

Case Study: Atypical Myocardial Infarction in a Man With Type 2 Diabetes

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Presentation

F.E., a 54-year-old man with a history of type 2 diabetes, hypertension, and Reiter's syndrome with prior hospitalizations for pneumonia and sepsis presented to the hospital emergency room complaining of chest pain, weakness, and fatigue. His chest pain was pleuritic in nature, worsening with movement and deep breathing. When he was motionless, the pain completely resolved.

F.E.'s electrocardiogram showed Q waves in leads II, III, and aVF, a new right bundle branch block, and mild ST segment elevation in leads V4 through V6. An urgent echocardiogram was ordered to differentiate between pericarditis and ischemia. The echocardiogram showed marked motion abnormalities in the inferior posterior, lateral wall. An initial troponin I was 238 ng/ml (normal range 0–2.5 ng/ml).

The patient was taken for emergent cardiac catheterization. This demonstrated an occluded right coronary artery that was opened with primary angioplasty and stent placement.

Questions

1. Is silent ischemia or atypical presentation of myocardial ischemia more common in diabetes?
2. What other disease states may predispose to the development of atypical chest pain syndromes?
3. What is the proposed mechanism for atypical or silent ischemia in diabetes?
4. Which patients with diabetes should undergo myocardial assessment?

Commentary

Manifestations of coronary artery dis-

ease (CAD) include overt, typical chest pain syndromes, atypical symptomatic ischemia, and asymptomatic or unnoticed ischemia. Previously unrecognized CAD may become apparent with abnormalities on a resting electrocardiogram including electrocardiographic left ventricular hypertrophy, nonspecific ST and T wave abnormalities, Q waves and interventricular conduction delays including bundle branch block. Silent CAD may also be recognized during an asymptomatic positive stress test.

For several years, it has been postulated that people with diabetes have a higher prevalence of asymptomatic or atypical CAD. The literature is far from clear on this point. What appears undeniable is that diabetes is an independent risk factor for the development of early CAD. In addition, the diagnosis of type 2 diabetes carries with it an increased risk of abnormal lipid profiles and hypertension (Syndrome X), both of which are independent risk factors for CAD. People with type 1 diabetes often lack other associated risk factors for atherosclerosis. Duration of diabetes seems to be the predominant predictor of CAD in these patients.

Silent myocardial ischemia was examined in the Framingham study.¹ In this cohort of 5,209 men and women, unrecognized anterior and inferior myocardial infarctions (MIs) were established by comparing biennial electrocardiograms.

More than 25% of all MIs in the Framingham cohort were discovered retrospectively, only after clear evidence of myocardial damage was noted on these routine electrocardiograms. Of these unrecognized MIs, 48% in men and 46%

in women were actually silent. The remaining unrecognized MIs were so atypical that neither the patient nor the attending physician entertained MI as a possible diagnosis.

Women had a higher incidence of unrecognized infarction than men (35 vs 28%) at all age levels. Hypertension was the only CAD risk factor, in both men and women, that was statistically correlated with unrecognized MI. This was a consistent finding even after excluding those patients with coexisting diabetes. In the cohort with diabetes, MI was unrecognized in 39% of men, a clear excess. In women, only 17% of the MIs were unrecognized, less than half the rate noted in the nondiabetic population. The authors offered no theory for these divergent findings.

Other studies have demonstrated an increased incidence of unrecognized CAD in patients with diabetes. In a case-control study, 41 of 132 patients with diabetes and 42 of 140 control subjects matched for age, sex, and risk factors other than diabetes, were noted to have electrocardiographic stress test evidence of myocardial ischemia.² To rule out possible false-positive stress tests, 36 of the 41 patients with diabetes and 34 of 42 control patients underwent coronary angiography. This demonstrated significant coronary narrowing in 39% of those with diabetes and in only 18% of the control subjects ($P < 0.05$). Other studies have demonstrated similar correlations between diabetes and silent or atypical ischemia.

Autonomic and sensory dysfunction have been postulated as possible mechanisms for unrecognized ischemia in patients with diabetes. A case-control

study involving 32 diabetic patients and 36 control subjects, all with typical anginal symptoms, tested this hypothesis by studying the anginal perceptual threshold, defined as the time from onset of 0.1 mV ST segment depression to the onset of anginal symptoms during treadmill stress testing.³ The results indicated that the perception of angina was significantly ($P < 0.001$) delayed in patients with diabetes compared to the control group, despite the fact that ST segment depression occurred earlier in the diabetic group. Further studies on patients with diabetes demonstrated significant autonomic dysfunction in the heart rate response to Valsalva and deep breathing, which were directly correlated with increased anginal perceptual threshold.

Clinical Pearls

1. Atypical or silent presentations of CAD may be more frequent in patients with diabetes.
2. Comorbid states such as hypertension may predispose patients with

- diabetes to a higher incidence of atypical or silent myocardial ischemia.
3. Autonomic dysfunction may in part explain altered anginal perception in diabetes.
 4. The American Diabetes Association 1998 consensus statement on Diagnosis of Coronary Heart Disease in People With Diabetes⁴ recommended the following indications for cardiac stress testing:
 - A. Typical or atypical cardiac symptoms
 - B. Resting electrocardiograph suggestive of ischemia or infarction
 - C. Peripheral or carotid occlusive arterial disease
 - D. Sedentary lifestyle, age >35 years, and plans to begin a vigorous exercise program
 - E. Two or more of the risk factors listed below in addition to diabetes
 1. Total cholesterol >240 mg/dl, LDL cholesterol >160 mg/dl, or HDL cholesterol <35 mg/dl

2. Blood pressure >140/90 mmHg
3. Smoking
4. Family history of premature CAD
5. Positive micro/macroalbuminuria test

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Case Study: Peripheral Neuropathy in Diabetes: Is It Diabetic Neuropathy?

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Presentation

T.T., a 26-year-old woman with type 1 diabetes diagnosed at the age of 14, presented with persistent burning pain in her lower extremities and upper extremity digital paresthesias that made her work as a dental hygienist difficult. Recently, her family had noted that she seemed to be stumbling at times. She reported that neither increased doses of a selective serotonin reuptake inhibitor (SSRI) nor trials of tricyclic antidepressants (phenytoin [Dilantin], carbamazepine [Eptol, Tegretol], or gabapentin [Neurontin]) had relieved her symptoms.

T.T. had no known history of diabetic retinopathy or nephropathy. She also denied resting tachycardia, orthostatic lightheadedness, early satiety, early morning nausea, changes in bowel habits, or postprandial sweating. She did note a history of depression, which was treated with counseling and medication. She also noted menstrual irregularity, dysmenorrhea, and premenstrual emotional lability. She had been treated with oral contraceptives in the past, but had discontinued these 6–8 months ago.

Her glycemic control had never been optimal despite a multiple-dose insulin program. Her hemoglobin A_{1c} (A1C) levels had typically been in the 8–9% range.

Exam revealed a moderately overweight (BMI 27 kg/m²) woman with a blood pressure of 138/85 mmHg with no orthostatic change and a resting pulse of 72 with no change with Valsalva maneuver. Lower extremity exam showed normal skin pigmentation, easily palpable

dorsalis pedis pulses, but decreased position sense as well as decreased sensation to 10-g monofilament testing.

Laboratory testing revealed an A1C of 8.2% (normal <6.5%); an albumin-to-creatinine ratio of 25 µg/mg (normal <30 µg/mg); and normal serum creatinine, complete blood count, total protein, sedimentation rate, and thyroid stimulating hormone.

When asked to bring in all over-the-counter and prescribed medications previously and currently used, the patient acknowledged taking pyridoxine (vitamin B6), a medication that she had started after reading on the Internet that it could help in the treatment of both premenstrual syndrome and carpal tunnel syndrome. She reported taking pyridoxine at a dosage of 200–500 mg daily for the past 6 months.

Questions

1. What is the differential diagnosis of peripheral neuropathy in people with diabetes?
2. What commonly used medications can be associated with peripheral neuropathy?
3. Are there any known benefits to the use of pyridoxine in a person with diabetes?

Discussion

Peripheral neuropathy has many potential etiologies yet is often quickly attributed to diabetes in diabetic patients, particularly in those with poorly controlled diabetes. The differential diagnosis includes metabolic etiologies, such as uremia, myxedema, amyloidosis, and

deficiency of vitamin B12, B6, or thiamine; toxic etiologies, such as ethanol or heavy metal exposure; and as a side effect of prescribed medications, including allopurinol (sold under various brand names), isoniazid (INH, Lanizid, Nydrasid), and nitrofurantoin (Macrochantin, Macrobid).

Peripheral neuropathy may also be associated with malignancy, such as lymphoma or bronchogenic or gastric carcinoma, and with infectious/inflammatory processes, such as monoclonal paraproteinemias, HIV, Lyme disease, borreliosis, or leprosy. In addition, it may also be associated with a variety of familial syndromes, such as Charcot-Marie-Tooth syndrome.¹

Providers must also recognize that over-the-counter remedies can have side effects including, in this instance, peripheral neuropathy. High-dose pyridoxine (B6) has been reported to cause sensory dysfunction and ataxia that improves after the vitamin is discontinued. Although initially believed to be related to mega-dose ingestion,² these symptoms have been reported in lower-dose users including those taking as little as 200 mg/day.³ Most patients note improvement or complete resolution of symptoms with discontinuation of pyridoxine. T.T. had substantial improvement within just 2–3 weeks of discontinuing pyridoxine.

Although neuropathy is a common complication of diabetes, it is important to be aware of other potential etiologies of neuropathy in diabetic patients to avoid missing an important diagnostic clue for a treatable condition. A careful

history should be obtained including use of both over-the-counter and prescription medications because commonly used agents can be associated with neuropathy.⁴⁻⁶

Treatment of specific problems, such as carpal tunnel syndrome, with pyridoxine has been thought at times to be beneficial,⁷ but not all data have supported this.⁸

Strongly encouraging patients to bring in all their medications can be a simple but helpful tool in making a more accurate diagnosis and effective therapeutic intervention.

Clinical Pearls

1. The differential diagnosis of peripheral neuropathy in diabetic patients is not limited to diabetes, but rather may have a variety of metabolic, toxic, inflammatory, malignant, infectious, and familial causes.

2. A thorough history and appropriate laboratory testing are needed to ensure completeness of the search for these etiologies. This should include a review of all over-the-counter medications being used about which patients may not initially volunteer information.
3. Several medications commonly used by people with diabetes may be associated with neuropathy.
4. Evidence of a beneficial role for pyridoxine in the treatment of neuropathy is inconclusive.

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