

CASE IN POINT

Rhabdomyolysis Occurring After Use of Cocaine Contaminated With Fentanyl Causing Bilateral Brachial Plexopathy

Lauren Dobrie^a; Talin Handa^a; Igor Sirotkin, MD^b; Angel Cruz, MD^b; Demetrios Konstas, MD^b; and Esther Baldinger, MD^b

Background: Rhabdomyolysis is caused by muscle overuse, trauma, prolonged immobilization, drugs, or toxins. As rhabdomyolysis progresses, swelling and edema can compress surrounding structures. Few cases of the phenomenon occurring as a sequela of substance use have been described.

Case Presentation: We present a 68-year-old male patient with rhabdomyolysis following use of crack cocaine contaminated with fentanyl. The patient had 0/5 strength bilaterally and bilateral absent reflexes in the upper extremities. Sensation was markedly decreased, as he was unable to feel temperature,

pinprick sensation, or general touch. Creatine phosphokinase level was elevated at 21,292 IU/L. On magnetic resonance imaging, there was abnormal signal in the lower neck bilaterally. It is presumed that muscular edema resulted in partial narrowing of the thoracic outlet bilaterally with corresponding mass effect on the traversing brachial plexus.

Conclusions: This is the seventh case of brachial plexopathy secondary to rhabdomyolysis precipitated by opioid use that has been reported in the literature. Prospective studies should examine treatment for this condition.

The brachial plexus is a group of interwoven nerves arising from the cervical spinal cord and coursing through the neck, shoulder, and axilla with terminal branches extending to the distal arm.¹ Disorders of the brachial plexus are more rare than other isolated peripheral nerve disorders, trauma being the most common etiology.¹ Traction, neoplasms, radiation exposure, external compression, and inflammatory processes, such as Parsonage-Turner syndrome, have also been described as less common etiologies.²

Rhabdomyolysis, a condition in which muscle breakdown occurs, is an uncommon and perhaps underrecognized cause of brachial plexopathy. Rhabdomyolysis is often caused by muscle overuse, trauma, prolonged immobilization, drugs, or toxins. Substances indicated as precipitating factors include alcohol, opioids, cocaine, and amphetamines.^{3,4} As rhabdomyolysis progresses, swelling and edema can compress surrounding structures. Therefore, in cases of rhabdomyolysis involving the muscles of the neck and shoulder girdle, external compression of the brachial plexus can potentially cause brachial plexopathy. Rare cases of this phenomenon occurring as a sequela of substance use have been described.^{1,5-9} Few cases have been reported in the literature.

The following case report describes a patient who experienced rhabdomyolysis fol-

lowing use of crack cocaine contaminated with fentanyl, which subsequently caused bilateral brachial plexopathy.

CASE PRESENTATION

A 68-year-old male patient with a history of polysubstance use disorder presented to the emergency department with complete loss of sensory and motor function of both arms. He had fallen asleep on his couch the previous evening with his arms crossed over his chest in the prone position. He reported using crack cocaine earlier that day that was later discovered to be contaminated with fentanyl. The patient reported using no other substances, including alcohol. When he woke about 7 hours later, the patient's arms were completely paralyzed.

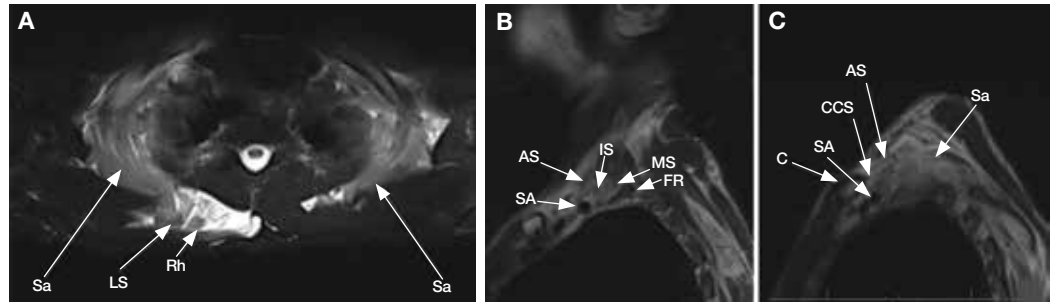
On admission, the patient presented with an agitated mental status. The patient presented with 0/5 strength bilaterally in the upper extremities (UEs) accompanied by numbness and tingling. Radial pulses were palpable in both arms. All UE reflexes were absent, but patellar reflex was intact bilaterally. On hospital day 2, the patient was awake, alert, and oriented to person, place, and time and could provide a full history. The patient's cranial nerves were intact with shoulder shrug testing mildly weak at 4/5 strength. The patient had 0/5 strength bilaterally and bilateral absent reflexes in the UEs.

Author affiliations can be found at the end of this article.

Correspondence:

Lauren Dobrie
(laurendobrie@knights.ucf.edu)

Fed Pract. 2022;39(6).
Published online June 16.
doi:10.12788/fp.0280

FIGURE Magnetic Resonance Images

Abbreviations: AS, anterior scalene; C, clavicle; CCS, costoclavicular space; FR, first rib; IS, interscalene space; LS, levator scapulae; MRI, magnetic resonance image; MS, scalene muscles; Rh, rhomboid; SA, subclavian artery; Sa, serratus anterior. A, Axial MRI wide field of view cervical/upper thoracic spine demonstrating abnormal increased signal in the shoulder girdle musculature greater on the right; arrows indicate Sa, LS, and Rh muscles; B, Sagittal T2 MRI of the brachial plexus demonstrating abnormal increased signal involving the right AS and MS; C, Sagittal T2 MRI brachial plexus demonstrating abnormal increased signal involving the right Sa and AS.

Sensation was markedly decreased, as he was unable to feel temperature, pinprick sensation, or general touch in both UEs. Coordination of the UEs could not be tested due to weakness. No response could be elicited from the median or ulnar nerve bilaterally on somatosensory evoked potential study. The lower extremities were intact to movement, sensation, coordination, and reflexes.

Serum electrolytes and glucose levels were normal. The creatine phosphokinase (CPK) level was elevated at 21,292 IU/L. Creatinine and blood urea nitrogen levels were elevated at 1.7 mg/dL and 32 mg/dL, respectively. Serum B12, thyroid-stimulating hormone, and hemoglobin A_{1c} levels were normal. Urine drug screen was positive for cocaine metabolite and fentanyl but negative for other substances, including alcohol. The patient stated emphatically he had only used crack cocaine, so it was presumed that the crack cocaine had been contaminated with fentanyl.

Computed tomography (CT) of the head was normal and revealed no acute intracranial process. Further imaging studies included magnetic resonance imaging (MRI) of the brain and spinal cord and subsequently of the brachial plexus. There was no evidence of a spinal cord or intracranial lesion. However, there was abnormal signal in the lower neck greater on the right side suggesting an edematous inflammatory process involving part of the shoulder girdle musculature. This included the trapezius, levator scapula,

rhomboid, and serratus anterior muscles, as well as prominent fluid signal in the right supraclavicular fossa. The abnormal signal was less prominent on the left and involved the serratus anterior muscle. To a lesser extent, there also was involvement of the distal attachment site of the anterior and middle scalene muscles on the right greater than the left. It is presumed that muscular edema resulted in partial narrowing of the thoracic outlet bilaterally with corresponding mass effect on the traversing brachial plexus, resulting in the patient's symptoms (Figure).

Due to the absence of evidence of spinal cord injury, presence of normal motor and sensory function of the lower extremities, an elevated CPK level, signal hyperintensities of the muscles of the shoulder girdle, and the patient's history, the leading diagnosis at this time was brachial plexopathy secondary to focal rhabdomyolysis.

Over the next week, the patient regained some motor function of the left hand and some sensory function bilaterally. At 8 weeks postadmission, a nerve conduction study showed prolonged latencies in the median and ulnar nerves bilaterally. The following week, the patient reported pain in both shoulders (left greater than the right) as well as weakness of shoulder movement on the left greater than the right. There was pain in the right arm throughout. On examination, there was improved function of the arms distal to the elbow, which was better on the right side despite the associated pain (Table).

TABLE Strength, Sensation, and Reflex Progression

Reflex Tests	At Admission		10 d Postadmission		9 wk Postadmission	
	Right	Left	Right	Left	Right	Left
Shoulder abduction	0	0	1	1+	4-	3
Elbow flexion	0	0	3	3+	4-	3
Wrist extension	0	0	3	3+	4	4
Elbow extension	0	0	3	3+	4-	3+
Finger flexion	0	0	3	3+	4	4-
Finger abduction	0	0	3	3+	4	4-
Sensation, pinprick and light touch	Absent in C5-T1		Decreased (< 25%) in C5-T1		Decreased (< 50% sensation) in C6; hypersensitivity in C5 and T1 on right arm; decreased sensation in C7 on left arm	
Deep tendon reflexes	Absent		Not assessed		1+ in biceps; all other reflexes absent	
Tone	Flaccid		Reduced		Reduced	

There was atrophy of the left scapular muscles, hypothenar eminence, and deltoid muscle. There was weakness of the left triceps, with slight fourth and fifth finger flexion. The patient was unable to elevate or abduct the left shoulder but could elevate the right shoulder up to 45°. Sensation was decreased over the right outer arm and left posterior upper arm, with hypersensitivity in the right medial upper and lower arm. Deep tendon reflexes were absent in the upper arm aside from the biceps reflex (1+). All reflexes of the lower extremities were normal. It is interesting to note the relative greater improvement on the right despite the edema found on initial imaging being more prominent on the right.

DISCUSSION

Rhabdomyolysis is a condition defined by myocyte necrosis that results in release of cellular contents and local edema. Inciting events may be traumatic, metabolic, ischemic, or substance induced. Common substances indicated include cocaine, amphetamines, acetaminophen, opioids, and alcohol.¹⁰ It classically presents with muscle pain and a marked elevation in serum CPK level, but other metabolic disturbances, acute kidney injury, or toxic hepatitis may

also occur. A more uncommon sequela of rhabdomyolysis is plexopathy caused by edematous swelling and compression of the surrounding structures.

Rare cases of brachial plexopathy caused by rhabdomyolysis following substance use have been described. In many of these cases, rhabdomyolysis occurred after alcohol use with or without concurrent use of prescription opioids or heroin.⁷⁻⁹ One case following use of 3,4-methylenedioxy-N-methylamptamine (MDMA) and marijuana use was reported.¹ Another case of concurrent brachial plexopathy and Horner syndrome in a 29-year-old male patient following ingestion of alcohol and opioids has also been described.⁵ The rate of occurrence of this phenomenon in the general population is unknown.

In the case of our patient, cocaine metabolite and fentanyl were the only substances found on urine drug screen. The patient had used crack cocaine that had presumably been contaminated with fentanyl, a high potency synthetic opioid. The rate of fentanyl contamination of street drugs is variable. It is a subject of high concern, considering the increasing rates of synthetic opioid overdose-related deaths. According to the US Centers for Disease Control and Prevention, synthetic opioids

have played a role in the increasing rates of cocaine-related overdose deaths. Conversely, in more than half of all overdose deaths involving fentanyl derivatives, patients also tested positive for cocaine, methamphetamine, or heroin. In recent studies conducted in various cities in the northeastern US, rates of fentanyl metabolite detection were much higher than rates of reported fentanyl use.¹¹ Cases of crack cocaine contamination with fentanyl derivatives have been reported in Canada and Washington.¹²

The pathophysiology of rhabdomyolysis caused by substance use has not been definitively identified, but it is hypothesized that the cause is 2-fold. The first insult is the direct toxicity of the substances to myocytes.^{8,9} The second factor is prolonged immobilization in a position that compresses the affected musculature and blood supply, causing both mechanical stress and ischemia to the muscles and brachial plexus. This prolonged immobilization can frequently follow use of substances, such as alcohol or opioids.⁹ Cases have been reported wherein rhabdomyolysis causing brachial plexopathy occurred despite relatively normal positioning of the arms and shoulders during sleep.⁹ In our case, the patient had fallen asleep with his arms crossed over his chest in the prone position with his head turned, though he could not recall to which side. Although he stated that he had slept in this position regularly, the effects of fentanyl may have prevented the patient from waking to adjust his posture. This position had potential to compress the musculature of the neck and shoulders and restrict blood flow, resulting in the focal rhabdomyolysis seen in this patient. In theory, the position could also cause a stretch injury of the brachial plexus, although a pure stretch injury would more likely present unilaterally and without evidence of rhabdomyolysis.

Chronic ethanol use may have been a major contributor by both sensitizing the muscles to toxicity of other substances and induction of CYP450 enzymes that are normally responsible for metabolizing other drugs.⁸ Alcohol also inhibits gluconeogenesis and leads to hyperpolarization of myocytes, further contributing to their susceptibility to

damage.⁹ Our patient had a prior history of alcohol use years before this event, but not at the time of this event.

Our patient had other known risk factors for rhabdomyolysis, including his long-term statin therapy, but it is unclear whether these were contributing factors in his case.¹⁰ Of the medications that are known to cause rhabdomyolysis, statins are among the most commonly described, although the mechanism through which this process occurs is not clear. A case of rhabdomyolysis following use of cocaine and heroin in a patient on long-standing statin therapy has been described.¹³ Our review of the literature found no cases of statin-induced rhabdomyolysis associated with brachial plexopathy. It is possible that concurrent statin therapy has an additive effect to other substances in inducing rhabdomyolysis.

Parsonage-Turner syndrome, also known as neuralgic amyotrophy, should also be included in the differential diagnosis. While there have been multiple etiologies proposed for Parsonage-Turner syndrome, it is generally thought to begin as a primary inflammatory process targeting the brachial plexus. One case report describes Parsonage-Turner syndrome progressing to secondary rhabdomyolysis.⁶ In this case, no primary etiology was identified, so the Parsonage-Turner syndrome diagnosis was made with secondary rhabdomyolysis.⁶ We believe it is possible that this case and others may have been misdiagnosed as Parsonage-Turner syndrome.

Aside from physical rehabilitation programs, cases of plexopathy secondary to rhabdomyolysis similar to our patient have largely been treated with supportive therapy and symptom management. Pain management was the primary goal in this patient, which was achieved with moderate success using a combination of muscle relaxants, antiepileptics, tramadol, and serotonin-norepinephrine reuptake inhibitors. Some surgical approaches have been reported in the literature. One case of rhabdomyolysis of the shoulder girdle causing a similar process benefitted from fasciotomy and surgical decompression.⁷ This patient had a complete recovery of all motor functions aside from shoulder abduction at 8 weeks postoperation, but neuropathic

pain persisted in both arms. It is possible our patient may have benefitted from a similar treatment. Further research is necessary to determine the utility of this type of procedure when treating such cases.

CONCLUSIONS

This case report adds to the literature describing focal rhabdomyolysis causing secondary bilateral brachial plexopathy after substance use. Further research is needed to establish a definitive pathophysiology as well as treatment guidelines. Evidence-based treatment could mean better outcomes and quicker recoveries for future patients with this condition.

Author affiliations

^aUniversity of Central Florida College of Medicine, Orlando

^bC.W. Bill Young Department of Veterans Affairs Medical Center, Bay Pines, Florida

Author disclosures

The authors report no actual or potential conflicts of interest or outside sources of funding with regard to this article.

Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of *Federal Practitioner*, Frontline Medical Communications Inc., the US Government, or any of its agencies. This article may discuss unlabeled or investigational use of certain drugs. Please review the complete prescribing information for specific drugs or drug combinations—including indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.

Ethics and consent

Informed consent was obtained from the patient in the presence of a witness. Patient identifiers were removed to protect the patient's identity.

References

- Eker Büyüksireci D, Polat M, Zinnuroğlu M, Cengiz B, Kaymak Karataş GK. Bilateral pan-plexus lesion after substance use: A case report. *Turk J Phys Med Rehabil*. 2019;65(4):411-414. doi:10.5606/tftrd.2019.3157
- Rubin DI. Brachial and lumbosacral plexopathies: a review. *Clin Neurophysiol Pract*. 2020;5:173-193. doi:10.1016/j.cnp.2020.07.005
- Oshima Y. Characteristics of drug-associated rhabdomyolysis: analysis of 8,610 cases reported to the US Food and Drug Administration. *Intern Med*. 2011;50(8):845-853. doi:10.2169/internalmedicine.50.4484
- Waldman W, Kabata PM, Dines AM, et al. Rhabdomyolysis related to acute recreational drug toxicity—a euro-den study. *PLoS One*. 2021;16(3):e0246297. doi:10.1371/journal.pone.0246297
- Lee SC, Geannette C, Wolfe SW, Feinberg JH, Sneag DB. Rhabdomyolysis resulting in concurrent Horner's syndrome and brachial plexopathy: a case report. *Skeletal Radiology*. 2017;46(8):1131-1136. doi:10.1007/s00256-017-2634-5
- Goetsch MR, Shen J, Jones JA, Memon A, Chatham W. Neuralgic amyotrophy presenting with multifocal myonecrosis and rhabdomyolysis. *Cureus*. 2020;12(3):e7382. doi:10.7759/cureus.7382
- Tonetti DA, Tarkin IS, Bandi K, Moosy JJ. Complete bilateral brachial plexus injury from rhabdomyolysis and compartment syndrome: surgical case report. *Oper Neurosurg (Hagerstown)*. 2019;17(2):E68-e72. doi:10.1093/ons/opy289
- Riggs JE, Schochet SS Jr, Hogg JP. Focal rhabdomyolysis and brachial plexopathy: an association with heroin and chronic ethanol use. *Mil Med*. 1999;164(3):228-229.
- Maddison P. Acute rhabdomyolysis and brachial plexopathy following alcohol ingestion. *Muscle Nerve*. 2002;25(2):283-285. doi:10.1002/mus.10021.abs
- Giannoglou GD, Chatzizisis YS, Misirli G. The syndrome of rhabdomyolysis: pathophysiology and diagnosis. *Eur J Intern Med*. 2007;18(2):90-100. doi:10.1016/j.ejim.2006.09.020
- Meacham MC, Lynch KL, Coffin PO, Wade A, Wheeler E, Riley ED. Addressing overdose risk among unstably housed women in San Francisco, California: an examination of potential fentanyl contamination of multiple substances. *Harm Reduct J*. 2020;17(1). doi:10.1186/s12954-020-00361-8
- Klar SA, Brodtkin E, Gibson E, et al. Notes from the field: fentanyl-fentanyl overdose events caused by smoking contaminated crack cocaine - British Columbia, Canada, July 15-18, 2016. *MMWR Morb Mortal Wkly Rep*. 2016;65(37):1015-1016. doi:10.15585/mmwr.mm6537a6
- Mitarittono M, Lupo M, Greco I, Mazza A, Cervellin G. Severe rhabdomyolysis induced by co-administration of cocaine and heroin in a 45 years old man treated with rosuvastatin: a case report. *Acta Biomed*. 2021;92(S1):e2021089. doi:10.23750/abm.v92iS1.8858