Initial genetic results for Brugada syndrome and hypertrophic cardiomyopathy patients in Brunei Darussalam

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Introduction: Mutations in at least 12 genes encoding the sodium, calcium and potassium channels are associated with Brugada syndrome (BrS), and mutations in 11 sarcomere protein genes are known to cause hypertrophic cardiomyopathy (HCM). We aim to look at the genetic results of our local patients having BrS and HCM.

Methods: For BrS, probands with type 1 electrocardiograms (spontaneous or flecainide-induced), and for HCM, probands with clinical diagnosis of HCM were included. For genetic tests, 1 ml of saliva was collected via self-collection kit (Oragene-DNA:OG-500) after fasting for 30 minutes, or 3 ml blood was taken in 2 EDTA tubes. Informed consents were obtained. Salivary samples were sent to Genelabs Diagnostics, and blood samples to Cardiogenomics in Singapore for genetic tests.

Result: 30 patients had genetic tests (BrS: N = 24; HCM: N = 6) between December 2014 and April 2019 (mean age: 45.87 +/- 14.58 years, 60% males) {Table 1}. For the BrS cohort, 5 have genes associated with BrS. All are apparently unrelated. 3 (S1, 21, 23) have SCN5A, and 2 (S6, 8) have CACNA1C. S1 had recurrent palpitations, spontaneous type I ECG and reproducibly inducible ventricular fibrillation (VF) leading to primary prevention implantaible cardioverter defibrillator (ICD) implant. S21 and S23 have asymptomatic flecainide-induced Brugada type 1 ECG. S6 had syncope, family history of premature sudden death, fever-induced type I ECG and reproducibly inducible VF aged 19 years. An ICD was recommended but patient declined it. S8 was asymptomatic. 5 BrS patients (S2, 4, 5, 15, 16) who were clinically deemed to be at high risk of sudden death had ICD implants but none had a pathogenic gene that is associated with BrS. Other genetic findings in BrS patients included genes that are associated with HCM (MYL2, MYH6, MYH7, MYBPC3), dilated cardiomyopathy (MYH6, MYL2, MYH7, DCS2, MYBPC3, HFE), arrhythmogenic right ventricular cardiomyopathy [ARVC] (DCS2), non compaction cardiomyopathy (MYH7, MYBPC3), and restrictive cardiomyopathy (MYL2, MYH7). For the HCM cohort, 1 (S26) has MYH7, a pathogenic gene associated with HCM. She had myomectomy for severe left ventricular outflow tract obstruction (LVOTO) aged 4 years. 1 (S25) has MYH6, a variant of uncertain significance. 1 asymptomatic patient (S27) having a likely clinical diagnosis of HCM, and a strong family history of premature sudden death has PKP2, a pathogenic gene associated with ARVC. 1 (S28) had myomectomy for HCM with severe LVOTO, and primary prevention ICD implant but his genetic test was negative. All patients are alive at follow-up.

Conclusion: In our local small cohort, pathogenic genes associated with BrS and HCM are seen. Hence we may offer genetic cascade testing in clinically unaffected first-degree relatives with the aim of identifying asymptomatic relatives for clinical follow-up, sudden death risk stratification and prevention.