



## Case of Desmoplakin Cardiomyopathy Treated with Heart Transplantation.

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### Background:

- Desmoplakin (DSP) is a protein that links cardiac desmosomes to intermediate filaments. It is needed for normal transmission of force within the myocardium. It is found in other cell types, including skin and hair, as well.
- DSP gene abnormalities were first described in arrhythmogenic right ventricular cardiomyopathy (ARVC). However, there is growing evidence of variable phenotypes of DSP gene abnormalities and distinguishing between different types of cardiomyopathies.
- DSP cardiomyopathy (CM) is associated with episodic myocardial injury that leads to left ventricular fibrosis, resulting in systolic dysfunction and subsequent ventricular arrhythmias.
- DSP CM is described in cases of recurrent episodic myocarditis, and can be associated with curly hair and calloused skin.
- There is a lack of specific diagnostic criteria for arrhythmogenic cardiomyopathies, though there are increasing recommendations for genetic screening and cardiac MRI when there is sufficient clinical suspicion.

### Case Presentation:

- **HPI:** A 67 year old male presents with progressive shortness of breath and fatigue that has been intermittent for several months.
- **PMH:** Previous cardiac arrest from VT at age 51, shortly after which he received an AICD placed with nonobstructive cardiomyopathy seen on angiography.
- **Surgical History:** No significant surgeries
- **Social History:** No significant smoking, alcohol, or other substance use
- **Family History:** arrhythmia in mother in her 70s, heart attacks in two grandparents in their 70s, early death of unknown cause in one grandparent, and two cousins that have AICDs
- **Medications:** sotalol, digoxin

### Clinical Course:

- The patient was relatively healthy from a cardiac standpoint prior to episode of ventricular tachycardia (VT) at age 51, shortly after which he had automatic implanted cardioverter-defibrillator (AICD) placed and nonobstructive, non-ischemic cardiomyopathy (NICM) on angiography.
- The patient was regularly seen at clinic for management of NICM. He was maintained on sotalol and digoxin from age 56 and onwards given history of VT storm. His left ventricular ejection fraction (LVEF) varied between 15-25% on multiple exams over the years. He was on below-target doses of goal directed medical therapy (GDMT) due to medication intolerances.
- He was first seen at advanced heart failure clinic at age 63. At this time, he had genetic testing that resulted in positive desmoplakin (DSP) gene abnormality and confirmed hereditary form of cardiomyopathy (DSP c699G>A (pTrp233\*)) variant.
- For this recent presentation at age 67, the patient was admitted for heart failure exacerbation. He had a right heart catheterization (RHC) on hospital day 2, was found to have elevated pulmonary capillary wedge pressure (PCW), and was started on milrinone. On hospital day 5, the patient declined, a rapid response team (RRT) was called, the patient went into VT, was shocked by his ICD, underwent brief CPR, was intubated, and transferred to the intensive care unit (ICU). He self extubated the next day. He was listed for heart transplant as status 2 while remaining on milrinone and with impella CP at P8.
- He underwent orthotopic heart transplant (OHT) and impella explant, which was complicated by bleeding and primary graft dysfunction. Intraoperatively, he was initially supported with intraaortic balloon pump (IABP) but then transitioned to venous-arterial extracorporeal membrane oxygenation (VA ECMO) and remained in the cardiac ICU.
- The ECMO settings were weaned and the balloon pump and ECMO were removed on post operative day 3.

### Results:

- The pathology report of the native heart described "fatty replacement of right lateral apical and anterior apical and basal ventricular wall and near-transmural fatty replacement of the posterobasal ventricular wall with focal transmural thinning and patchy replacement fibrosis."

### Conclusions:

- DSP CM is a distinct form of hereditary cardiomyopathy that differs from typical dilated cardiomyopathies.
- The clinical manifestations and expressivity of DSP CM is variable, depending on the specific gene mutation.
- Cardiac MRI can be helpful to further characterize DSP CM.
- Moderate-severe primary graft dysfunction in heart transplant is not uncommon and affects 3-7% of recipients.

### Literature:

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