyocardial biopsy to look for rejection. When the biopsy samples were evaluated under the microscope, they were noted to have no signs of cellular antibody-mediated rejection. But they found acellular, eosinophilic, extracellular matrix material deposits that were suspicious for amyloid. So they then performed an additional stain with Congo red, and it was positive, which is consistent with amyloid deposition. They then did further immunohistochemical testing, which was positive for antibodies against the transthyretin amyloid fibrils, and the tissue was sent off for liquid chromatography and tandem mass spectrometry, which is the gold standard for confirming amyloid. And it did, in fact, confirm the transthyretin type amyloid deposition. And then, to differentiate what type of ATTR she may have, she underwent genetic testing, which was negative for ATTR variant, so she was then diagnosed with what we call wild-type ATTR. And then she was started on appropriate disease-modifying therapy tafamidis, which is a TTR stabilizer.

And what's so amazing about this case is that when we went back and looked at her original cardiac explant from the time of her transplant, she had no amyloid at that time. This suggests that she developed and deposited these ATTR amyloid fibrils in this new heart over the subsequent 21 years.

The consideration of a diagnosis of cardiac amyloidosis in a post-heart transplant population has historically been not necessary as the median survival post-transplant is only 12 years, and the average age at the time of transplant is in the 50s. So people on average are

living until their 70s, but given improvements in immunosuppression regimens and monitoring protocols, people are living 20 or 30 years out from transplant. So it provides the opportunity for patients to develop non-heart transplant age-related conditions, such as ATTR wild-type amyloidosis.

So in general, we are learning that cardiac amyloidosis is much more common than we used to realize in the general population. About one in eight patients with heart failure with preserved ejection fraction have ATTR wild-type amyloid cardiomyopathy, and greater than 20 to 25 percent of octogenarians die with this form of amyloid in their heart. It may be the same for our heart transplant patients, but we do not routinely check biopsies on our patients this many years out from transplant. So while this likely is a rare scenario, this is an important reminder to think about de novo ATTR wild-type amyloidosis as part of the differential in our older heart transplant population who present with unexplained progression of restrictive cardiomyopathy, a drop in left ventricular ejection fraction, or arrythmias.

Announcer:
That was Dr. Lily Stern discussing her recent case study on wild-type ATTRwt-CM and heart transplantation. To access this and other episodes in our series, visit *Heart Matters* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!