

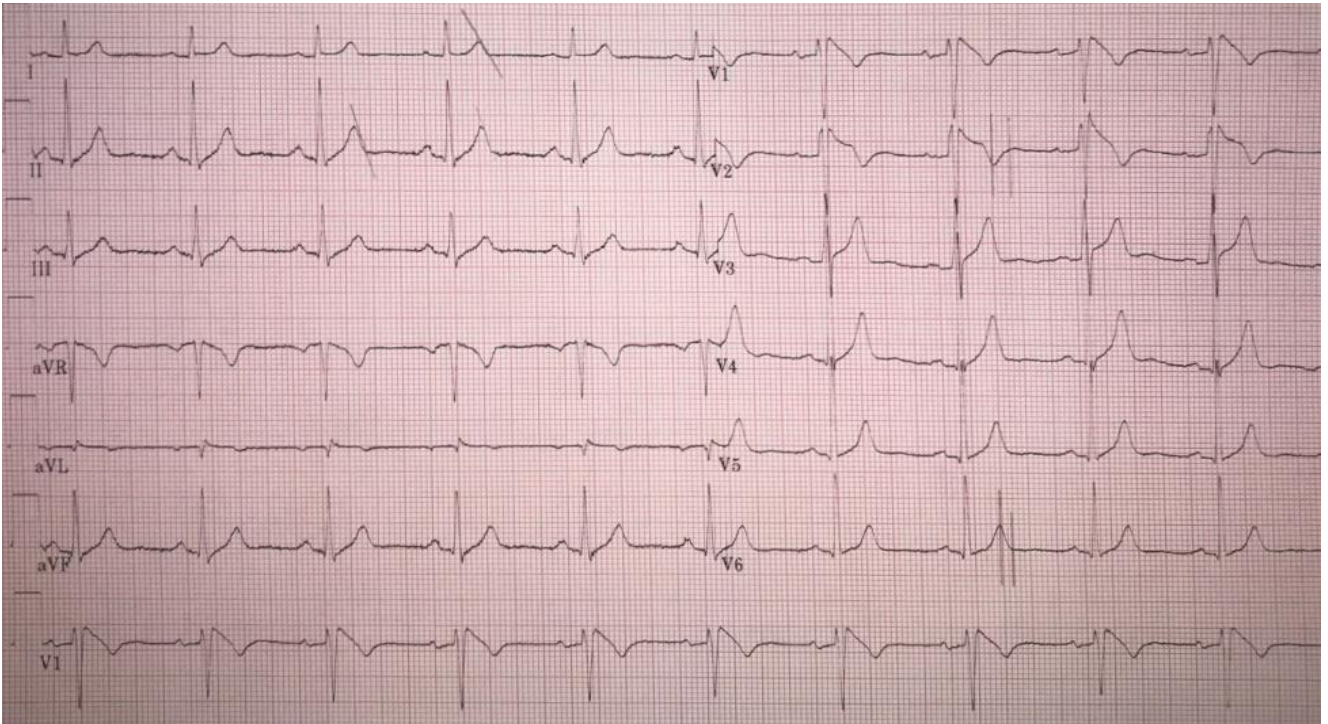
Supplemental Material

Table S1. Quality assessment of observational study included in the systematic review with MINORS criteria.

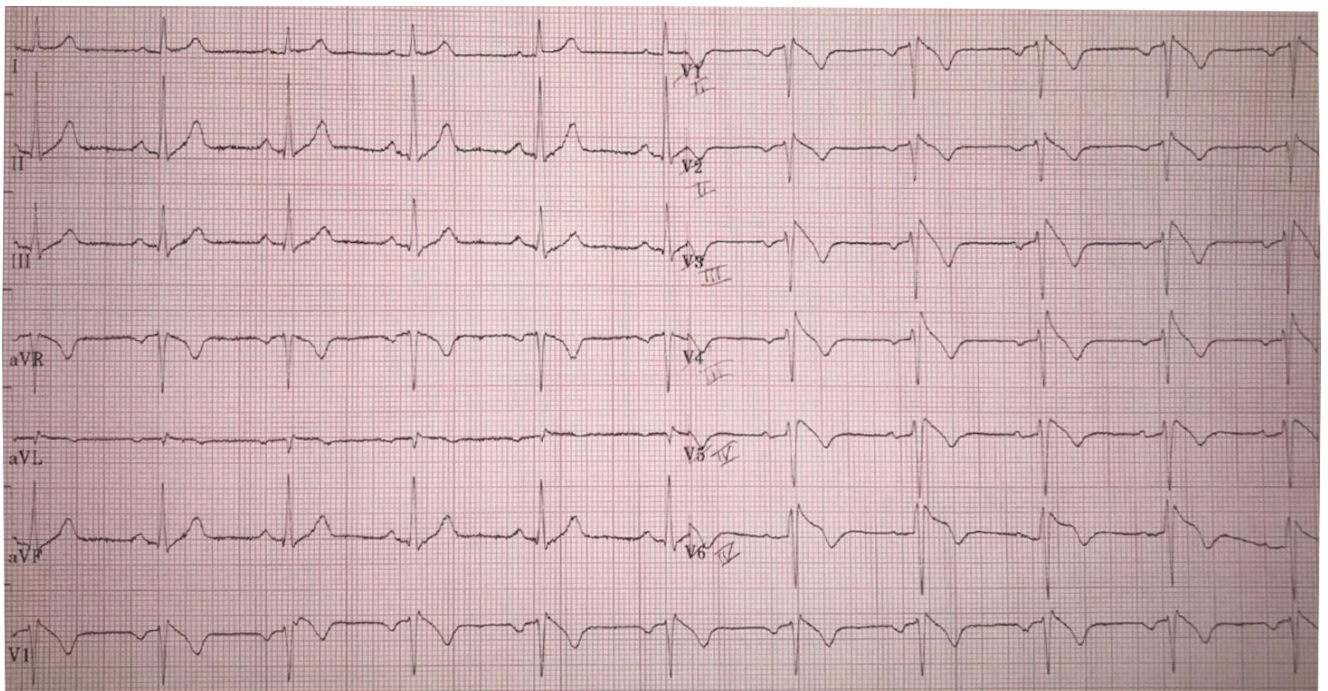
References	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12
<i>Migliore et al.</i> ²³	2	1	0	2	2	2	1	0	0	0	0	2
<i>Delise et al.</i> ¹⁷	2	2	0	2	2	2	2	0	0	0	0	1
<i>Morita et al.</i> ²⁶	2	2	0	2	2	0	1	0	0	0	0	2
<i>Mugnai et al.</i> ⁴³	2	2	0	2	2	0	1	0	0	0	0	1
<i>Ragab et al.</i> ⁴⁴	2	1	0	2	2	0	1	0	0	0	0	1
<i>Ragab et al.</i> ³¹	2	1	0	2	2	0	1	0	0	0	0	2
<i>Sakamoto et al.</i> ³⁸	2	2	2	2	2	2	2	2	0	0	0	2
<i>Probst et al.</i> ²⁰	2	2	2	2	2	2	1	0	0	1	0	2
<i>Sakamoto et al.</i> ³⁹	2	2	0	2	2	0	1	0	0	0	0	2
<i>Calò et al.</i> ²⁵	2	1	2	2	2	1	1	2	0	0	0	2
<i>Maury et al.</i> ²²	2	1	0	2	2	2	1	0	0	0	0	2
<i>Crea et al.</i> ³⁵	2	2	0	0	0	0	2	0	0	0	0	1
<i>Uchimura-Makita et al.</i> ³⁷	2	2	0	2	2	2	2	0	0	0	0	2
<i>Kawata et al.</i> ³³	2	2	0	2	2	0	2	0	0	0	0	2
<i>Rollin et al.</i> ²¹	2	1	0	2	2	2	1	0	0	0	0	2
<i>Maury et al.</i> ⁴²	2	1	0	2	2	0	1	0	0	0	0	1
<i>Priori et al.</i> ⁶	2	1	2	2	2	2	2	2	0	0	0	2
<i>Ohkubo et al.</i> ²⁹	2	2	0	2	2	2	2	0	0	0	0	1
<i>Nishii et al.</i> ¹⁹	2	2	0	2	2	2	1	0	0	0	0	1
<i>Nakano et al.</i> ¹⁸	2	1	0	2	2	2	2	0	0	0	0	2
<i>Letsas KP et al.</i> ⁴¹	2	1	0	2	2	0	2	0	0	0	0	1
<i>Shimeno et al.</i> ³⁴	2	2	2	1	1	2	2	2	0	0	0	1
<i>Sarkozy et al.</i> ³²	2	1	0	2	2	2	1	0	0	0	0	1
<i>Morita et al.</i> ²⁷	2	2	2	2	2	0	1	2	0	0	0	1
<i>Tada et al.</i> ³⁶	2	2	2	2	2	2	2	2	0	0	0	2
<i>Takagi et al.</i> ²⁴	2	2	2	0	0	2	1	2	0	0	0	2
<i>Babai Bigi et al.</i> ³⁰	2	2	0	2	2	2	2	0	0	0	0	1
<i>Juhani Junttila et al.</i> ²⁸	2	1	0	2	2	0	1	0	0	0	0	2
<i>Castro Hevia et al.</i> ⁴⁰	2	2	2	0	0	2	2	2	0	0	0	2

Q: question. In every item the following points were assigned: "Not reported (0 point)", "Reported but inadequate (1 point), or "Reported and adequate (2 point)". Q1: A clearly stated aim; Q2: Inclusion of consecutive patient; Q3: Prospective collection of data; Q4: Endpoints appropriate to the aim of the study; Q5: Unbiased assessment of the study endpoint; Q6: Follow-up period appropriate to the aim of the study; Q7: Loss to follow up less than 5%; Q8: Prospective calculation of the study size; Q9: An adequate control group; Q10: Contemporary groups; Q11: Baseline equivalence of groups. Q12: Adequate statistical analyse

Figure S1. Case 1.



A

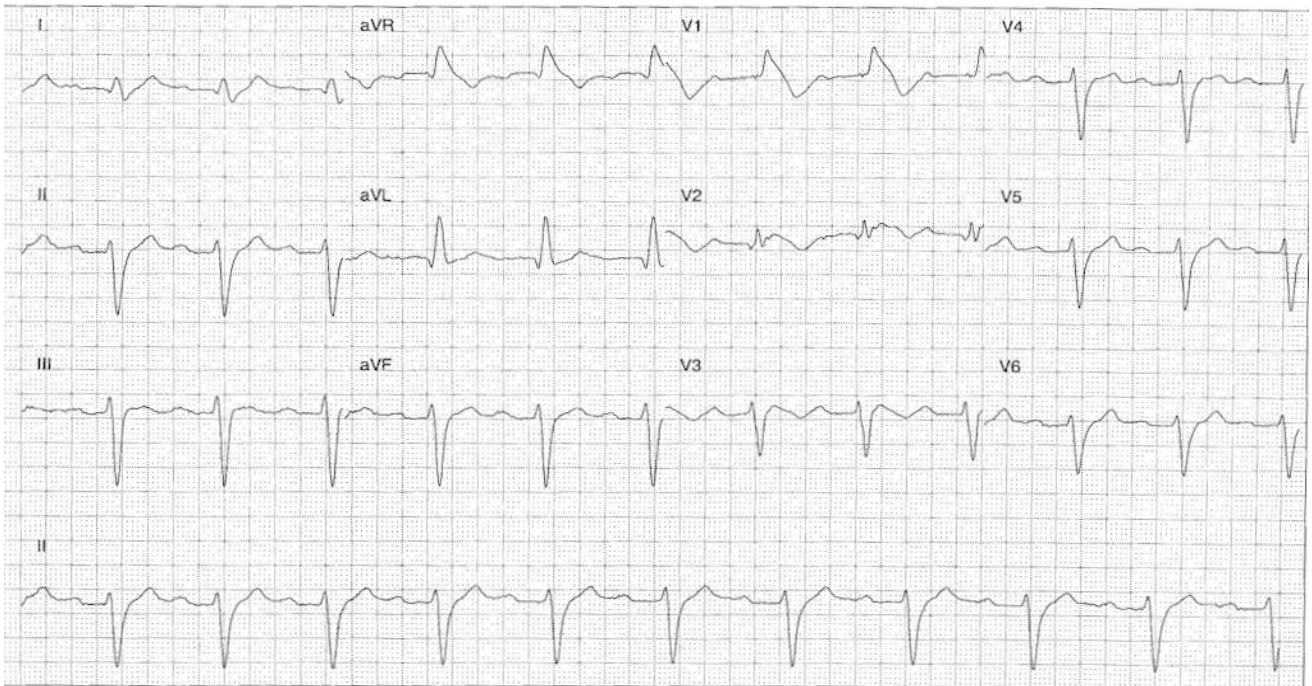


B

Case 1: these two ECGs are from the same asymptomatic 22 years old male with no history of familial sudden death. Normal echocardiogram and cardiac MRI. No gene mutations found. **A:** (standard 12

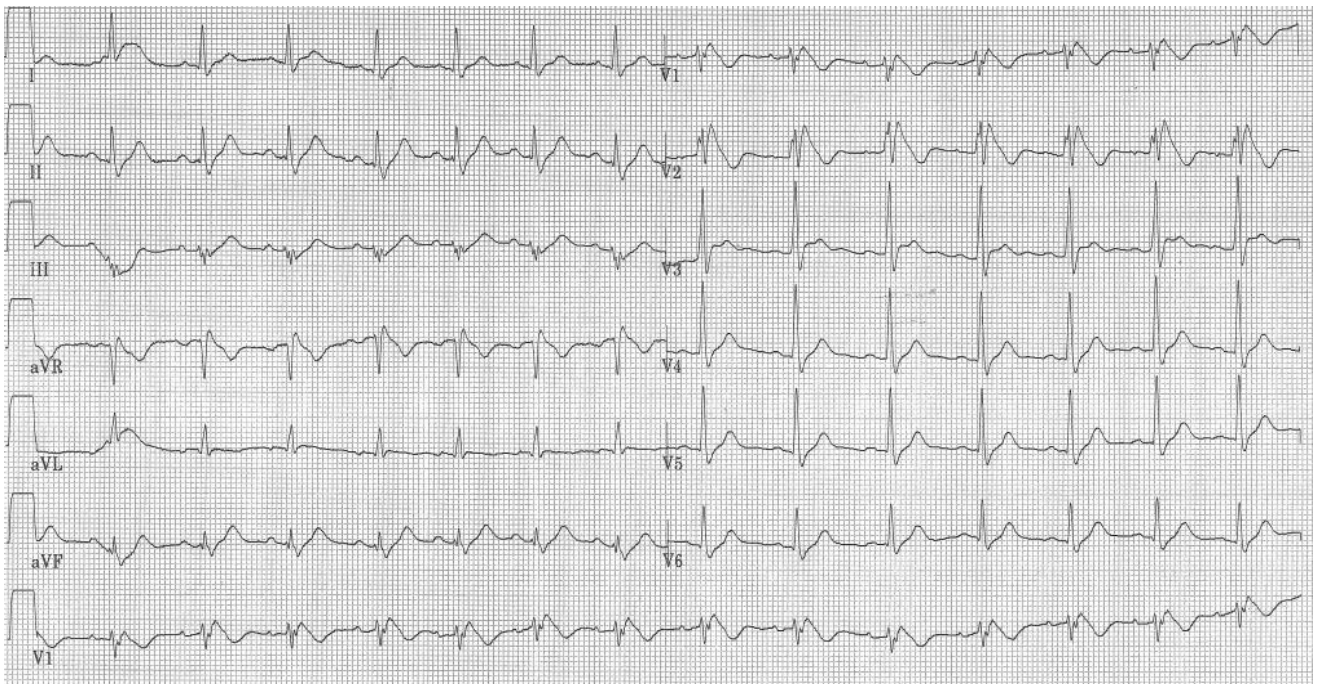
lead ECG) normal sinus rhythm, normal PR interval and QRS complex (duration and axis), ST segment elevation ≥ 2 mm in right precordial leads (V1–V2) followed by a concave or straight ST segment with a negative symmetric T-wave (type 1 Brugada pattern). **B:** (V1 and V2 along the 2nd, 3rd, 4th intercostal space) type 1 Brugada pattern expressed in all the modified precordial leads. In Case 1 ECG there are no additional arrhythmic signs inside the type 1 Brugada pattern. We can identify this as a “low risk pattern”.

Figure S2. Case 2.



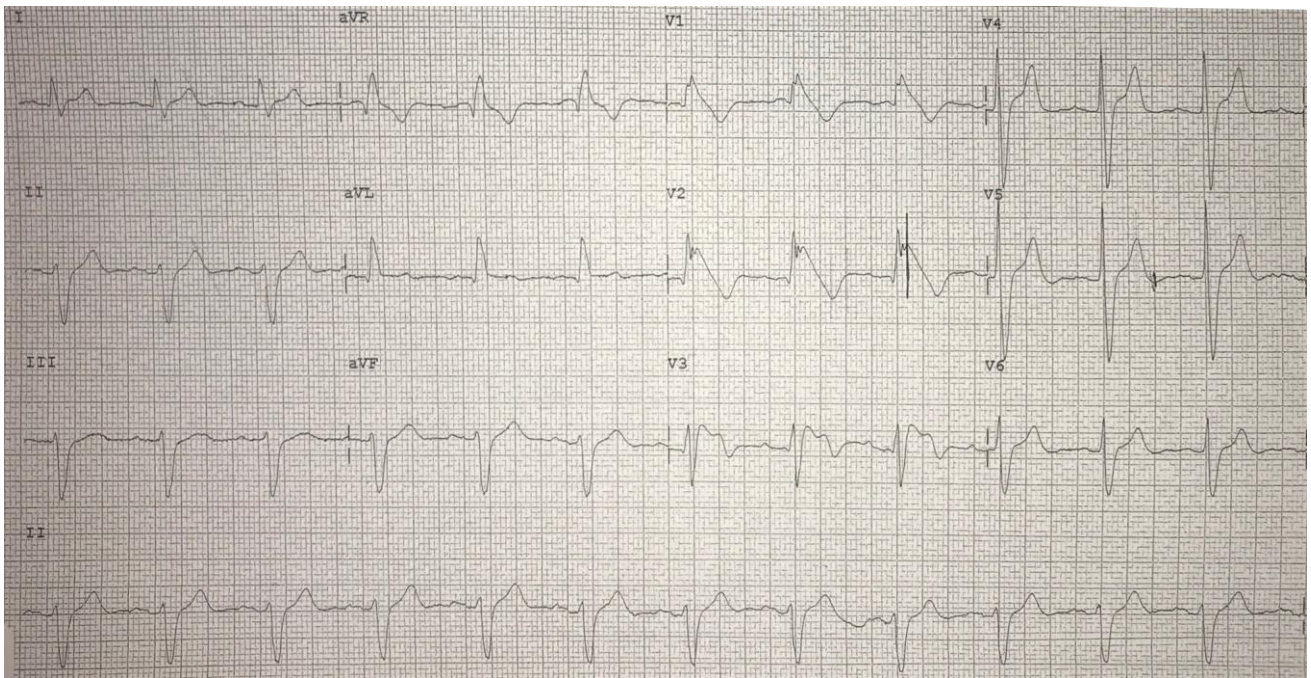
Case 2: 51 years old male with previous cardiac arrest. Multiple appropriate ICD interventions on VT/VF (one per year). Mild left ventricular hypertrophy at echocardiogram and cardiac MRI. SCN5A and Myosin gene mutations were found. **Figure S2:** (standard 12 lead ECG) normal sinus rhythm, first degree atrio-ventricular block (PR interval 340 ms), prolonged QRS duration (160 ms), left anterior hemiblock, type 1 Brugada pattern in V2 but also in lead aVR. In this ECG we have multiple arrhythmic signs as first degree AV block, prolonged QRS duration and type 1 Brugada pattern in the peripheral leads. We can identify this as “high risk pattern”.

Figure S3. Case 3.



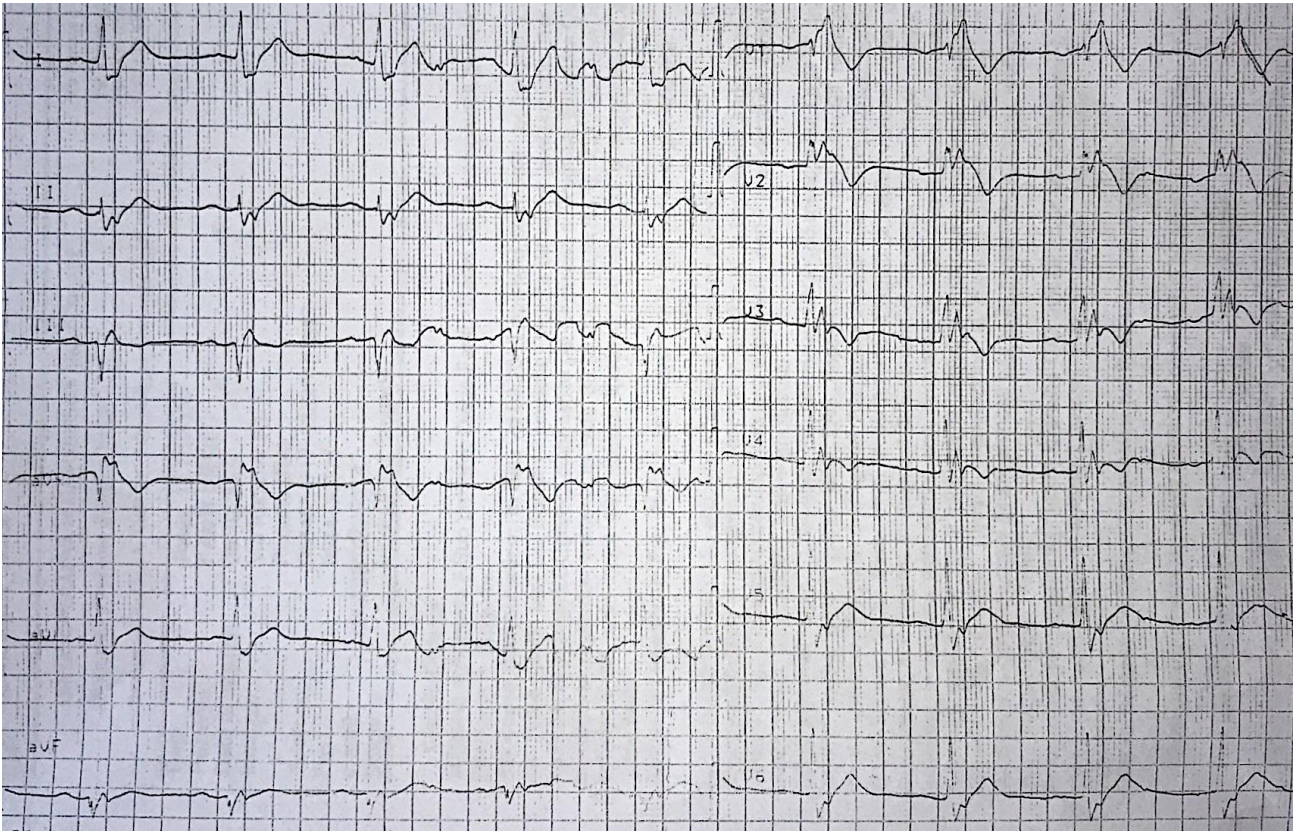
Case 3: 43 years old male with aborted cardiac death. He had multiple appropriate ICD interventions on polymorphic ventricular tachycardia. Father and paternal grandfather with sudden cardiac deaths in their forties. Normal echocardiogram and cardiac MRI. Novel pathogenetic mutation in the lamin A/C gene was found⁶¹. **Figure S3:** (standard 12 lead ECG): normal sinus rhythm; normal PR interval, prolonged QRS interval in V2 (135 ms), multiple notching of QRS complex in right precordial leads, tall R wave in lead aVR, deep S wave in V5 - V6 and DI, type 1 Brugada pattern in V1 - V2. In this ECG we have multiple arrhythmic signs as prolonged QRS duration in V2, fragmented QRS, aVR sign and deep S wave in lateral leads. We can identify this as “high risk pattern”.

Figure S4. Case 4.



Case 4: 74 years old man with ICD placed when he was 55 years old after ventricular arrhythmias induced during programmed electrical stimulation. He had only one appropriate ICD intervention for VF in his follow-up. He has paroxysmal atrial fibrillation. No family history of sudden cardiac death. Normal echocardiogram. No gene mutations found. **Figure S4:** (standard 12 lead ECG) normal sinus rhythm, first degree atrio-ventricular block (PR interval 220 ms), prolonged QRS duration (140 ms), left anterior hemiblock, fragmented QRS in right precordial leads, tall R wave in lead aVR, profound S wave in V5 - V6 and DI, Tzou criteria, type 1 Brugada pattern in V1 - V2 and type 2 Brugada pattern in V3. In this ECG, similar to Case 2 ECG, we have multiple arrhythmic signs as first degree AV block, prolonged QRS duration, fragmented QRS, aVR sign, Tzou criteria and deep S wave in lateral leads. We can identify this as “high risk pattern”.

Figure S5. Case 5.



Case 5: 55 years old man with aborted sudden cardiac while sleeping. No ICD interventions during follow-up. No history of familiar sudden death. Normal echocardiogram and cardiac MRI. SCN5A gene mutation was found. **Figure S5:** (standard 12 lead ECG) normal sinus rhythm, first degree atrio-ventricular block (PR interval 240 ms), prolonged QRS duration in V2 and DII (180 ms), fragmented QRS in right precordial leads, tall and prolonged R wave in lead aVR, deep S wave in V5 - V6 and DI - aVL, Tzou criteria, high depolarization dispersion, type 1 Brugada pattern in V1 - V2. Here we have almost all the arrhythmic signs as first degree AV block, prolonged QRS duration, fragmented QRS, aVR sign, Tzou criteria and deep S wave in lateral leads. We can identify this as a “very high risk pattern”.