Case Study: Dilated Cardiomyopathy

Clinical Overview
A 32 year-old female presents to clinic with palpitations. ECG and holter monitor showed frequent PVCs of multiple morphologies, and her echo showed normal LVEF. After 6 months, her PVC burden worsened, and she had developed paroxysmal atrial fibrillation and biventricular dilation. Due to the unclear etiology of her cardiomyopathy, either the result of her arrhythmia or familial cardiomyopathy, genetic testing was ordered for dilated cardiomyopathy (DCM). A heterozygous nonsense mutation was found in LMNA, which is known to be associated with DCM with conduction system disease Genetic testing with the GeneDx 27 gene DCM panel detects mutations in over 30% of familial DCM cases.

Patient Information:
Age: 32 Specimen: Blood

Referral diagnosis: 32 year-old female presenting frequent PVCs of multiple morphologies, and biventricular dilation.

Family history: Family history is significant for her father who died at age 52 from heart failure. No other reported family history of arrhythmia, cardiomyopathy, or sudden cardiac death.

Diagnostic Summary:
POSITIVE. Heterozygous Arg225Stop mutation in LMNA. GeneDx tests not only for genes associated with isolated DCM, but also genes associated with multisystem disorders such as mitochondrial disease and Danon disease. Distinguishing the different genetic causes of ventricular dilation is extremely important, as the clinical management for DCM may differ based on which gene is the cause of disease.

DCM gene sequencing panel: Sequence analysis of 27 genes associated with DCM revealed the Arg225Stop (R225X) mutation in LMNA, previously reported, multiple times, in association with various features in the laminopathy clinical spectrum. LMNA mutations are associated with a wide variety of phenotypes including arrhythmias, DCM with conduction system disease, and skeletal myopathy. DCM caused by mutations in LMNA typically presents in early to mid-adulthood and is usually accompanied by significant conduction system disease. Some patients also present with elevated serum CK levels with or without muscle dystrophy.1

Diagnostic Implications:
Although DCM can be inherited, ventricular dilation can also be acquired as a result of ischemic heart disease, normal aging, valvular heart disease, toxins such as alcohol and cocaine, infectious disease, and pregnancy. In addition, dilated cardiomyopathy can occur as a late manifestation of hypertrophic cardiomyopathy. Idiopathic DCM is a dilated ventricle without any identifiable cause. Genetic testing as part of a clinical evaluation can define the diagnosis and assist in determining appropriate management. The patient was counseled for management of LMNA-related DCM, with consideration for an ICD for control of her arrhythmias. Additionally, the patient’s two asymptomatic brothers could be tested for the Arg225Stop mutation to predict their risk of developing DCM and/or arrhythmias in the future.

References: