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# Bupivacaine Induced Cardiac Toxicity Mimicking An Acute Non-ST Segment Elevation Myocardial

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**Keywords:** Post pacemaker placement NSTEMI; Cardiogenic shock; Complete heart block; Local anesthesia; Bupivacaine; Cardiac toxicity; Myocardial infarction.

## Abstract

Bupivacaine is widely used as a local anesthetic. Central Nervous System (CNS) and cardiovascular toxicity were reported. There have been very few case reports in the past showing association of bupivacaine induced cardiac toxicity, mostly in young healthy patients. We present a unique case of bupivacaine induced cardiac toxicity in a 69-year-old male with multiple comorbidities mimicking an acute non-ST segment elevation myocardial infarction without CNS toxicity. We initially diagnosed the patient as having acute non-ST segment elevation myocardial infarction, but his impaired cardiac function improved gradually. On the fifth day of admission, there was a spontaneous recovery of cardiac function. The patient was discharged home with a follow up nuclear stress test in 4 weeks showing no ischemic changes and complete resolution of patient's atypical symptoms. Therefore, we believe that bupivacaine has some direct role in causing injuries to the cardiac cell.

## Case presentation

69-year-old Caucasian male with previous history of hypertension, hyperlipidemia, non-obstructive coronary artery disease, diastolic congestive heart failure, insulin dependent type I diabetes mellitus, chronic kidney disease, obstructive sleep apnea, atrial fibrillation on Coumadin, tachy-brady syndrome, hypothyroidism was admitted for symptomatic bradycardia. Patient had a loop recorder placed a month ago for evaluation of palpitations, atrial fibrillation, and bradycardia. He was found to have significant bradycardia on the remote recordings and was suggested to go to the emergency room for further evaluation and management. He reported fatigue, generalized weakness and dizziness during these episodes. He also reported mild diarrhea a few days prior to admission without any abdominal pains, chest pains and shortness of breath. The Rest of The (ROS) was negative except as stated above. On admission he was found to be in complete heart block with heart rate of 35bpm on initial EKG. He was saturating 97% on room air, respirations 8-10, and BP 142/53.

PMH: As stated above

Surgical History: appendectomy, cholecystectomy

Allergies: Penicillin, Versed, Fentanyl, Doxycycline,

Social history: former smoker quit many years ago, non-alcoholic, and non-drug abuser.

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Family history: Both parents had CAD and HTN,

**Physical Examination**

GENERAL: Patient was well nourished, somnolent but easily awakened to voice. HEENT: Head: No signs of trauma. Conjunctiva clear, pupils reactive to light bilaterally. Extraocular movements intact. Normal oropharynx.

NECK: supple, full range of motion, no cervical adenopathy, No JVD or tracheal deviation.

CARDIAC: s1/s2, bradycardia, no murmurs, or gallops

LUNGS: No respiratory distress, clear to auscultation bilaterally.

ABDOMEN: Soft, nontender to palpation.

EXTREMITIES: No leg edema. Calves nontender to palpation.

SKIN: No notable rashes.

NEURO: Somnolent but easily awakens to voice. Alert and oriented x 3. No focal deficits.

Initial work up in the Emergency room includes labs and imaging. Covid negative. Flu negative. Troponin (13) negative. Magnesium within normal limits. Comprehensive metabolic panel shows elevated BUN and creatinine at 74 and 2.6, respectively, slightly increased from baseline. Otherwise, all other labs were unremarkable. INR at 2.0 on coumadin. APTT elevated to 45. VBG: pH 7.36, PCO2 56. CBC shows Hemoglobin of 9.7. When trended, the last hemoglobin was 10.4, otherwise, unremarkable CBC. TSH is within normal limits.

IMAGING: Chest x-ray shows no acute pathology.

EKG shows complete heart block with rate of 37. No ST or T wave changes compared to previous EKG.

**Hospital course**

Patient was admitted to ICU and during the course in ICU he was initially noted to be in hypertensive urgency. He was given hydralazine and minoxidil to optimize the blood pressure with successful results. Cardiology, EP and Nephrology were consulted. He was placed on cardiac monitor, and transcutaneous temporary pacemaker pads were applied. All anti-chronotropic agents including beta blockers and nodal blocking agents were withheld. The decision was made to place a permanent pacemaker the next morning. The patient underwent permanent pacemaker placement. It was done under local IV sedation and local infiltration of bupivacaine. The procedure was tolerated well, however, shortly after return to the intensive care unit the patient experienced tachycardia 130-150s and hypotension BP 60/40. EKG showed sinus tachycardia with some nonspecific ST segment changes. He had two episodes of nonbilious, non-bloody vomiting with nausea. He denies any chest pains. A limited echo was done at that time and showed no effusion. The patient continued to have difficulty overnight with nausea, vomiting, and general complaints of feeling unwell. Serial troponins were checked and were up trending. On the physical exam, he was noted to have significant hypotension, tachycardia, and hypoxemia. He appeared mildly diaphoretic with poor skin color. His incision site on the chest looked clean with no signs of infection, swelling or hematoma. Lungs were clear to auscultation but diminished bilateral bases. Heart sounds normal without murmur, gallop, or rubs. Abdomen was soft and nontender with positive bowel sounds. No hepatosplenomegaly. Abdominal aorta normal without bruits. Chest X-ray showed bilateral pleural effusion and pulmonary vascular congestion. Comprehensive metabolic panel revealed worsening renal functions suspecting ATN. He was treated with supportive care. He also had elevated troponins and was thought to be due to an NSTEMI. The patient remained asymptomatic from this. A heparin drip was not started on the patient as his INR was 1.9 as it was still therapeutic from his home warfarin treatment. The plan was to optimize medical management. The patient had a coronary angiogram a few months ago prior to this and showed non obstructive CAD. Labs showed leukocytosis to 20,000 with slightly increased neutrophils. Aspiration pneumonia from vomiting was considered. CT chest was ordered and showed findings of consolidation and bilateral pleural effusion. Patient was started on IV vancomycin and Zosyn. He was fluid resuscitated after consulting with Nephrology. Despite volume resuscitation he continued to have low blood pressure, he was eventually started on phenylephrine drip. He was found to be acutely ill with chronic renal insufficiency. Nephrology recommended continuing IV fluids, holding all nephrotoxic agents. The patient did require supplemental oxygen up to 10 L/min. This was gradually titrated down and the patient's renal function gradually improved back to his baseline. Once he was titrated off oxygen his mentation improved, and he was more alert and oriented. High-sensitivity troponin peaked at 5,364 before down trending. He was eventually stable and transferred out of the ICU. He was subsequently placed on guideline-directed medical therapy. He continued to show improvement and eventually returned to his baseline functioning. He did have an echocardiogram done that showed a new left ventricle EF 40% to 45% with akinesis of the anterolateral and apical myocardium. Cardiologists felt the patient would be best served to follow-up for an outpatient cardiac catheterization or stress test depending on the clinical situation. He was stable on medical management for discharge home. EP also agreed with this management. The patient felt like he had improved back to his baseline self and was comfortable with the plan for discharge home with close outpatient follow-up with his nephrologist, cardiologist, and electrophysiologist. The patient followed up in 2 weeks and remained asymptomatic. A nuclear stress test was performed four weeks later and was negative for any ischemic changes.

## Discussion

We presented a case of reversible LV dysfunction which occurred immediately after administration of bupivacaine. Initial clinical presentation was atypical with features of acute coronary syndrome/NSTEMI. He had mild dyspnea, elevated troponins post procedure without any chest pains, no EKG change and very mild regional wall motion abnormality by echocardiogram.

We considered the patient as having an acute non-ST segment elevation myocardial infarction. However, there were several atypical features of acute non-ST segment elevation myocardial infarction in this case. First, the patient was admitted for symptomatic bradycardia without any chest pains or shortness of breath. His initial troponins on admission were negative. Second, the patient had nausea, vomiting; atypical symptoms occurring immediately after pacemaker placement and bupivacaine use. Third, the regional wall motion abnormality on the echocardiogram was minimal with no pericardial effusion and no EKG changes.

We also considered viral myocarditis, stress cardiomyopathy, coronary spasm, hypovolemic shock, septic shock, and adverse reaction to the bupivacaine drug as differential diagnoses. Al-

though the patient had some clinical features like those of stress cardiomyopathy, he did not show all the classic findings. Therefore, we believe that this patient developed cardiac side effects from the bupivacaine injection.

Bupivacaine is related to CNS and adverse cardiovascular effects. CNS side effects usually occur before the cardiovascular signs and symptoms. These include tongue numbness, lightheadedness, visual disturbances, and muscular twitching. More fatal side effects include convulsions, coma, and respiratory arrest. Not only does bupivacaine induce CNS toxicity, but also arrhythmia and myocardial depression due to the blocking of sodium channels in the cardiovascular system. Bupivacaine significantly decreases the maximum diastolic potential and the action potential amplitude in myocardial tissue and prolongs the ratio of the effective refractory period to action potential duration. In that mechanism, bupivacaine produces a depression of myocardial conduction and negative inotropic action.

In a review of the literature, some reports on the adverse effects of bupivacaine were found. In animal studies; hypotension, respiratory arrest, ventricular tachycardia, and ventricular fibrillation after bupivacaine administration. In the human, 12 volunteers (healthy men) received intravenous injections of bupivacaine, and they developed depression of cardiac conductivity and contractility. In addition, Coven et al.10 also reported two cases with an accelerated idioventricular rhythm during spinal anesthesia using bupivacaine for caesarean section. Furthermore, Cotileas et al.11 reported a case like ours, in which bupivacaine induced myocardial depression and pulmonary edema were described in a healthy young woman with epidural anesthesia. Although she had normal cardiac enzyme levels.

We believe that Bupivacaine can directly damage the myocardium. Sztark et al.12 demonstrated that mitochondrial adenosine triphosphate (ATP) synthesis was decreased by bupivacaine in isolated rat heart mitochondria because it acted as an un-coupler between oxygen consumption and phosphorylation of adenosine diphosphate and as an inhibitor of respiration. Consequently, the decrease in cellular ATP resulted in an increased rate of anaerobic glycolysis, which may result in the accumulation of lactic acid and inorganic phosphates from hydrolysis of phosphate esters, cumulating in reduced intracellular ph. Finally, the myocardial cell membrane is injured and intracellular molecules such as cardiac enzymes are released to the bloodstream, unless the condition is reversed. Not only does bupivacaine decrease cellular ATP from a molecular biological point of view, but it also decreases coronary blood flow and myocardial oxygen consumption in preparation of isolated perfused guinea pig heart, according to Langendorff.13 Therefore, an increased rate of anaerobic glycolysis may be accelerated, and the myocardial membrane injury may be incrementally aggravated.

## Conclusion

Based on the above data, we suggest that bupivacaine may induce direct myocardial injury and release cardiac enzymes into the bloodstream causing acute coronary syndrome-like manifestations. Clinicians should be aware of the side effects of this commonly used anesthetic.

## Declarations

### Ethics approval and consent to participate

Informed verbal and written consent were obtained from the patient. All specific identifying information regarding the patient was de-identified. This case report did not include any new or experimental treatment different from the current guidelines for the management of Atrial fibrillation and ACS, hence approval from an ethics committee was not required.

### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

### Competing interests

The authors declare that they have no conflicts of interest.

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