A 32-year-old male pharmacist complained of having had palpitations for the past month. Using his index finger and tapping the table top, he replicated a pattern that simulated extrasystoles. He exercised daily, running 3 miles and lifting weights for 1½ hours and was asymptomatic prior to, during, and after exercise. There was no past history of illness or allergies, and he was not taking any medications on a regular basis. He had a lean physical habitus and his weight had been stable. Family history revealed that both parents were being treated for essential hypertension; one sister was living and well.

On physical examination: height 5 ft 11 in (1 m 80), weight 172 lb (78 kg; in street clothes and stocking feet), pulse 72/min, and blood pressure 150/90 mm Hg. The cardiac examination revealed a regular sinus rhythm of 72/min, normal S1 and S2, and no murmurs were heard. The jugular venous pulses were normal. No bruits were heard over the carotid arteries. The inferior extremity arterial pulses were brisk and normal.

An electrocardiogram revealed a regular sinus rhythm and was within normal limits (Figure 1). An echocardiogram revealed a normal left and right ventricle, with normal left ventricular contractility. A comprehensive metabolic panel revealed all values to be within the normal range. Thyroid function tests were normal and the high-sensitivity C-reactive protein was 0.10 mg/dL (within the normal range). A lipid profile revealed: cholesterol 213 mg/dL (5.51 mmol/L), high-density lipoprotein 68 mg/dL (1.76 mmol/L), low-density lipoprotein 128 mg/dL (3.31 mmol/L), and triglycerides 83 mg/dL (0.94 mmol/L). A 24-hour Holter recording the following day revealed a basic sinus rhythm averaging 84 beats/minute. The maximum heart rate was 182 sinus-conducted beats per minute recorded during his daily 3-mile running exercise (Figure 2). No arrhythmias were recorded during the tachycardia; however, ventricular premature beats were seen at slower heart rates (Figure 3; 132/min). No symptoms were reported during the entire 24-hour Holter recording. The absence of arrhythmias during a high level of exercise when heart rates of 182 sinus-conducted beats per minute were recorded was unexpected in a patient who demonstrated ventricular premature beats at rest. After being advised as to the results of his tests, he refused all additional cardiac testing or therapy.

This case illustrates that exercise can eliminate ventricular ectopic beats occurring during rest or low-grade activity, a finding rarely reported in the literature.  

QUESTIONS

1. What clinical management is indicated in this case?
   a. reassurance
   b. no pharmacological therapy
   c. discontinue exercise
   d. β-blocker therapy
   e. quinidine sulfate
   f. statin therapy

2. What physiological events associated with exercise can lead to arrhythmias?
   a. activation of the sympathetic nervous system
   b. an increase in circulating catecholamines
   c. an increase in sympathetic tone
   d. an increase in automaticity
   e. any of the above

3. Repolarization changes with exercise stress testing aid in evaluating the coronary circulation. What other marker is associated with an
increase in cardiac mortality during exercise stress testing?
   a. change in regional wall motion
   b. exercise-induced cardiac arrhythmias
   c. lipid profile
   d. genetic subtypes

4. Exercise-induced ventricular arrhythmias (EIVAs) increase the risk of mortality in healthy individuals.
   a. true
   b. false
   c. perhaps

5. Physiological and pathological sequences that predispose to arrhythmias during exercise may include which of the following?
   a. electrolyte imbalance
   b. acidosis
   c. heightened sympathetic tone
   d. genetic and pharmacological alterations of ion channel function
   e. all of the above

6. Which variables limit detection and reliability of EIVA?
   a. inaccurate analysis of arrhythmias
   b. reliance on technician’s interpretation of arrhythmias
   c. disabling of arrhythmia detection functions
   d. any of the above

7. Management of EIVA in asymptomatic patients involves which of the following?
   a. β-blocker therapy
   b. genetic testing
   c. echocardiographic analysis
   d. serial electrocardiograms
   e. nuclear stress imaging
   f. all of the above

8. Physiological variables that influence EIVA include which of the following?
   a. age
   b. ischemia
   c. gender
   d. all of the above

ANSWERS
1. a. reassurance
d. β-blocker therapy
f. statin therapy

Ventricular premature beats at rest or low-grade activity that is eliminated by exercise-induced sinus tachycardia have a favorable prognosis. On the other hand, post-exercise ventricular premature beats are
indicative of a serious prognosis. Reassurance and β-blocker therapy are advised, as well as a statin because of the dyslipidemia.

2. e. any of the above

Physiological changes that occur with exercise may precipitate arrhythmias by activating the sympathetic nervous system, which increases circulating catecholamines. An increase in sympathetic tone and automaticity may lead to premature beats and re-entrant arrhythmogenic circuits. In a pathological myocardial substrate, atrial fibrillation can occur as a result of left atrial enlargement, mitral regurgitation, or ventricular dysfunction. Ventricular arrhythmias can occur as a result of electrolyte imbalance, myocardial stretch, baroreceptor activation, or ischemia. Genetic mutations, either spontaneous or as familial forms (eg, long QT or the Brugada syndrome), may alter normal cellular depolarization and/or repolarization processes, predisposing to EIVA.

3. b. exercise-induced cardiac arrhythmias

The physical examination and history are prognostic clues for cardiac events. Exercise stress testing stratifies asymptomatic patients with an intermediate probability of coronary artery disease
Exercise stress tests measure several variables associated with cardiac risk, such as poor exercise capacity, exercise-induced electrocardiographic ischemia, hypotension, and impaired heart rate response to exercise. Premature ventricular beats induced during exercise can be a result of stress-induced myocardial ischemia and indicate an increased mortality risk.

Recent trials have analyzed exercise-induced arrhythmias employing concise cardiac end points, longer follow-up periods, and streamlined study populations. The poor prognosis when EIV A occurs is related to the concomitant presence of CAD, exercise-induced ischemia with exercise, or the presence of premature ventricular beats at rest. Exercise-induced supraventricular arrhythmias may increase the risk of developing atrial fibrillation.

4. a. true

Variations in population protocols, length of follow-up, and end points have created controversies regarding the significance of EIVA. EIVA is defined as any premature ventricular beat or sustained ventricular beats (3 or more). The prognosis of resting premature ventricular beats has not been adequately reported. EIVA was associated with an increase in cardiac risk in the healthy population. In patients with CAD, EIVA indicates an increased incidence of abnormal left ventricular ejection fraction. The maximal heart rate and EIVA are independent predictors of cardiac events. EIVA in the recovery period is a stronger predictor of cardiac death.

5. e. all of the above

An arrhythmia implies that there are increases in excitability and/or catecholamine sensitivity; however, the mechanisms of exercise-induced arrhythmias have not been established (eg, re-entrant, enhanced automaticity, after-depolarizations). Physiological and pathological sequences occur during exercise that can predispose to arrhythmias. The physiological events include electrolyte, pH, and autonomic changes. Pharmacological and genetic influences affect conduction properties and are arrhythmogenic.

Electrolytes, pH, Autonomic Tone

Alterations in serum potassium concentration facilitate arrhythmogenesis; however, the changes in serum potassium levels that accompany exercise are well tolerated. Vigorous exercise doubles the serum potassium concentration, decreases pH, and raises catecholamine levels greater than 10-fold. An anti-arrhythmic interaction between catecholamines and hyperkalemia may protect the heart from exercise-induced chemical stress. Catecholamines may offset the harmful cardiac effects of hyperkalemia and acidosis by increasing inward calcium currents that improve or maintain the integrity of potassium-depolarized action potential in the myocyte. When these changes occur at rest or during ischemia, the risk of arrhythmia and cardiac arrest is increased.

The antagonistic product of hyperkalemia, acidosis, and norepinephrine is reduced in the setting of ischemia or infarction, or during the post-exercise period when plasma potassium is low and adrenergic tone is high. Malignant exercise-induced arrhythmias occur in the recovery period of exercise when there is combined electrolyte and sympathovagal imbalance, particularly when ischemia is present. The
heightened risk of arrhythmias can be minimized by cool-down activities.

Pharmacological, Genetic Mutations

Alteration in conduction channels (sodium, potassium) and physiological response to exercise may lead to cardiac arrhythmias. Anti-arrhythmic agents increase EIVA by enhancing or attenuating function of specific ion channels. Genetic mutations can also lead to arrhythmia formation. A long QT syndrome subtype (potassium channel) has been linked to exercise-induced sudden cardiac death. Familial catecholaminergic polymorphic ventricular tachycardia is a rare arrhythmogenic disease that manifests with EIVA or stress-induced syncope, ventricular arrhythmia, or sudden cardiac death.

Miscellaneous

Variations in electrical patterns may herald or precipitate EIVA. Peri-exercise ventricular tachycardia was preceded by 2 different patterns: short-long-short RR interval sequence or a regular RR pattern.

6. d. any of the above

Several variables limit the reliability and detection of EIVA: (a) lack of consensus regarding definition and outcome that is related to variations in population and exercise protocols, inconsistent end points, and poor reproducibility; (b) reliance on the technician for identification of arrhythmias (computers and software algorithms currently detect and record arrhythmias); (c) exercise-associated “noise” (artifacts) such as electrical or musculoskeletal interference (the electromechanical “noise” produced by exercise creates artifacts that make arrhythmia recognition difficult); and (d) exercise-associated “noise” forces technicians to disable the arrhythmia detection function in order to record a definable trace. Recent exercise testing instruments accurately record electrocardiographic data during and after exercise. The stored and digitized signals undergo analysis by software programs that have Holter-like “noise”-reduction algorithms.

7. f. all of the above

The literature has not clarified which patients with EIVA who have no CAD risk factors require additional tests. β-Blocker therapy is indicated for symptomatic arrhythmias. In asymptomatic patients with EIVA, echocardiography, serial electrocardiograms, and nuclear stress imaging are indicated to evaluate for ischemia. Genetic testing provides data independent of clinical or environmental variables. The risks of arrhythmias are products of environmental factors and genetic substrates. Stratification of patients based upon genetics helps in determining the risk for serious cardiac events.

8. a. age
   b. ischemia

There is a direct relationship between age (>40 years) and the prevalence of EIVA. Either the aging process or the various age-related comorbidities contribute to EIVA. EIVA has been evaluated in relationship to the presence or risk of myocardial ischemia. Since arrhythmogenesis is a common characteristic of acute coronary occlusions and coronary syndromes, the presence of EIVA is prognostic. EIVA is more frequent in patients with CAD, and they have a greater tendency for ischemic-exercise echocardiographic changes and are at maximum risk for a cardiac event.

SUMMARY

Ventricular arrhythmias can be seen during exercise testing. The significance and prognosis of EIVA have been reviewed in the literature, but a consensus has not been reported to date. A ventricular arrhythmia induced by stress or exercise is a stimulus for cardiac evaluation and aggressive treatment of risk factors. Finally, exercise training reduces or eliminates exercise-induced arrhythmias, supporting a favorable prognosis.

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REFERENCES


SELECTED REFERENCES
