Review Article

Severe Chest Pain of Non-Cardiac Origin in a Patient with Coronary Artery Disease: A Case Report and Literature Review

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ABSTRACT

Chest pain is one of the most common reasons for emergency department presentation and remains a leading cause of hospital admission worldwide. While acute coronary syndrome is the primary concern, particularly in older adults and patients with established coronary artery disease, the majority of chest pain cases are ultimately attributable to non-cardiac etiologies. Distinguishing cardiac from non-cardiac causes is clinically challenging, especially when initial investigations suggest significant underlying coronary pathology.

We present the case of a 69-year-old male with extensive cardiovascular comorbidities, including prior coronary artery bypass grafting, who presented with severe, persistent chest pain refractory to standard anti-ischemic therapy. Initial evaluation raised concern for non–ST-elevation myocardial infarction based on symptoms, risk profile, and imaging findings. Despite appropriate cardiac management, the patient's symptoms persisted and his clinical course deteriorated, prompting further investigation. Subsequent imaging revealed severe acute cholecystitis complicated by hepatic abscess formation, which was identified as the true source of his chest pain.

This case underscores that non-cardiac conditions, particularly acute biliary pathology, can closely mimic acute coronary syndromes and may present with chest pain unresponsive to conventional cardiac therapies, even in patients with known coronary artery disease. Clinicians should maintain a broad differential diagnosis and reassess refractory chest pain systematically to avoid diagnostic delay, reduce morbidity, and ensure timely, targeted management.

Keywords: Chest pain, Non-cardiac chest pain, Acute cholecystitis, Coronary artery disease, Emergency medicine.

INTRODUCTION

Chest pain is one of the most frequent and clinically significant presenting complaints in emergency departments (EDs) worldwide. In the United States alone, chest pain accounts for approximately 6–7% of all adult ED visits, translating to an estimated 7–8 million presentations annually (Cairns & Kang, 2021). Because chest pain may represent life-threatening conditions such as acute coronary syndrome (ACS), pulmonary embolism, or aortic dissection, emergency evaluation is often intensive and resource-driven, prioritizing rapid risk stratification and exclusion of cardiac ischemia.

Despite this focus, the majority of patients presenting with chest pain are ultimately found to have non-cardiac etiologies. National studies indicate that only a small proportion of chest pain presentations result in a life-threatening diagnosis, with acute coronary syndrome accounting for most of these cases, while a substantial number of patients are discharged with a diagnosis of non-cardiac or nonspecific chest pain (Hsia et al., 2016). Furthermore, up to half of non-cardiac chest pain cases lack a clearly identifiable cause at the time of evaluation, contributing to diagnostic uncertainty and challenges in management (Wertli et al., 2019).

Diagnostic complexity is further heightened in older adults and in patients with established coronary artery disease. Advancing age and pre-existing cardiovascular disease significantly increase baseline risk for ACS, often leading clinicians to prioritize cardiac etiologies even when symptoms are atypical or refractory to standard therapy. Current clinical guidelines emphasize structured risk assessment, serial cardiac biomarkers, and appropriate imaging; however, these approaches may inadvertently delay recognition of extra-cardiac sources of chest pain in high-risk populations (Gulati et al., 2021).

The objective of this case report is to highlight a rare but clinically important non-cardiac cause of chest pain severe acute cholecystitis in a patient with known coronary

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artery disease. By illustrating the diagnostic challenges and clinical consequences of anchoring on cardiac pathology, this case underscores the importance of maintaining a broad differential diagnosis and reassessing patients with persistent or unexplained chest pain.

CASE PRESENTATION

Patient Information

The patient was a 69-year-old male with multiple cardiovascular and metabolic comorbidities. His medical history was significant for coronary artery disease status post coronary artery bypass grafting, type 2 diabetes mellitus, hypertension, dyslipidemia, prior ischemic cerebrovascular accident, and Bell's palsy. He also had a documented history of atrial septal defect repair. There was no recent history of trauma, alcohol misuse, or illicit drug use. His cardiovascular risk profile was therefore considered high based on age, comorbid conditions, and prior coronary revascularization.

Clinical Presentation

The patient presented to the emergency department via emergency medical services with acute-onset central chest pain. The pain was described as compressive in quality, non-radiating, and severe, with an intensity of 7 out of 10. Symptoms began suddenly and persisted despite pre-hospital administration of aspirin and multiple doses of sublingual nitroglycerin. Associated symptoms included nausea, vomiting, and shortness of breath.

He denied fever, cough, diaphoresis, orthopnea, paroxysmal nocturnal dyspnea, lower-extremity edema, palpitations, or diarrhea. On arrival, vital signs revealed severe hypertension with a blood pressure of 216/102 mmHg. Given his extensive cardiovascular history and symptom profile, the initial clinical suspicion for acute coronary syndrome was high.

Diagnostic Assessment

Initial laboratory evaluation revealed mild but rising cardiac troponin levels, raising concern for myocardial injury, although values did not reach levels diagnostic of ST-elevation myocardial infarction. Additional laboratory findings included hyperglycemia, hypomagnesemia, and an elevated hemoglobin A1c, reflecting poor long-term glycemic control. Serial troponin assessment was performed in accordance with recommended protocols for chest pain evaluation (Hollander, 2016).

Electrocardiography demonstrated a right bundle branch block with nonspecific T-wave changes. While these findings were not diagnostic of acute ischemia, they were interpreted in the context of the patient's high-risk profile and known coronary artery disease (Brush et al., 1985; Hathaway et al., 1998).

Advanced imaging with computed tomography angiography (CTA) using a triple rule-out protocol was performed to evaluate for coronary ischemia, pulmonary embolism, and aortic pathology. Imaging revealed severe multivessel coronary artery disease, including occluded grafts and high-grade stenoses, as well as marked dilation of the main and left pulmonary arteries. No evidence of acute aortic dissection or pulmonary embolism was identified (Ayaram et al., 2013; Litt et al., 2012).

Clinical Course and Initial Management

Based on the patient's presentation and diagnostic findings, guideline-directed medical therapy for suspected acute coronary syndrome was initiated, including antiplatelet therapy, high-intensity statin, beta-blocker optimization, nitrate therapy, and aggressive blood pressure control (Gulati et al., 2021). Despite these interventions, the patient's chest pain persisted.

Over the ensuing hospital course, the patient developed worsening systemic symptoms, including hypotension, fever, altered mental status, acute kidney injury, and new oxygen requirements. These findings were not fully explained by a primary cardiac process and prompted reconsideration of the initial working diagnosis.

Identification of Non-Cardiac Etiology

Given the patient's clinical deterioration and lack of response to cardiac therapy, further diagnostic evaluation was pursued. Cross-sectional imaging of the chest, abdomen, and pelvis revealed extensive inflammatory changes surrounding the gallbladder, associated with trace ascites and suspected hepatic abscess formation. These findings were concerning for severe acute cholecystitis with possible gallbladder perforation.

Blood cultures subsequently grew *Escherichia coli*, confirming a systemic infectious process. The constellation of imaging, microbiological results, and clinical presentation supported a final diagnosis of severe acute cholecystitis with secondary hepatic abscess formation, explaining the patient's refractory chest pain and systemic illness.

Therapeutic Intervention and Outcome

The patient underwent percutaneous cholecystostomy tube placement by interventional radiology due to high surgical risk. The procedure resulted in drainage of purulent material and rapid clinical improvement. Broad-spectrum intravenous antimicrobial therapy was initiated and later tailored based on culture sensitivities.

Following intervention, the patient's fever resolved, hemodynamics stabilized, renal function improved, and chest pain significantly diminished. He was discharged in stable condition with plans for prolonged antibiotic therapy, outpatient

Table 1: Summary of Initial Laboratory and Imaging Findings

Parameter	*Result*	*Interpretation*
Troponin (serial)	Mild elevation with upward trend	Suggestive but non-diagnostic
ECG	RBBB, nonspecific T-wave changes	No acute ischemia
CTA triple rule-out	Severe multivessel CAD	High ischemic burden
Pulmonary arteries	Marked dilation	Possible chronic pathology

follow-up with surgery, cardiology, and infectious disease, and continued supportive care.

LITERATURE REVIEW

Overview of Non-Cardiac Causes of Chest Pain

Non-cardiac chest pain represents a substantial proportion of chest pain presentations in emergency and acute care settings. While cardiac ischemia remains the primary diagnostic concern, studies consistently demonstrate that most patients evaluated for chest pain do not ultimately have an acute coronary syndrome (Ringstrom & Freedman, 2006). Non-cardiac chest pain encompasses a wide range of etiologies, including pulmonary, gastrointestinal, musculoskeletal, psychiatric, and systemic inflammatory conditions. The clinical challenge lies in the considerable symptom overlap between cardiac and non-cardiac causes, as many extra-cardiac conditions can present with substernal discomfort, dyspnea, and autonomic symptoms that closely resemble myocardial ischemia.

Systematic evaluations of chest pain highlight the limitations of symptom-based diagnosis alone. Even classic anginal descriptors lack sufficient sensitivity and specificity to reliably differentiate ischemic from non-ischemic causes, reinforcing the need for structured diagnostic algorithms and serial assessments (Fanaroff et al., 2015). As a result, non-cardiac chest pain remains a diagnosis of exclusion in many cases, often reached only after extensive cardiac evaluation.

Gastrointestinal Disorders Mimicking Acute Coronary Syndromes

Gastrointestinal pathology is a well-recognized but frequently underappreciated source of chest pain that may closely mimic acute coronary syndromes. Conditions such as gastroesophageal reflux disease, esophageal spasm, peptic ulcer disease, pancreatitis, and biliary tract disease can produce chest discomfort that is indistinguishable from cardiac ischemia based on clinical features alone (Khan & Nair, 2002).

Biliary disease, particularly acute cholecystitis, may present with referred pain to the chest or shoulder due to shared neural pathways between the diaphragm and thoracic structures. Case reports and observational studies have documented presentations of acute cholecystitis complicated by mediastinal or thoracic symptoms, occasionally leading to initial misdiagnosis as cardiac or pulmonary pathology (Jagminas & Silverman, 1996). These presentations are especially misleading when chest pain predominates and abdominal symptoms are mild or delayed, as seen in critically ill or elderly patients.

Diagnostic Challenges in Patients with Established Coronary Artery Disease

The evaluation of chest pain in patients with known coronary artery disease presents unique diagnostic challenges. Pre-existing CAD significantly increases the pre-test probability of ACS, often leading clinicians to anchor on a cardiac etiology even when clinical findings are atypical or when patients fail to respond to guideline-directed anti-ischemic therapy. This diagnostic anchoring may delay consideration of alternative causes and contribute to prolonged hospital stays and increased healthcare utilization (Hollander et al., 2016).

Table 2: Major Non-Cardiac Causes of Chest Pain and Distinguishing Clinical Features

Category	*Examples*	*Key Distinguishing Features*
Gastrointestinal	GERD, esophageal spasm, cholecystitis	Relation to meals, abdominal tenderness, nausea
Pulmonary	Pneumonia, pulmonary embolism, pleuritis	Pleuritic pain, hypoxia, cough
Musculoskeletal	Costochondritis, rib fracture	Reproducible pain with palpation
Psychiatric	Anxiety, panic disorder	Hyperventilation, sense of doom
Systemic/ Inflammatory	Autoimmune disorders, infections	Fever, inflammatory markers

Additionally, abnormal baseline electrocardiographic findings, prior revascularization, and chronically elevated cardiac biomarkers can complicate interpretation of diagnostic tests in this population. In such cases, persistent or worsening symptoms despite appropriate cardiac management should prompt systematic reassessment and expansion of the differential diagnosis to include non-cardiac sources, particularly infectious or intra-abdominal processes.

DISCUSSION

Diagnostic Reasoning and Evolution of the Clinical Picture

The patient presented with acute, central chest pain in the context of significant pre-existing coronary artery disease (CAD) and multiple cardiovascular risk factors. Initial assessment appropriately prioritized exclusion of life-threatening cardiac etiologies, including acute coronary syndrome (ACS) and complications of prior CABG (Hollander et al., 2016; Gulati et al., 2021). Despite guideline-directed therapy including dual antiplatelet therapy, nitrates, beta-blockade, and statins the patient's pain persisted, indicating that the chest pain was not fully explained by myocardial ischemia alone.

The evolution of additional systemic findings, including hypotension, fever, altered mental status, and laboratory evidence of infection, prompted reevaluation of alternative causes. This highlights the dynamic nature of clinical reasoning in complex patients, where initial high-probability diagnoses may overshadow emerging signs of a non-cardiac etiology (Grailey & Glasziou, 2012). A structured iterative approach reassessing the patient's condition with each new clinical development was critical in identifying the ultimate diagnosis of severe acute cholecystitis complicated by hepatic abscesses.

Pathophysiology of Referred Chest Pain in Biliary Disease

Biliary pathology, including acute cholecystitis, can mimic cardiac chest pain through viscerosomatic convergence and shared neural pathways. The gallbladder and associated biliary tract are innervated by visceral afferent fibers that enter the spinal cord at levels T5–T9, overlapping with the cardiac sympathetic distribution (Khan & Nair, 2002). This convergence can result in referred pain perceived as substernal or epigastric discomfort, occasionally radiating to the chest or scapula, which may clinically resemble angina.

Inflammatory processes in the gallbladder can further exacerbate visceral nociception, leading to persistent, poorly localized pain that is unresponsive to standard anti-ischemic therapies. In this patient, systemic inflammatory response, including fever and elevated lactate, reinforced the non-cardiac origin of pain and prompted imaging of the hepatobiliary system, ultimately confirming the source.

Importance of Reassessment in Refractory Chest Pain (Grailey & Glasziou, 2012)

This case underscores the necessity of continuous reassessment in patients whose symptoms do not respond to initial therapy. Refractory chest pain should trigger consideration of non-cardiac etiologies, particularly when evolving clinical signs suggest infection, gastrointestinal pathology, or pulmonary complications. Failure to reassess may delay definitive treatment, increase morbidity, and prolong hospital stay.

Reevaluation involves:

- Reconsidering the differential diagnosis in light of new findings
- Ordering appropriate imaging beyond the cardiac-focused workup
- Consulting relevant specialties (e.g., surgery, infectious disease, interventional radiology)
- Adjusting management strategies based on dynamic clinical data

Comparison with Previously Reported Cases

Several reports in the literature have documented non-cardiac causes of chest pain mimicking ACS, including biliary disease, pancreatitis, and esophageal pathology (Jagminas & Silverman, 1996; Ringstrom & Freedman, 2006; Fanaroff et al., 2015). Like our patient, these cases often involved patients with significant cardiac risk factors, which initially biased the diagnostic focus toward coronary causes.

The unique aspects of this case include:

- Presentation in a patient with extensive multivessel CAD and prior CABG
- Lack of response to intensive cardiac therapy, which emphasized the need for a broader differential
- Identification of severe acute cholecystitis complicated by hepatic abscesses as the primary pain source

This comparison reinforces the clinical principle that even in high-risk cardiac populations, atypical presentations of non-cardiac disease must remain a consideration, and multidisciplinary approaches can expedite diagnosis and improve outcomes.

CONCLUSION

This case highlights several important clinical lessons regarding the evaluation and management of severe chest pain in patients with established coronary artery disease. First, it underscores that not all chest pain in high-risk cardiac patients originates from the heart. Despite extensive cardiovascular comorbidities and objective evidence of coronary artery disease, this patient's chest pain was ultimately caused by severe acute cholecystitis complicated by hepatic abscess formation. Clinicians should therefore remain vigilant for atypical presentations and avoid diagnostic anchoring solely on cardiac pathology.

Second, the case emphasizes the critical importance of maintaining a broad differential diagnosis. Refractory chest pain should prompt systematic reassessment and consideration of non-cardiac etiologies, particularly gastrointestinal, pulmonary, infectious, or musculoskeletal conditions that may mimic acute coronary syndromes. Iterative clinical evaluation, integration of evolving signs and laboratory results, and timely use of advanced imaging modalities are essential to avoid diagnostic delays and reduce morbidity (Grailey & Glasziou, 2012; Khan & Nair, 2002).

Finally, this case has significant implications for emergency and inpatient clinical practice. It demonstrates the value of dynamic, patient-centered diagnostic reasoning and multidisciplinary collaboration, particularly when standard therapies fail. Incorporating structured reassessment protocols for refractory chest pain may improve recognition of uncommon or non-cardiac causes, ensure prompt intervention, and optimize patient outcomes. By highlighting the intersection of cardiac risk and non-cardiac pathology, this report reinforces the need for a careful, methodical, and flexible approach to chest pain management in complex patients.

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