Chest Pain and ST Segment Elevation Attributable to Cholecystitis: A Case Report and Review of the Literature

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Chest pain with electrocardiographic changes is usually a life-threatening presentation of cardiac ischemia. There are, however, a variety of noncardiac conditions that have been reported to mimic these clinical and electrocardiographic changes. An Asian woman presented with chest pain and ST segment elevations in the distribution of the left anterior descending artery. She had persisting chest pain and ST segment elevations that were refractory to medical therapy, leading to thrombolytic therapy and rescue angiography, which revealed no evidence of coronary artery disease by coronary catherization. Cholecystitis was subsequently diagnosed with hepatobiliary scintigraphy. The patient's fever and ST segment elevations promptly resolved with antibiotic treatment. Four previous cases of ST segment elevation attributed to cholecystitis have been reported. Although the electrocardiographic changes attributed to cholecystitis have been shown to be correctable, the pathophysiological mechanism underlying these changes remains unclear. Prompt recognition of cholecystitis can ensure appropriate treatment and may prevent the performance of unnecessary diagnostic and therapeutic interventions.

Introduction

Chest pain with electrocardiographic (ECG) changes is often a life-threatening presentation of cardiac ischemia. However, a variety of noncardiac conditions have been reported to mimic the ECG changes seen with ischemic heart disease, including cholecystitis,[1–9] pancreatitis,[10–13] and pneumonitis.[14] With these conditions, the changes usually manifest as diffuse, nonspecific, T wave inversions or ST segment depressions.[5–9] Although chest pain with ST segment elevation is considered to be nearly pathognomonic for cardiac injury, this presentation has also been described with gastric distention,[15] cholecystitis,[1–3] acute stroke, pericarditis, subarachnoid hemorrhage, neoplastic invasion of the myocardium, acute cor pulmonale, and hypothermia. Prompt recognition of these noncardiac causes may reduce morbidity and mortality rates, costs, and patient anxiety.

We report on a patient with chest pain with anterior ST segment elevation that resolved with treatment of the patient's cholecystitis. We are aware of only four previous cases of ST segment elevation attributable to cholecystitis.[1–4] We discuss our case, compare it with previously published reports, and review the potential association between gallbladder disease and heart disease, including the potential pathophysiological conditions underlying these ECG changes.

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This manuscript was received for review in June 2004. The revised manuscript was accepted for publication in February 2006.

Case Report

A 63-year-old Asian woman with diabetes mellitus, hypercholesterolemia, asthma, and tobacco use presented with a 24-hour history of intermittent, "band-like," substernal, chest pain, dyspnea, nausea with vomiting, and low-grade fever. The pain was not pleuritic and did not radiate. The patient denied cough, abdominal pain, chills, or changes in her bowel or bladder habits. Her medications were insulin, theophylline, and terbutaline.

The patient's blood pressure was 130/60 mm Hg, pulse rate was 110 beats per minute, respiratory rate was 18 breaths per minute, and temperature was 38.2°C. The patient appeared to be in mild distress. Her heart rate was regular, without murmurs, rubs, or gallops. The patient had scattered, diffuse, expiratory wheezes, with good air movement. Her bowel sounds were normal, and her abdomen was soft, nontender, and without palpable masses. The patient had no jugular vein distention or peripheral edema. Her musculoskeletal and dermatological examination results were normal.

Chemistry results were normal except for a glucose level of 200 mg/dL. The aspartate aminotransferase level was 46 U/L (normal range, 0–31 U/L), alanine aminotransferase level was 43 U/L (normal range, 0–31 U/L), bilirubin level was 0.6 mg/dL (normal range, 0–1.0 mg/dL), alkaline phosphatase level was 134 U/L (normal range, 39–117 U/L), and lactate dehydrogenase level was 361 U/L (normal range, 122–220 U/L). The serum amylase level was 61 U/L (normal range, 25–115 U/L). The complete blood count revealed a white blood cell count of 13,500 cells per mm^3 (82% neutrophils and 4% bands), hemoglobin level of 15.2 g/dL, and platelet count of 297,000 cells per μL (normal range, 250,000–450,000 cells per μL). Urinalysis results were normal except for glycosuria. The creatine phosphokinase level was 69 U/L (normal range, 0–203 U/L), and creatine kinase-MB was undetectable.

The chest X-ray revealed hyperinflation without cardiomegaly, effusion, or infiltration. An acute abdominal series showed a nonspecific bowel gas pattern, without evidence of obstruction. The initial ECG assessment demonstrated sinus tachycardia (rate, 110 beats per minute), with new 3- to 4-mm ST segment elevation in V1 to V3. An ECG recording from an outpatient visit several months before presentation did not demonstrate ST or T wave changes suggesting ischemia. The patient's chest pain and ECG abnormalities initially resolved after she received aspirin and nitroglycerin in the emergency department, and heparin was infused intravenously. Echocardiography

demonstrated normal left ventricular systolic function, without effusion, wall motion abnormalities, or valvular disease. The patient's chest pain and anterior ST segment elevation returned 5 hours after admission, prompting the administration of tissue plasminogen activator. Rescue coronary angiography was subsequently performed because of lack of clinical or ECG improvement. There was no evidence of coronary artery disease or coronary artery spasm. Empiric calcium channel blocker administration because of vasospasm failed to resolve the ST segment elevation.

Four hours after cardiac catheterization, the patient's temperature rose to 40.8°C. No new findings were noted on cardiopulmonary examination. However, the patient's bowel sounds had become hypoactive and her abdomen was distended. Laboratory tests at this time demonstrated a leftward shift in her complete blood count (white blood cell count of 9,400 cells per mm^3, with 71% neutrophils and 22% bands), with persisting, mildly elevated, liver enzyme levels. Intravenous ticarcillin/clavulonate acid therapy was started after additional blood cultures were obtained. Right upper-quadrant ultrasonography demonstrated gallbladder wall thickening without stones. Subsequent hepatobiliary scintigraphy confirmed cholecystitis.

Blood cultures grew *Klebsiella pneumoniae* on the second day of hospitalization. The patient's symptoms and ECG abnormalities completely resolved within 48 hours after initiation of antibiotic therapy. The patient had no enzymatic evidence of myocardial infarction, with a peak creatine phosphokinase level of 133 U/L (normal range, 0–203 U/L). Troponin was not available when this patient presented to our medical center (she presented before the advent of troponin use). Cholecystectomy was performed, and acute cholecystitis was confirmed through histopathological evaluation.

Discussion

We report on a 63 year-old woman with chest pain and ST segment elevation in the distribution of the left anterior descending artery, prompting thrombolysis and angiography. She had no evidence of coronary artery disease or spasm, and her ST segment abnormalities promptly resolved with antibiotic treatment. Cholecystitis was subsequently diagnosed with hepatobiliary scintigraphy and was confirmed histologically. ECG abnormalities have been reported with a variety of noncardiac conditions, and ST segment elevations with chest pain have been reported with cholecystitis,[1–3] gastric distention,[15] acute stroke, pericarditis, subarachnoid hemorrhage, neoplastic invasion of the myocardium, acute cor pulmonale, and hypothermia. Prompt recognition of these noncardiac causes of ECG changes can ensure appropriate treatment and may prevent unnecessary diagnostic and therapeutic maneuvers, which can lead to significant patient anxiety, morbidity, cost, and potentially death. Chest pain and ST segment elevations have also been described for takotsubo cardiomyopathy, a rare disorder that is associated with emotional stress and is likely attributable to increased sympathetic activity.

A diseased gallbladder has been long associated with heart disease.[16–18] Swartz and Herman[19] credited Gueneau de Mussey with associating these diseases as early as 1878. This association has prompted several studies examining the ECG effects of biliary distention.[20,21] In those studies, the ECG changes usually manifested as diffuse, nonspecific, T wave inversions or ST segment depressions.

We conducted a Medline literature search and reviewed the citations of the articles identified in this manner. We found only four previous cases of ST segment elevation attributed to cholecystitis (Table I).[1–4] Patient ages ranged from 46 to 64 years. Three of the patients presented with chest pain and one with abdominal pain. All four were men, and two had a history of coronary artery disease. The lack of coronary artery disease detected with angiography for our patient is notable, because this is only the second case of cholecystitis presenting with chest pain and ST segment elevation with no evidence of coronary artery disease with cardiac catheterization. Earlier studies with animals[20] and humans[21] suggested that the gallbladder could elicit ECG changes only if coronary artery disease was present.

Two of the four patients underwent cardiac catheterization, and one of the previously reported patients received thrombolytic therapy, without effect. All previous cases with ST segment changes diagnosed through 12-lead ECG evaluations ($n = 3$) showed ST segment elevations in the distribution of a single coronary artery, anterior ($n = 2$) or inferior ($n = 1$). Two patients had resolution of ECG changes after cholecystectomy, two had resolution of ECG changes without further treatment, and our patient had resolution of ECG changes after antibiotic therapy.

Although the ECG changes attributed to cholecystitis have been shown to be correctable in humans with surgery[5,22,23] and atropine treatment,[5] the pathophysiological mechanism underlying the ECG changes remains unclear. Gallbladder distention has been shown to increase heart rate, arterial blood pressure,[24,25] and plasma renin levels,[26] and studies in animals suggest that its effect on coronary blood flow may be a significant factor underlying these ECG changes.[27–29] Decreased coronary blood flow was demonstrated in dogs during distention of the common bile duct.[29] Additionally, distention of the common bile duct in pigs[28] demonstrated that the decreased coronary blood flow persisted with control of heart rate and arterial blood pressure. In this swine model, a reflexive reduction in coronary blood flow always occurred with gallbladder distention and exhibited a graded response to the magnitude of the distention. This reflex was abolished with bilateral cervical vagotomy but was unaffected by severing of the splanchnic nerves, suggesting a vagal afferent pathway. The coronary vasoconstriction of this reflex was unaffected by atropine and propranolol but was abolished with phentolamine, indicating that this reflex has an α-adrenergic sympathetic efferent. These animal study findings may also play an important role in humans and may explain how gallbladder distention during gallbladder disease may limit coronary flow, providing a mechanism for the association of gallbladder disease and myocardial ischemia.

Summary

To our knowledge, this is the fifth report of ST segment elevation attributable to cholecystitis and the first case to resolve with antibiotics. Contrary to historic belief that ST segment elevation in the setting of cholecystitis is seen only in patients with underlying coronary artery disease, we report the second

TABLE I

CASE REPORTS OF ST SEGMENT ELEVATIONS IN PATIENTS WITH GALLBLADDER DISEASE

Patient No.	Authors	Age (Years)	Gender	Distribution of ST Segment Elevations	CAD	Clinical Course
1	Doorey and Miller[3]	58	M	Inferior	Nonocclusive CAD; previous coronary stent	While awaiting surgery for cholecystitis, patient developed chest pain, shortness of breath, diaphoresis, and new ST segment elevations in inferior leads. Emergency catheterization revealed only mild CAD and no evidence of vasospasm. Enzyme tests were negative and ST segment elevation spontaneously resolved. Subsequent urgent cholecystectomy revealed acute and chronic cholecystitis
2	Ryan et al.[1]	46	M	Anterior	No	Patient presented with constant, substernal, nonpleuritic, chest pressure and pain that began at rest. Cardiac catheterization, enzyme tests, and echocardiography did not indicate cardiac pathology. Abdominal ultrasonography showed multiple stones, and patient had acutely inflamed gallbladder removed. ECG changes rapidly resolved after surgery
3	Clark[2]	57	M	Unknown (no 12-lead ECG tracing obtained)	Presumed (no cardiac studies reported)	Patient presented with severe substernal pain, with diaphoresis, vomiting, abdominal distress, and RUQ tenderness. Pain is alleviated by standing still. ECG testing indicated new, slight, ST segment elevation in one lead, with reciprocal depression in another. Several weeks after acute attack, cholecystograms were reported as showing evidence of chronic cholecystitis. ECG abnormalities gradually resolved without definitive treatment
4	Cohen[4]	64	M	Anterior	No	Patient present with diffuse abdominal pain, with radiation to scapula. Serial ECG testing demonstrated complete resolution over 48-hour period without elevations in lactate dehydrogenase or creatine kinase levels. Ultrasonography showed gallstones in neck of gallbladder. Elective cholecystectomy 1 month later revealed chronic cholecystitis and cholelithiasis
5	Present report	63	F	Anterior	No	Patient presented with chest pain and intermittent ST -segment elevations, prompting thrombolysis and angiography. She had no evidence of CAD, and her ST abnormalities promptly resolved with antibiotic treatment. Cholecystitis was subsequently diagnosed with hepatobiliary scintigraphy and confirmed histologically after cholecystectomy was performed

CAD, coronary artery disease; RUQ, right upper quadrant; M, male; F, female.

case of cholecystitis leading to ST segment elevation with no angiographic evidence of coronary artery disease.

Chest pain accompanied by ST segment elevation is typically regarded as a condition for which prompt thrombolysis or percutaneous coronary intervention is recommended by the American College of Cardiology and the American Heart Association.[30] This is the second reported case of thrombolytic therapy and the third reported case of cardiac catheterization for a patient with ST segment elevation attributable to cholecystitis. Heparin, thrombolytic therapy, and/or coronary angiography can lead to significant morbidity as well as death. In addition, there are significant costs and patient anxiety with such interventions. Furthermore, delays in diagnosing cholecystitis may lead to serious complications, including sepsis and death. When the initial diagnostic and/or therapeutic interventions for chest pain with ST segment elevation do not yield the expected results (i.e., normal cardiac enzyme levels and normal cardiac catheterization results), then alternative diagnoses should be considered, including a search for cholecystitis.

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