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ECG CASE STUDY

Giant Negative T Waves

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Marked T wave inversion in a life insurance applicant's ECG may suggest high risk. Careful analysis of the ECG, an informative attending physician statement, and judicious use of additional testing allows the medical director to put this striking ECG abnormality in its proper context.

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CASE SCENARIO

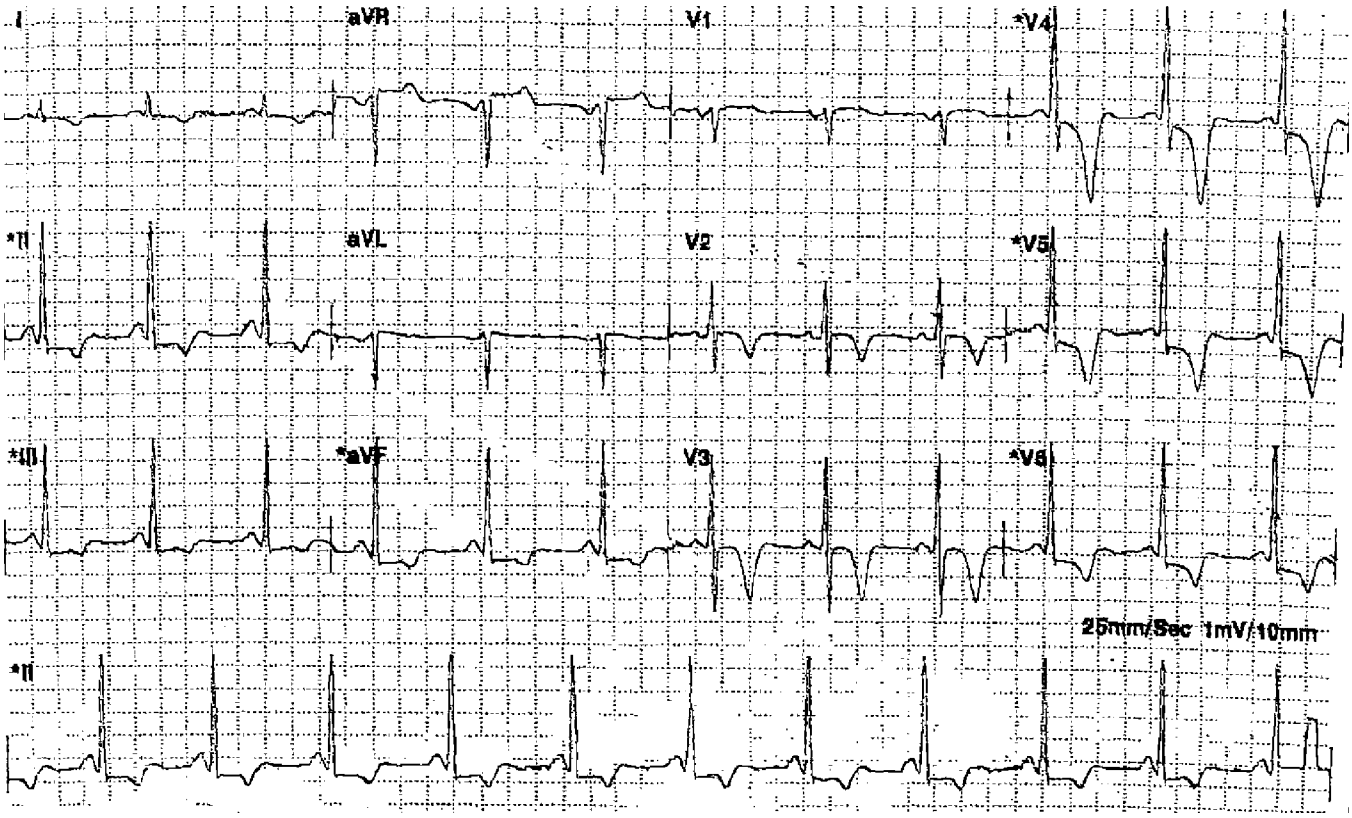
A 50-year-old chemical engineer is applying for $1,500,000 in whole life insurance. Five years prior to his application, he had a dizzy spell while at work. The company nurse took him to the emergency room of a nearby university medical center. Because of an abnormal electrocardiogram (ECG), he was admitted to the coronary care unit. His cardiac enzymes remained normal, and he was rapidly ambulated. Subsequent investigations including an exercise electrocardiogram, an exercise Thallium perfusion test and an echocardiogram were within normal limits. He was told that this dizziness was noncardiac in origin and that he had a normal heart. His future physical activity was not restricted.

Five years later at the time of his current application, he has had no further dizziness and remains asymptomatic. His past health is otherwise unremarkable. He remains physically active, playing singles tennis during the summer and basketball in a local league during the winter months. He is a non-smoker. Both parents died in their late 70s, and his 3 siblings are alive and well. His physical examination is normal. Routine lab work, including lipid analysis, is normal.

The Figure is an ECG obtained at the time of application for age and amount. Is the ECG normal or abnormal? If it is abnormal, what is the major abnormality? Does this abnormality indicate heart disease or could it be a normal variant? Does this abnormality have risk selection implications? Are there additional requirements, which you should request before making a risk selection decision?

ECG INTERPRETATION

The prevailing rhythm is sinus in origin with an average ventricular rate of 76 per minute. The PR interval is 0.14 second. The QRS complex is narrow, and the QT interval appears minimally shortened. The QRS axis in the frontal plane is normal (approximately +75°). The ECG is properly standardized,



Applicant's Electrocardiogram.

and the QRS voltages appear normal. In V_2 and V_3, the R/S ratio is ≥1, suggesting early transition (normally the transition zone where the QRS complex changes from predominantly negative to predominantly positive is between leads V_3–V_4).

The most striking feature in this ECG involves the T waves, which are inverted in leads I, II, III, AVF, V_2–V_6. In leads V_2–V_6, the T waves are sharply inverted and in V_4 reach a maximum depth of 14 mm from the baseline (these are referred to as ''giant negative T waves''). T waves in AVR, which are normally inverted, are distinctly upright. In leads V_2–V_4, the limbs of the T wave appear symmetric, while in the other leads with T wave inversion, the limbs of the T wave are asymmetric with a slow descending limb and rapid ascending limb. In leads II, III, AVF, V_4–V_6, the ST segments associated with the inverted T waves are depressed.

DIFFERENTIAL DIAGNOSIS

As a general statement, the causes of inverted T waves are quite varied so that this finding, in itself, is often regarded as nonspecific. The presence of giant negative T waves (≥10 mm in depth) does narrow the possibilities but is not pathonomic of any disorder. Similar T wave changes can be found in a variety of cardiac and non-cardiac disorders.[1,2]

In our analysis of this ECG, we should first ask whether such a pattern is recognized as one of the normal variant patterns. Normally, the T wave and QRS vectors are relatively concordant. Thus, in adults under physiologic conditions, the T wave is almost invariably positive in leads I and II, and in the lateral chest leads; it is normally inverted in AVR. In all other leads, it is variable. Certain general rules govern this variability. The T wave is normally upright in AVL and in AVF if the QRS is more than 5 mm tall, but may be inverted in the company of smaller R waves. In the precordial leads, the tendency to inversion of T waves diminishes with increasing age. In adult males, it is generally considered abnormal if the T wave is inverted in V_3–V_6. In normal women, the T wave in V_3 may be

shallowly inverted. The T in V_1 may be inverted normally at any age, and in V_2 it is sometimes normally negative.[3]

In children, T waves may normally be inverted in a number of anterior precordial leads. Persistence of T wave inversion in lead V_1 up to and including lead V_4 is a common normal ECG variant of childhood and is termed the *juvenile T wave pattern.* Occasionally, some adults show persistence of the juvenile T wave pattern, with more prominent T wave inversions in right to mid-precordial leads showing an rS or RS morphology.[2] In healthy young males, negative T waves may be seen in lead V_3 or V_4. This is sometimes referred to as the *isolated T negativity syndrome.* It comes and goes unpredictably and is not identified with any hemodynamic or metabolic process.[4] Inverted T waves may accompany the early repolarization pattern discussed in the last issue of the *Journal of Insurance Medicine.*[5] Inverted, often shallow, asymmetric T waves with the descending limb longer than the abruptly ascending limb, can be recorded in middle-aged women in the right precordial leads. Studies have shown no evidence of underlying heart disease.[6] The depth and widespread distribution of the T wave abnormalities in our applicant would rule out these normal variants.

In general, T wave abnormalities are divided into two types, primary and secondary. Any given individual may have one or the other, or both types. Primary T wave abnormalities are due to alterations in myocardial cellular electrophysiology such as those due to ischemia or injury. The changes are independent of changes in the QRS complex. Typically, primary T wave changes produce symmetric T wave inversion.

Secondary T wave abnormalities occur with conditions in which the sequence of ventricular activation is altered, such as in bundle branch block and ventricular hypertrophy. Electrocardiographically, such changes tend to produce ST depression and asymmetric T wave inversion. Our applicant's ECG illustrates both T wave morphologies with the typical symmetric primary T wave changes in V_3 and V_4 and typical asymmetric secondary T wave changes in II, III, AVF and V_6.

Five years ago, when the applicant appeared in the emergency room with his dizzy spell, presumably, his ECG was similar to the one illustrated in the Figure. In that context, it is understandable that primary consideration was given to ruling out acute coronary artery disease. The widespread distribution of the T wave abnormalities (coronary artery disease tends to be focal), the subsequent normal investigations and the persistence of the striking T wave changes for several years argue against coronary artery disease being the culprit.

Deep T wave inversion may also occur in a variety of non-coronary cardiac disorders, which may mimic coronary artery disease. Among these are the following conditions: stage 3 pericarditis, myocarditis, cardiac metastasis, athletic heart syndrome, hypertrophic cardiomyopathy, after bouts of tachycardia or ventricular pacing, and in some patients with complete heart block.[1,2]

Also, giant T wave inversion is not restricted to cardiac pathology. For this reason, the differential diagnosis includes non-cardiac causes such as severe brain injury due to subarachnoid or intracerebral hemorrhage, traumatic head injury, bilateral carotid endarterectomy, after vagotomy, cocaine abuse, flecainide intoxication, pheocromocytoma and acute gastrointestinal emergencies such as perforated ulcer, acute pancreatitis and acute cholecystitis.[1,2] In many of these non-cardiac situations, the T waves are asymmetric, wide, and associated with a prolonged QT interval. The absence of the above clinical contexts would rule out such causes in our applicant.

Because of our applicant's past history and his abnormal ECG, an attending physician's statement was requested. The above history was confirmed and an old ECG taken at the time of the emergency room visit was attached. It was similar to the ECG in Figure 1. A copy of a cardiologist's consultation was also enclosed. It concluded that the applicant's ECG was either a normal variant or possibly related to a latent or concealed pre-

excitation variant. The insurance company medical director, when reviewing the evidence with the underwriter, was suspicious that the original echocardiogram was suboptimal technically and suggested obtaining a repeat echocardiogram with special attention to the cardiac apex. Following initial resistance from the applicant, his agent and his cardiologist, a technically adequate echocardiogram was obtained. This revealed clear evidence of apical hypertrophic cardiomyopathy.

DISCUSSION

Clinicians are frequently confronted with ECG tracings showing deep T wave inversions, where the etiology is not immediately apparent. In the clinical context, the key question is whether the ECG abnormalities are related to some life-threatening cause such as myocardial ischemia/infarction or a cerebrovascular accident.

In the insurance risk evaluation setting, isolated major T wave abnormalities are an infrequent finding. However, their presence often carries a more serious prognostic implication than isolated minor T wave abnormalities.

Hypertrophic cardiomyopathy is a primary disease of cardiac muscle characterized by left ventricular hypertrophy in the absence of ventricular dilatation, and in the absence of a known cardiovascular or systemic stimulus to the development of hypertrophy. Patients with hypertrophic cardiomyopathy vary considerably in the distribution and extent of left ventricular hypertrophy. Frequently, the pattern of wall thickening is heterogeneous and contiguous segments of the left ventricle may differ greatly in thickness. This asymmetric hypertrophy is usually localized to the proximal ventricular septum and anterolateral free wall.

In 1976, a variant of hypertrophic cardiomyopathy was described, initially only in Japan, in which the hypertrophy was confined to the apex. In the first reports, the diagnosis was based on characteristic ECG findings consisting of pronounced negative T waves (>10 mm) in the precordial leads, ECG signs suggestive of left ventricular hypertrophy and a typical angiographic sign in which the silhouette of the left ventricular cavity appeared as an ''ace of spades'' at end diastole. Subsequently, the diagnosis was usually based on echocardiographic criteria: localized hypertrophy near the apex (beneath the origin of the chordae tendineae), a wall thickness in the apical region of at least 15 mm and a ratio of maximal apical thickness to posterobasal wall thickness of 1.5 or more.[8–11]

Although, in general, two-dimensional echocardiography is the method of choice for imaging and diagnosis in patients with hypertrophic cardiomyopathy, the echocardiographic diagnosis of apical hypertrophic cardiomyopathy may be more difficult. A ''normal'' study may not exclude the diagnosis. Ultrasound examination of the left ventricular apex by transthoracic echocardiography is occasionally inadequate as illustrated in our applicant. The apex is not seen in the parasternal view; and although apical views may show ventricular hypertrophy at the apex, there may be difficulties in getting an optimal echocardiographic window. There is also inherent foreshortening in this projection, so that hypertrophy may be missed or underestimated. The use of multiplane transesophageal echocardiography, image enhancement with intravenous contrast agents and magnetic resonance imaging all improve diagnostic accuracy.[7,12]

Although hypertrophic cardiomyopathy is the most common genetic cardiac disorder, its prevalence approximates 0.2% in the general population. Apical hypertrophic cardiomyopathy is most common in Japan where it accounts for about 25% of hypertrophic cardiomyopathy cases. Outside Japan, this condition is less frequent, constituting only 1%–2% of hypertrophic cardiomyopathy cases.[13]

The striking giant negative T waves, first reported in the Japanese series, were less pronounced in the later non-Japanese series. Several early follow-up studies have suggested a gradual increment in mean T wave inversion,

but more recent longer follow-up studies have disclosed diminution of both T wave negativity and QRS voltage with complete disappearance documented in some cases. Also the severity of T wave negativity can diminish during exercise testing.[10,14]

Very long-term follow-up of patients with apical hypertrophic cardiomyopathy is limited by the fact that the disease was only recognized as a distinct entity within hypertrophic cardiomyopathy since 1976. Studies of apical hypertrophic cardiomyopathy in the Japanese population have indicated a benign prognosis in patients with this condition. A less favourable outcome was initially reported from non-Japanese patients but more recent studies have found apical hypertrophic cardiomyopathy to be associated with a rare occurrence of cardiovascular morbidity and mortality. However, severe clinical manifestations, including sudden cardiac death, severe ventricular arrhythmias and apical infarction with aneurysm formation have been described in case reports.

A recent large long-term study from Toronto,[12] showed a benign long-term prognosis in North American patients with apical hypertrophic cardiomyopathy—15-year mortality was similar to age- and gender-matched general population mortality. One third of their patients developed unfavorable clinical events and potentially life-threatening complications, such as myocardial infarction, arrhythmias and stroke. Despite this significant morbidity, the majority of patients did not show any deterioration in their functional class, and approximately half remained totally asymptomatic during follow-up.[12]

In summary, giant negative T waves on an applicant's ECG raise a number of prognostically important possibilities for the medical director to consider. The severity and distribution of the abnormalities usually exclude normal variants. The screening context of an insurance applicant's ECG will exclude acute cardiac and non-cardiac causes of this abnormality. Consideration of the distribution and morphology of the T wave abnormally and the QT interval may point towards the underlying cause. Finally, in the presence of a very abnormal electrocardiogram suggesting high risk, judicious use of additional testing such as an echocardiogram may demonstrate an alternative diagnosis on which one can base an offer.

REFERENCES

1. Martinez-Lopez J. Reading T leaves. *J La State Med Soc.* 2000;152:8–9.
2. Goldberger A. Deep T wave inversions: ischemia, cerebrovascular accident, or something else? *ACC Current Journal Review.* 1996; Nov/Dec:28–29.
3. Marriott HJL. *Practical Electrocardiography.* 7th ed. Baltimore/London: Williams & Wilkins; 1983:21–22.
4. Lipman BS, Dunn M, Massie E. *Clinical Electrocardiography.* 7th ed. Chicago, Ill: Year Book Medical Publishers Inc; 1984;337–338.
5. MacKenzie R. Asymptomatic ST segment elevation. *J Insur Med.* 2004;36:86–89.
6. Fisch C. The abnormal ECG in the absence of cardiac disease. *ACC Current Journal Review.* 1997:69–73.
7. Crowley J, Dardas P, Shapiro L. Assessment of apical hypertrophic cardiomyopathy using transoesophageal echocardiography. *Cardiology.* 1997;88: 189–196.
8. Sakamoto T, Tei C, Murayama M. Giant T-wave inversion as a manifestation of asymmetrical apical hypertrophy of the left ventricle. *Jpn Heart J.* 1976;17:611–629.
9. Yamaguchi H, Ishimura T, Nishiyama S, et al. Hypertrophic nonobstructive cardiomyopathy with giant negative T-waves (apical hypertrophy). *Am J Cardiol.* 1979;44:401–412.
10. Smolders W, Rademakers F, Conraads V, Snoeck J. Apical Hypertrophic Cardiomyopathy. *Acta Cardiol.* 1993;48:369–383.
11. Webb J, Sasson Z, Rakowski H, et al. Apical hypertrophic cardiomyopathy: clinical followup and diagnostic correlates. *J Am Coll Cardiol.* 1990;15:83–90.
12. Eriksson M, Sonnenberg B, Woo A, et al. Long-term outcome in patients with apical hypertrophic cardiomyopathy. *J Am Coll Cardiol.* 2002;39:638–645.
13. Halkin A, Keren G, Stone G, Holmes D, Rosenschein U. Apical hypertrophic cardiomyopathy: truly a benign entity or not benignly a true entity? *Isr Med Assoc J.* 2002;4:203–204.
14. Koga Y, Katoh A, Matsuyama K, et al. Disappearance of giant negative T waves in patients with the Japanese form of apical hypertrophy. *J Am Coll Cardiol.* 1995;26:1672–1678.