Genetic testing in presumed cardiac sarcoidosis

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Background: Cardiac sarcoidosis (CS) is a difficult to diagnose inflammatory heart disease. Certain types of genetic cardiomyopathy have been reported to masquerade as inflammatory cardiomyopathy. The utility of genetic testing in the evaluation of inflammatory cardiomyopathy is not completely explored and data regarding the prevalence of genetic cardiomyopathies in patients with presumed CS is limited.

Methods: We retrospectively analyzed patients evaluated from May 2020 to October 2022 in our Cardiac Sarcoid Clinic diagnosed with presumed CS as inferred by either fluorodeoxyglucose positron emission tomography (FDG-PET) - computed tomography (CT) or cardiac magnetic resonance (CMR) or both. Pertinent demographic, genetic, electrocardiographic, and imaging data for these patients was extracted from the electronic medical record.

Results: Genetic testing was obtained in 47 (22%) of the 213 presumed CS patients, among whom 43 (91%) presented with suspected isolated CS, and 4 (9%) with possible cardiac involvement in the setting of systemic sarcoidosis. Among the patients who underwent genetic testing, 10 (21%) had a pathogenic or likely pathogenic (P/LP) variant(s) in a genetic cardiomyopathy-susceptibility gene, including DSP (n=2), LMNA, FHL1, TPM1, MYBPC3, NRAS, MYH7 (n=2) and TTN (n=2) genes. All P/LP patients had FDG uptake, and in those with CMR data, 100% had late gadolinium enhancement. The seven patients with P/LP who underwent endomyocardial biopsy had no evidence of granulomatous inflammation. Immunosuppression was initiated in 60% of the P/LP patients before knowledge of genetic results.

Conclusion: Patients suspected to have CS may have concomitant or primarily genetic cardiomyopathy that may masquerade as an inflammatory phenotype. Genetic testing should be considered in these patients, not only to clarify the diagnosis and its prognostic and therapeutic implications, but also to offer cascade screening for the family of patients with P/LP variants who otherwise would not have been considered to have a heritable disease.