

Unrecognized Postoperative Opioid-Induced Movement Disorder: A Case Report

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A 22-year-old man, with a medical history significant for posttraumatic stress disorder and chronic pain, underwent ankle surgery at the United States Naval Hospital, Yokosuka, Japan. His immediate postoperative course was complicated by episodic muscle rigidity, necessitating admission for diagnostic evaluation. The differential was necessarily broad and included local anesthetic toxicity, medication mediated effect, seizures, serotonin syndrome, and malignant hyperthermia. Cultural and systemic differences in patient care delivery at a Japanese hospital helped to elucidate the mechanism. This case highlights cultural differences in pain management and navigates the differential of an acute onset movement disorder in the immediate postoperative period. (A&A Practice. 2021;15:e01448.)

GLOSSARY

OIMD = opioid-induced movement disorder

The presentation of an opioid-induced movement disorder (OIMD) varies and is associated with low- and high-dose opioid administration in acute and chronic care settings.¹⁻⁴ Some studies suggest an etiology associated with metabolite accumulation, while others indicate a direct result of opioid or serotonergic receptor-mediated activity in the setting of polypharmacy.^{1,2} Not surprising is that the pathophysiology of OIMD is equally complex and not fully understood. The variable presentation, combined with variable timing, likely contributes to the underreporting of the disorder. As such, the incidence and prevalence are not well described. The severity of postoperative movement disorders varies from subacute to life-threatening. Therefore, early identification of the etiology and prompt intervention are crucial. Cases of opioid-induced chest rigidity with ventilatory compromise requiring naloxone administration have been reported. However, the disorganized movement in a patient with adequate spontaneous ventilation and normal cognition may not prompt consideration of an opioid trigger. Here, we characterize the immediate postoperative

occurrence of an OIMD and discuss the differential diagnosis. We are incredibly grateful to the patient for providing Health Insurance Portability and Accountability Act authorization to publish this case report successfully.

REPORT

A 22-year-old man (176 cm; 77 kg), with a medical history significant for posttraumatic stress disorder and chronic back pain, presented to the Ambulatory Procedures Unit at the United States Naval Hospital, Yokosuka, Japan, for ankle surgery. He denied routine medication use, except occasional tramadol for his back pain and sertraline for post-traumatic stress disorder. He was a nonsmoker and reported no alcohol or recreational drug use. The patient underwent an unremarkable ankle surgery with general endotracheal anesthesia. He was induced with propofol, lidocaine, fentanyl, and rocuronium. Anesthesia was maintained with sevoflurane using an oxygen/air mixture. Additional doses of fentanyl were administered (total 125 µg), and common peroneal block with liposomal bupivacaine was performed using a landmark technique at the end of surgery. He received cefazolin, ondansetron, ketorolac, and acetaminophen. Shortly after arrival in the postanesthesia care unit, the patient complained of increasing pain despite the administration of fentanyl (250 µg), ketamine (15 mg), and morphine (4 mg). The surgeon was notified and returned to the postanesthesia care unit to evaluate the patient. In the setting of increasing patient agitation, pain, and an equivocal sensory physical examination, the surgeon elected to administer an additional 20 mL of 0.25% bupivacaine near the common peroneal nerve using a landmark technique. Fifteen minutes after the fentanyl, morphine, ketamine, and repeat peripheral nerve block administration, he reported minimal pain relief with a numeric rating scale score of 6/10. He soon developed episodic involuntary whole-body muscle contractions that manifested in a relapsing-remitting fashion with dystonic features. These muscle contractions persisted for 20 to 40 seconds, were associated with tachycardia, and occurred every 5 minutes. In between episodes, his muscles

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were relaxed, and he appeared to breathe normally with pulse oximetry of 95% to 98% and a ventilatory rate of 13 to 15 breaths per minute. It is noteworthy that he had normal neurocognitive function during the episodes. Laboratory evaluation was unremarkable (normal glucose, basic metabolic profile, calcium, and magnesium). Diazepam (5 mg) was administered with little effect. Ultimately, the recurrent nature of his muscle contractions resulted in a desaturation event, necessitating consideration of intubation. After administration of 100 mg propofol, mask ventilation was performed, and the muscle contractions abated. An arterial blood gas obtained at the time was unremarkable. He was subsequently placed on a dexmedetomidine infusion (titrated to 0.8 µg/kg/h) and transferred to the intensive care unit for further monitoring. Within 2 hours of intensive care unit admission, the patient developed hypotension and bradycardia, which resolved after the dexmedetomidine infusion was stopped. Four hours after cessation of the dexmedetomidine, he had staring spells and visual hallucinations. He was then transferred to a local Japanese hospital for magnetic resonance imaging and neurologic consultation. With limited resources and specialty care, overseas US military hospitals often collaborate with host nation hospitals for optimum patient care. Despite ongoing postoperative pain, the patient did not receive any opioids at the Japanese hospital, secondary to cultural differences. He was instead treated with nonsteroidal antiinflammatory medications and acetaminophen. His neurologic examination was normal, and magnetic resonance imaging was unremarkable. He had no further episodes at the Japanese hospital. He was diagnosed with pseudo-seizures and transferred back to our facility on postoperative day 2. Shortly after his return, he was administered 0.25 mg hydromorphone intravenously for a numeric rating scale score of 8. Within 2 minutes of administration, he experienced a single self-resolving episode of whole-body muscle contraction. Additional opioid therapy was discontinued. In the subsequent 24-hour period, he had no further episodes. His pain improved over time with nonsteroidal antiinflammatory medication and acetaminophen as needed. He had an unremarkable electroencephalogram on postoperative day 3, and the patient was discharged to home on postoperative day 4 without the need for oral analgesia. During his 3-week follow-up visit, he reported no recurrence of symptoms.

DISCUSSION

Witnessing whole-body muscle contractions in the postoperative setting is unsettling. Providers must act quickly to navigate the differential of critical etiologies. A nonexhaustive differential diagnosis includes several life-threatening pathologies: local anesthetic systemic toxicity, serotonin syndrome, neuroleptic malignant syndrome, malignant hyperthermia, ketamine-mediated seizure activity, conversion disorder (pseudo-seizures), and OIMD.

As the patient was able to answer questions during these episodes, it was deemed unlikely to be a seizure, ketamine-mediated seizure, or neuroleptic malignant syndrome. The patient denied symptoms associated with local anesthetic toxicity, including tinnitus, metallic taste, circumoral or tongue numbness, nausea, or confusion. The patient was afebrile and not tachycardic or hypertensive between episodes.

Serotonin syndrome was considered, given that tramadol has direct serotonin releasing effect and inhibits serotonin reuptake via serotonin transporter inhibition.⁵ Selective serotonin reuptake inhibitors are known to increase the serotonergic activity of tramadol by inhibiting cytochrome P450 2D6.⁶ In addition, ketamine acts on the opioid receptor and enhances opioid-induced signaling.⁷ Opioids are associated with serotonin reuptake inhibition and possess direct serotonergic activity.⁸ Specifically, fentanyl produces an efflux of serotonin and binds to 5-hydroxytryptamine 1A and 5-hydroxytryptamine 2A receptors.⁸ In our case, occasional use of tramadol and a selective serotonin reuptake inhibitor may have resulted in increased serotonin concentrations. The successive administration of multiple serotonergic agents (ie, fentanyl, ondansetron, ketamine) may have precipitated the manifestation of serotonergic neuromuscular hyperactivity without serotonin syndrome.

As the patient demonstrated immediate recurrence of his symptoms upon opioid challenge, OIMD seems a more likely cause of his condition. The pathophysiology of OIMD is complex and not fully understood. Some studies suggest that abnormal patient movement is an indirect result of morphine-3-glucuronide or hydromorphone-3-glucuronide accumulation in the plasma.¹ Harm reduction literature from North America's first legal supervised injection site observed that muscle rigidity and dyskinesia are among the most common atypical presentations for opioid overdose.⁹ Opioid receptor antagonists have been reported as a potential treatment for L-3, 4-dihydroxyphenylalanine-induced dyskinesia, a significant complication in the treatment of Parkinson disease.¹⁰ Activation of the mu-opioid receptors has been shown to block the activation of and reduce the production of cyclic adenosine monophosphate in spiny projection neurons located in the basal ganglia responsible for initiating and controlling movements.¹¹ Potentiation of opioid-mediated signaling by ketamine may also have contributed in this case.⁷ Since an OIMD was not considered in the immediate postoperative period, naloxone therapy was not considered to reverse the muscle contractions. It is possible that this patient had an underlying genetic predisposition unmasked by the concomitant serotonergic activity and opioid administration. We are unaware of any pharmacogenetic evaluation that can help identify such a predisposition. Genetic evaluation of pathways where the metabolism of fentanyl and hydromorphone overlap is reasonable to consider given that both medications were given immediately before muscle contractions.

The unintended interlude from opioid therapy sheds light on striking cultural differences. Opioid use is less common in Japan than in the United States, especially for acute pain.¹² In a study by Onishi et al,¹² Japanese respondents reported far fewer opioid prescriptions than United States respondents for both acute (49.4% vs 97.0%) and chronic pain (63.7% vs 90.9%; $P < .001$ for both). As indicated in the Japan Society of Pain Clinicians guidelines, opioid therapies are mostly restricted to cancer patients.¹³ In addition, Japan has one of the lowest pain-free labor and delivery rates among developed countries. According to a representative study by the Japanese health ministry, only 6.1% of Japanese women (36,849 of 608,450) are administered epidural analgesia during delivery, compared with 73.1% (1,920,368 of 2,625,950) in the United States.^{14,15} Our clinical collaboration

with Japanese physicians revealed this stark difference in opioid prescription patterns between the 2 countries and helped to reveal a likely etiology for this case.

In conclusion, we have presented and discussed the etiology of an acute onset movement disorder. We identified an OIMD as the likely etiology of our patient's symptoms. Providers should consider OIMD as an etiology for movement disorders in the postoperative setting and consider treatment with naloxone even in the absence of ventilatory compromise. ■■

DISCLOSURES

Name: Kumiko Chino, MD.

Contribution: This author helped present the idea, develop the theory, and write the case report.

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Contribution: This author supported and supervised the case report's possible etiology and edited the writing of the case report.

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