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Case Report

Possible Bupivacaine Induced Hepatitis Following Wide Awake, Local Anesthesia, No Tourniquet Carpal Tunnel Surgery: A Case Report

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In this case report, we present a novel occurrence of acute hepatitis 2 weeks after local bupivacaine injection for wide awake, local anesthesia, no tourniquet carpal tunnel release. Laboratory and biopsy analysis confirmed cholestatic, drug-induced hepatitis that was successfully managed with conservative treatment. With a paucity of potential bupivacaine-induced hepatitis cases reported within the literature, the importance of broad differential diagnosis, meticulous medication reconciliation, and consideration of this rare complication should not be understated by the astute hand surgeon.

In recent years, hand surgery using the WALANT (wide awake, local anesthesia, no tourniquet) technique has become increasingly common when compared to other anesthetic techniques such as intravenous regional anesthesia (IVRA)/Bier block.[1] Several studies, including those by Iqbal et al[2] and Ralte et al[3] have demonstrated equivalent functional outcomes between WALANT and IVRA. Moreover, Ayhan et al[4] compared 24 patients with bilateral carpal tunnel syndrome (CTS), with one side treated under WALANT and the other under IVRA. The study demonstrated similar pain ratings in the two treatment arms, but demonstrated significantly better intraoperative patient experience and duration of anesthesia in the WALANT group.[4] WALANT surgery still poses risk of complications; notably, those associated with the use of local anesthetics, such as lidocaine and bupivacaine. Local anesthetic toxicity can include perioral numbness, metallic taste, muscle twitching, and anxiety, whereas more serious complications can include cardiotoxicity or neurologic issues. However, few reports of bupivacaine-induced hepatic injury exist, with none documented in the hand surgery literature. This case report presents the novel occurrence of possible bupivacaine-induced hepatitis following WALANT carpal tunnel release (CTR). Through this presentation, we would like to aid clinicians in identifying local anesthesia as a potential etiology of acute hepatitis following WALANT hand surgery. Written informed consent was obtained from this patient.

Case Report

An 80-year-old right-handed man presented to the University of Massachusetts orthopedic hand clinic with a chief complaint of constant bilateral hand pain and paresthesias for 8 months. His symptoms had progressed in severity over time with his left side worse than right, causing frequent night-time awakenings. His numbness was localized to the distal tips of his left thumb, index, middle, and ring fingers, and he complained of stereognosis and difficulty picking up small objects.

At the time of presentation, a brief medical history was obtained that was notable for coronary artery disease and previous myocardial infarction status after stent placement, hyperlipidemia, hypothyroidism, shingles, gastroesophageal reflux, and previous smoking history. Physical examination, EMG, and nerve conduction study findings were consistent with CTS. The patient thereafter consented to an open left CTR under WALANT.

The surgery was performed in an outpatient ambulatory surgical center by the senior author (MDJ), a hand fellowship trained surgeon, using WALANT techniques. Using 8 mL of 1% lidocaine with epinephrine buffered with 2 mL of sodium bicarbonate on a 25 G needle, a wrist block in line with the planned incision site was performed. A standard 2 cm miniopen incision in line with the

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Table 1
The Patient's Laboratory Values Presented in Relation to the Procedure*

Lab value	Before surgery	POD11	POD16	POD19	POD59
AST	25	97	74	70	39
ALT	37	144	108	69	35
T bili	0.5	6.2	12.4	16.3	1.2
D bili		5.0		15.2	0.7
Alk Phos	70	203			123

AIH, autoimmune hepatitis; ALT, alanine transaminase; AST, aspartate aminotransferase; CMV, cytomegalovirus; D bili, direct bilirubin; EBV, Epstein–Barr virus; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis; POD, postoperative day; T bili, total bilirubin.
* PSC/PBC/AIH antibody testing; EVB, CMV all negative.

radial border of the ring finger and Kaplan's cardinal line was used to release the carpal tunnel. The wounds were closed in an interrupted fashion using nylon sutures, and the wound edges and subcutaneous tissues were infiltrated with less than 10 mL of 0.5% bupivacaine. In the immediate postoperative period, he recovered well and took acetaminophen and ibuprofen for pain relief.

Two weeks after surgery, the patient presented with dark urine and painless jaundice. He reported chills, nausea without emesis, and postprandial abdominal pain. He was noted to have hyperbilirubinemia and transaminitis; computed tomography (CT) was negative for obstructive pathology. He was then discharged and referred for gastroenterology consultation. On postoperative day 16, he represented to an outside hospital with persistent symptoms of jaundice, dark urine, and pale stools. Gastroenterology recommended cholestyramine and careful medication reconciliation. Right upper quadrant ultrasound and magnetic retrograde cholangiopancreatography (MRCP) were obtained without concerning findings. Histological analysis of an ultrasound-guided liver biopsy demonstrated widespread canalicular and focal ductular cholestasis, mixed inflammation of the portal tracts and lobular parenchyma with feathery degeneration of hepatocytes, and patchy neutrophilic infiltration, consistent with cholestatic, drug-induced liver injury. Gastroenterology recommended discharge given clinical improvement with conservative measures. He was re-evaluated 6 weeks after surgery by gastroenterology. All pertinent laboratory values are included in Table 1. At this time, the patient revealed additional notable medical history. The patient reported prior exposure to viral hepatitis A, which resolved spontaneously. He reported a family history of undifferentiated cirrhosis, causing the death of two brothers. Following a right shoulder arthroscopy (30 years prior to presentation) and a left shoulder arthroscopy (20 years prior to presentation), the patient experienced jaundice and fatigue thought to be a recurrence of his hepatitis secondary to general anesthesia and postoperative oxycodone-acetaminophen medication, respectively. In both instances, his symptoms self-resolved without further sequelae. In both cases, he was injected with 0.25% bupivacaine with morphine, offering an additional explanation of his hepatitis. Given his biopsy results, prior history of hepatitis after local anesthesia with bupivacaine, and his marked improvement in his symptoms and laboratory findings, the gastroenterology team deemed bupivacaine-induced liver injury the most likely etiology of this presentation. He was recommended to follow-up for FibroScan in 6 months and to fully return to normal activity.

Discussion

This case report presents a patient who developed acute hepatitis and hyperbilirubinemia in the postoperative period following CTR with use of bupivacaine. This scenario has not been previously described in the existing literature. There are general symptoms commonly associated with local anesthetic toxicity, ranging from perioral numbness, metallic taste, muscle twitching, and anxiety to more severe neurologic or cardiac complications. However, each local anesthetic carries its own side effect profile, with each drug's individual pK_a, lipophilicity, and protein binding determining the pharmacokinetics and toxicity. Bupivacaine has a pK_a of 8.1, high lipophilicity, and high protein binding, which gives it slow onset time, high potency, and long duration of action.[5] It is also associated with cardiotoxicity and methemoglobinemia. Its action inhibits sodium, potassium, and voltage-gated calcium channels impacting the functioning of ventricular myocytes, decreasing cardiac contractility, and increasing the risk of cardiac toxicity and arrhythmias.[6] Risk for toxicity is considered dose dependent, with the recommendation to inject the minimum volume required for desired analgesia. Toxicity risk is also affected by the technique used. Although the use of tourniquets has been considered protective against some systemic toxicities of local anesthetics, there does not appear to be a notable difference in complication rates related to anesthetic toxicity between WALANT procedures and those using tourniquets.[1]

There is limited evidence from case reports of bupivacaine-induced hepatic injury. One case series by Chintamaneni et al[7] reported on three patients without previous liver disease who underwent herniorrhaphy with bupivacaine infusion catheter, who developed hepatitis symptoms within 1 month. Their symptoms included jaundice, anorexia, fatigue, pruritus, and dark urine. Each patient had conjugated hyperbilirubinemia and considerable transaminitis with alanine transaminase (ALT) predominance and underwent right upper quadrant ultrasound and MRCP. One patient underwent biopsy demonstrating mild portal and periportal fibrosis, consistent with cholestatic adverse drug reaction. All three improved with supportive care. Chowdhury et al[8] described a 68-year-old woman with no prior liver disease who developed fatigue, anorexia, and nausea 2 weeks after bupivacaine catheter placement for arthroscopic shoulder surgery. She had elevated total bilirubin levels of 10.2 mg/dL with alkaline phosphatase, ALT, and aspartate aminotransferase levels of 924 U/L, 429 U/L, and 279 U/L, respectively. CT, ultrasound, MRCP, and portal vein doppler were negative. Additional work-up including acetaminophen and ethanol levels, SARS-CoV2, hepatitis panel, Epstein–Barr virus antigen, and urine toxicology were negative. Her symptoms resolved with conservative management. This case echoes our patient's prior case of hepatitis following shoulder surgery. Slone et al[9] discussed a 51-year-old man with no liver disease presenting with similar symptoms 2 weeks after hemorrhoidectomy with liposomal bupivacaine injection, with aspartate aminotransferase levels 173 U/L, ALT 651 U/L, alkaline phosphatase 353 U/L, total bilirubin 7.3 mg/dL, and negative MRCP. CT-guided liver biopsy showed "centrilobular cholestasis with associated lobular necroinflammatory activity suggestive of drug-induced liver injury." His symptoms also improved with conservative management.

As evidenced here, drug-induced hepatitis secondary to bupivacaine is a rare, but documented complication of this local anesthetic. The physiology behind bupivacaine-induced liver injury remains unclear. Yokoyama et al[10] theorizes that injury can be because of allergic reaction or a metabolic abnormality. Our patient had no signs consistent with allergy; thus, a metabolic abnormality is the more likely cause. However, in all the above cases, bupivacaine was administered using an infusion catheter or as a local injection of liposomal bupivacaine. The present case report is the first to describe the possibility of nonliposomal bupivacaine-induced hepatic injury secondary to local injection, especially in the hand surgery setting.

Although the previously documented case reports included patients without prior liver disease, our patient's history of hepatitis may have played a role in his response to the medication. Bupivacaine, an amide anesthetic, is metabolized to its inactive

form by the liver. If this patient had underlying hepatic dysfunction, he may have been at increased risk for developing toxicity from a normally well tolerated dose of bupivacaine. Although not a factor to this case, underlying renal impairment is another risk factor for toxicity.[11] Patients with cardiac dysfunction are also at increased risk for toxicity as they may be more sensitive to myocardial depression and arrythmias. In addition, decreased cardiac function that limits hepatic and renal perfusion may contribute to slower metabolism and clearance. However, even with these conditions, a local anesthetic dose adjustment is not usually necessary.[12] Given the frequency with which hand surgeons use local anesthetic injections, it is important to be aware of this rare possible complication and potential associated risk factors.

Conflicts of Interest

No benefits in any form have been received or will be received related directly to this article.

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