ESC European Society of Cardiology

European Heart Journal - Case Reports (2018) **2**, 1–6
doi:10.1093/ehjcr/yty120

CASE REPORT

Sudden cardiac death: the finish line as a beginning: a true endurance race in a case report

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Received 7 November 2017; accepted 9 October 2018; online publish-ahead-of-print 20 November 2018

Background The benefits of exercise are well documented. Intensive exercise for more than 4 h per week is associated with cardiovascular remodelling, including increases in ventricular dimensions, wall thickness, and left ventricular mass. These changes are influenced by sex, ethnicity, and type and duration of exercise. In highly trained endurance athletes, exercise is often associated with electrocardiographic changes at rest.

Case summary A well-trained endurance athlete underwent cardiac investigation after his 33-year-old brother died while jogging. A resting 12-lead electrocardiogram showed significant first degree atrioventricular block (AVB), and longer monitoring revealed advanced AVB. This led to further testing and exercise restrictions.

Discussion Although most electrocardiographic changes are related to athletic performance, the distinction between normal variants, often exaggerated by the physiology of the conditioned athlete, and myocardial or electrical disease may be challenging. Athletes should undergo comprehensive cardiovascular evaluation, with management based on these results.

Keywords Athlete • Heart • Sports cardiology • Endurance training • Sudden cardiac death • Case report

Learning points

- Athletes perform physical activity beyond the recommended levels, which induces cardiac electrical, structural and functional adaptive alterations.
- These alterations are influenced by age, sex, ethnicity, type of sport, and training intensity. They can overlap with morphologically mild forms of primary cardiomyopathies.
- Physicians responsible for cardiovascular care of athletes should correctly differentiate athlete's heart from cardiomyopathy. Decisions for eligibility or sports disqualification may have significant implications to the individual.

Introduction

Sudden cardiac death (SCD) in young patients during leisure sports activities is a rare but tragic event.[1] Subsequently, first degree family relatives should be carefully screened for suspicious abnormal cardiac signs or symptoms. Screening can be disease oriented when the proband has a known diagnosis or can be general otherwise. Because regular intensive exercise induces adaptive cardiac remodelling, it is necessary to differentiate between harmless alterations and dangerous conditions, situations that frequently overlap in athletes.

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Timeline

Timeline of the events and follow-up of our patient using 24 hour Holter monitoring

Ten years prior to brother's sudden cardiac death (SCD)	Performed intensive dynamic training and moderate static training for bicycle marathons.
From five years prior to brother's SCD	Endurance training for 3 hours per day for ultra-trail running events.
Initial evaluation and beginning of detraining period	• Resting 12-lead electrocardiogram (ECG) showed sinus rhythm with a first degree atrioventricular block (AVB) block of 360 ms. • Ambulatory 24 hour Holter registration showed a maximum PQ interval of 630 ms with multiple episodes of type I second degree AVB. Multiple type II second degree AVB was observed during the daytime, and two periods of type 2:1 advanced AVB at night. • Treadmill stress test (TST) showed a normal increase in heart rate during exercise and no abnormal AV conduction or arrhythmias. • Normal transthoracic echocardiography (TTE). • CMR showed normal cardiac morphology and function with no evidence of LGE. • Blood cell counts; liver, renal and thyroid function tests; and toxicology tests were normal. • Negative for the *LMNA* gene
After 1 month	Ambulatory 24 hour Holter registration showed a maximum PQ interval of 500 ms with no episodes of type I second degree AVB. Maintains type II second degree AVB during the daytime but no longer periods of type 2:1 advanced AVB.
After 2 months	Ambulatory 24 hour Holter registration showed a maximum PQ interval of 520 ms with 5 episodes of type I second degree AVB. Reduces to 1 type II second degree AVB during night time and no periods of type 2:1 advanced AVB.
After 6 months	Ambulatory 24 hour Holter registration showed a maximum PQ interval of 500 ms with 1 episode of type I second degree AVB, 5 type II second degree AVB during night time and no periods of type 2:1 advanced AVB.
After 12 months	Ambulatory 24 hour Holter registration showed a maximum PQ interval of 400 ms with no episodes of second degree or higher AVB.

Case presentation

The patient was a healthy 37-year-old man, without any past medical history, who had participated in semi-professional training for bicycle marathons for over 10 years. During the previous 5 years, he took part in ultra-trail running events, which requires endurance training for 3 h per day.

The patient's brother, at age 26 years, was referred to a cardiologist for an asymptomatic abnormal electrocardiogram (ECG). Features of his ECG included sinus bradycardia, incomplete right bundle branch block, ST-segment elevation from V2 to V6 and T wave inversion in leads I, avL, and V6. Cardiovascular magnetic resonance imaging (CMR) showed a dilated left ventricle (LV) with a moderately depressed ejection fraction (EF 41%), hypertrabeculation that did not meet the criteria for non-compaction cardiomyopathy (NCC) and patchy late gadolinium enhancement (LGE) in the anterolateral wall. He was diagnosed with dilated cardiomyopathy with a moderately depressed EF related to myocarditis with no active myocardial inflammation and not meeting NCC criteria and was prescribed an angiotensin-converting enzyme inhibitor. This examination also led to a diagnosis of Hodgkin's lymphoma (HL), for which he underwent chemoradiotherapy with total disease regression. He subsequently underwent genetic testing for alterations in genes associated with NCC (*TAZ* and *LDB3*) and dilated cardiomyopathy (*MYH7*, *ACTC1*, *TNNT2*, and *TPM*), as well as tests for GM1 gangliosidosis, Morquio B and Fabry disease, but all were negative. Four months after his last evaluation and 3 years after being cured of HL, he collapsed in ventricular fibrillation during his regular jog and subsequently died. His last treadmill stress test (TST) showed excellent functional capacity and increased PQ interval duration (320 ms) during the recovery period. Transthoracic echocardiography (TTE) showed a normal LV, an EF of 48% and a global longitudinal strain of -15%. He did not undergo a follow-up CMR and a post-mortem analysis was not performed. Possible causes of death were ventricular arrhythmia due to myocardial fibrosis identified on initial CMR or coronary artery disease due to previous exposure to chemotherapy and radiotherapy.

Following his brother's death, our patient underwent a thorough cardiac evaluation. Cardiovascular and respiratory examination were unremarkable. A resting 12-lead ECG showed sinus rhythm with a first degree atrioventricular block (AVB) of 360 ms (*Figure 1*). Ambulatory 24 h Holter registration showed a maximum PQ interval of 630 ms (*Figure 2A*) with multiple episodes of Type I second degree AVB (*Figure 2B*). Multiple Type II second degree AVB (*Figure 2D*) was observed during the daytime, and two periods of type 2:1 advanced AVB (*Figure 2C*) at night. The patient was always asymptomatic during follow-up.

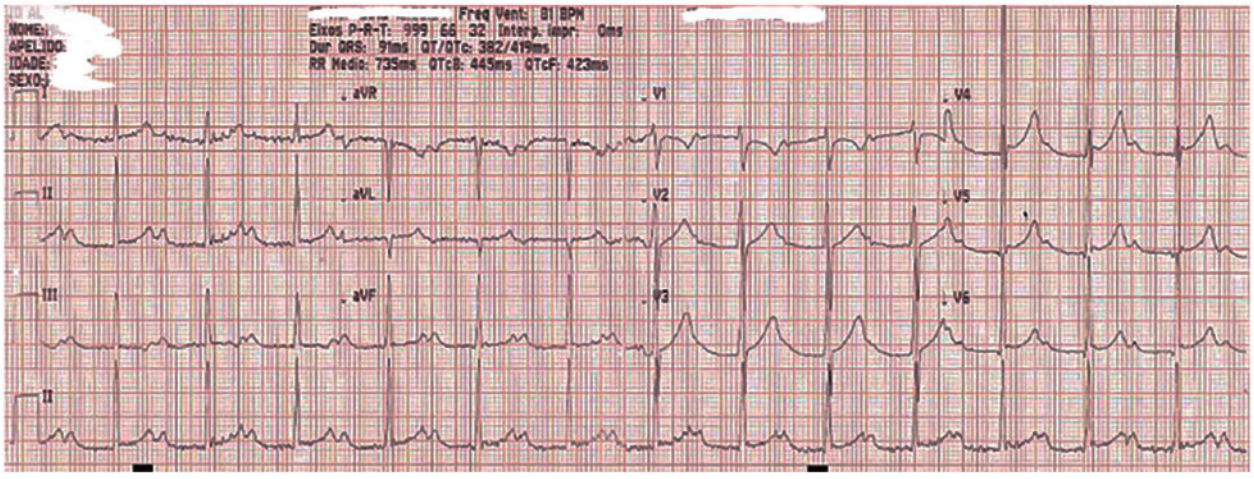

Figure 1 Baseline 12 lead electrocardiogram showing first degree atrioventricular block (PQ 360 ms).

The patient underwent an electrophysiology evaluation, and detraining was recommended. He was totally compliant with detraining and underwent regular 24 h Holter registration. Treadmill stress test showed a normal increase in heart rate during exercise and no abnormal AV conduction or arrhythmias. Transthoracic echocardiography was normal, and CMR showed normal cardiac morphology and function with no evidence of LGE. His blood cell counts; liver, renal, and thyroid function tests; and toxicology tests were normal. He was negative for the *LMNA* gene. Sarcoidosis was unlikely because of his normal CMR and normal blood levels of angiotensin conversion enzyme. After 1 year of deconditioning, there was clear regression of higher forms of AVB (*Table 2*).

Discussion

Electrocardiogram manifestations in athletes are associated with combinations of high vagal tone and increased chamber dimensions induced by training.[2] Although resting PQ ≥400 ms may be normal in a well-trained athlete, it should prompt further evaluation for cardiac conduction disease.[3] Information regarding symptoms and family history are of utmost importance in guiding further investigations of these overlapping conditions. Our patient was evaluated because of his family history of SCD with no definitive diagnosis.

The TST showed an appropriate increase in heart rate with PQ interval normalisation and no other conduction alterations. In asymptomatic athletes with no family history of cardiac disease or SCD, the disappearance of vagotone-induced alterations under exercise conditions would be sufficient to prevent further evaluation. However, ambulatory 24 h ECG monitoring in our patient revealed high grade AVB.

Mobitz Type II second degree AVB and 2:1 advanced AVB are abnormal findings in athletes, regardless of family history, and further evaluation is required.[3] Although TTE and CMR excluded the possibility of structural abnormalities in our patient, the possibility of a familial cardiomyopathy without phenotype expression could not be excluded. Because his brother experienced unclear conduction disease, with first degree AVB during recovery from his last TST, our patient was tested for LMNA gene mutations. Mutations in this gene have been associated with more than ten clinical entities and are among the primary causes of inherited dilated cardiomyopathy frequently associated with conduction system disease.[4,5] The LMNA gene and its variants were not found, suggesting that high vagal tone alterations induced by training were more likely.

The effect of intense training on conduction pathways has been described, with increased parasympathetic activity and/or decreased sympathetic tone and adaptation at rest resulting in a longer resting refractory period for AV node conduction.[6,7] Physiologically, an increase in sinus rate is normally associated with a concomitant shortening of the AV nodal refractory period enabling a 1:1 ventricular response. In contrast, neither the infranodal nor the distal conducting system is under vagal influence; therefore, vagolytic manoeuvres cannot shorten their refractory periods. Mild exertion can therefore help to differentiate between physiological conditioning and cardiac conduction tissue disease. Lesions in patients with Type I second degree AVB are usually located in the AV node, whereas Type II second degree AVB lesions are infranodal. The vagolytic effect, as mediated by exercise, tends to improve or abolish Type I second degree AVB, but has no effect on type II second degree AVB because the more distally sited lesion is beyond vagal influence.[7,8] Therefore, as in our patient, second degree AVB disappears during physiological sinus tachycardia. Thus, the refractory period of the relevant conducting system is likely under vagal influence, and the block is likely nodal or in the proximal conducting system.

Clinical practice guidelines recommend that athletes with Mobitz Type II second degree AV block with wide QRS receive a permanent pacemaker (PPM), and that a PPM be considered for athletes with a narrow QRS.[9] Although PPM implantation is proven safe in long-distance runners, the deleterious effects of right ventricular pacing and complications of implantation should not be forgotten.[10,11]

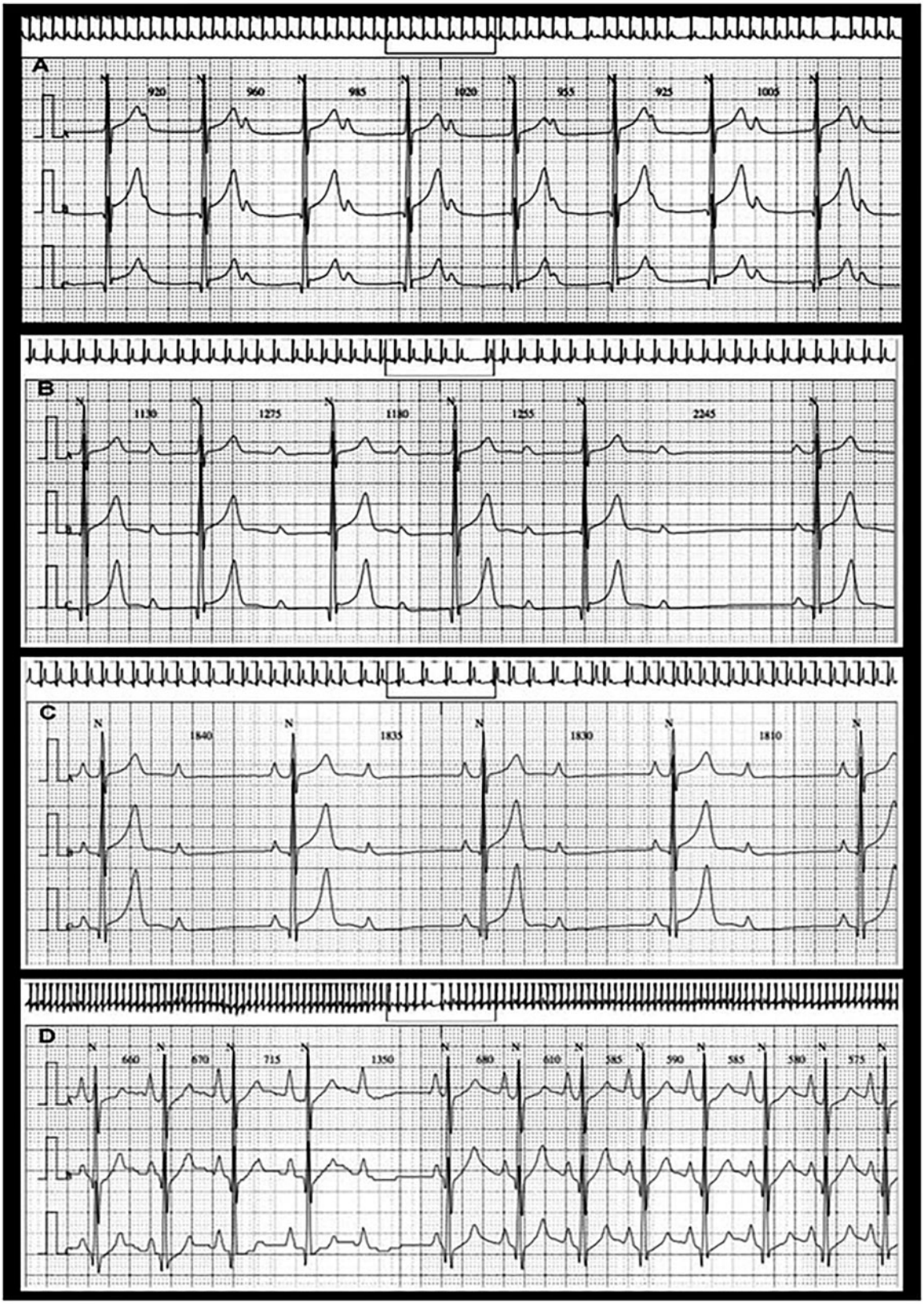

Figure 2 Electrocardiogram strips from baseline 24 h Holter monitoring showing all the degrees of atrioventricular block found; (*A*) maximum first degree atrioventricular block (PQ 630 ms). (*B*) Second degree Mobitz I atrioventricular block; (*C*) advanced degree 2:1 atrioventricular block; (*D*) second degree Mobitz II atrioventricular block.

Table 1 Clinical, exercise training, and echocardiographic characteristics of our patient (Case A) and his relative (Case B)

		Case A	Case B
Clinical	Age (years)	38	33
	Weight (kg)/height (cm)	83/187	78/182
	Rest HR (b.p.m.), BP (mmHg)	45, 110/70	59, 115/70
	Rest PQ interval (ms)	400	120
Exercise training	Weekly training (h)	21	6
	Career training (years)	5	—
	Maximal HR (b.p.m.)	178	180
Echocardiography	RAV, LAV (mL/m^2)	17, 20	17, 20
	RVEDA/RVESA (cm^2/m^2)	12.5/7	13.1/7.1
	RV S' (cm/s)	17	16
	EF (%)	64	50%
	GLS LV (%)	-24%	-15%
	LVEDVI (mL/m^2)	65	69
	E/A LV	1, 2	1, 3
	E/E' LV	8	7

A, peak late atrial filling left velocity; BP, systemic systolic and diastolic blood pressure; E, peak early filling left velocity; E/A, E/A ratio; E', velocity of myocardial diastolic motion by tissue Doppler; EF, ejection fraction; GLS, global longitudinal strain; HR, heart rate; LAV, left atrial volume; LV, left ventricle; LVEDVI, left ventricular end-diastolic volume index; RAV, right atrial volume; RV, right ventricle; RVEDA, right ventricle end-diastolic area; RVESA, right ventricle end-systolic area; S', velocity of the tricuspid annular systolic motion by tissue Doppler.

Table 2 Twenty-four-hour Holter parameters of our patient during detraining follow-up

	Time of detraining				
Holter parameters	**Baseline**	**1 month**	**2 month**	**6 month**	**12 month**
Minimum HR (b.p.m.)	34	44	46	43	42
Maximum HR (b.p.m.)	142	132	142	150	124
Average HR day, night (b.p.m.)	70, 67	80, 57	80, 61	83, 63	72, 54
Maximum RR (ms)	2910	1995	1895	2085	1670
Maximum PQ interval (ms)	630	500	520	500	400
Bradycardia <40 b.p.m. total duration (min)	7	<1	0	0	0
2nd AVB Type I Maximum RR (ms)	4	0	5	1	0
	2245	—	1895	1600	—
2nd AVB Type II Maximum RR (ms)	2	3	1	5	0
	2910	1995	1865	2085	—
Advanced 2:1 AVB Maximum RR (ms)	2	0	0	0	0
	1846	—	—	—	—
Premature ventricular beats	4	3	3	8	8
Premature supraventricular beats	2	—	6	—	2

This table sums up the findings in our patient's Holter monitoring registers during 1 year of detraining. Significant regression in the conduction defects were found in the first month with disappearance of advance 2:1 high degree AVB. During the total period of follow-up higher forms of conduction block regressed. After 1 year of detraining there remains a first degree AVB of 400 ms. AVB, atrioventricular block; HR, heart rate.

These findings suggest that detraining with regular rhythm monitoring was an appropriate choice for the patient. The number of debatable safe options in leadless monitoring devices (e.g. Nuubo 30 Sportbeat®, Zio® XT Patch), which allow cardiac rhythm monitoring for longer periods with high athlete compliance, is increasing.[12,13] After being informed of the advantages and disadvantages, our patient chose not to participate in any moderate to high intensity sports.

The results in the present patient highlight the importance of differentiating between exercise-induced and disease-related cardiac findings in athletes. These findings also emphasise the role of sports

cardiology knowledge in improving clinical decisions on eligibility and disqualification from athletic competition.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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