



Contents lists available at ScienceDirect

Journal of Hand Surgery Global Online

journal homepage: www.JHSGO.org

Case Report

Isolated Compartment Syndrome of the Hand After Intravenous Doxycycline Infiltration Injury

Abigail R. Tirrell, BS,^{*} Manas Nigam, MD,[†] Rex W. Hung, MD[†]^{*} Georgetown University School of Medicine, Washington, DC[†] Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC

ARTICLE INFO

Article history:

Received for publication July 10, 2021

Accepted in revised form December 8, 2021

Available online January 10, 2022

Key words:

Compartment syndrome

COVID-19

Doxycycline

Hand surgery

Isolated compartment syndrome of the hand, although uncommon, can lead to considerable functional deficits if not treated promptly. The most common etiologies are related to trauma, burns, or electric injuries; however, some cases have been reported after intravenous infiltration events, particularly rapid intravenous contrast injection. In this case report, we describe the development of compartment syndrome in the hand of a critically ill patient with COVID-19 pneumonia and sepsis 16 days after doxycycline infiltration injury. She presented with worsening pain, swelling, bullous eruption, and intrinsic minus hand posturing. Emergent surgical release of intrinsic hand compartments and evacuation of a hematoma resolved her symptoms and preserved hand function. Early recognition and surgical intervention of compartment syndrome of the hand after infiltration injury in medically complex patients will reduce morbidity in this patient population.

Copyright © 2021, THE AUTHORS. Published by Elsevier Inc. on behalf of The American Society for Surgery of the Hand. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Compartment syndrome results from high tissue pressure in enclosed osseofascial spaces that prevents adequate perfusion required for tissue viability; pressures above 30 mm Hg or within 30 mm Hg of the diastolic blood pressure can lead to muscle ischemia, necrosis, contraction, and nerve injury.¹ This syndrome is a medical emergency requiring immediate surgical intervention to release compartments and to increase oxygen delivery to tissues, preventing loss of function and high morbidity.¹

Rare cases of isolated compartment syndrome of the hand have been reported, with the most common etiologies traumatic in nature, typically vascular injury, thermal burns, or electrical burns.¹ Other incidences, although less prevalent, have resulted from intravenous infiltration injuries, infection, or insect bites.¹ Infiltration injuries are typically self-limiting. However, those reported to precipitate compartment syndrome most often involved pressurized administration of intravenous fluids.² In the case

below, we describe the delayed development of compartment syndrome in the hand of a patient 16 days after an intravenous doxycycline infiltration injury in the setting of anticoagulation therapy for COVID-19 pneumonia. To our knowledge, this is the first report of hand compartment syndrome after doxycycline infiltration.

Case Report

A 72-year-old woman presented with a 1-week history of cough, shortness of breath, and weakness. She was hypoxic to oxygen saturation of 80% and was admitted for COVID-19 pneumonia superimposed with bacterial pneumonia and sepsis. Her past medical history was notable for hypertension, hypothyroidism, and obesity.

The treatment of COVID-19 pneumonia initially involved a 10-day course of dexamethasone, albuterol, and nasal cannula oxygen. She was prophylactically placed on therapeutic dosing of enoxaparin, the standard of care at that time for patients with COVID-19, in response to reports of systemic hypercoagulability. Blood cultures grew gram-positive cocci in clusters, and vancomycin, meropenem, and doxycycline were initiated. On hospitalization day (HD) 2, an intravenous piggyback set to gravity containing doxycycline 100 mg in 100 mL of normal

Declaration of interests: No benefits in any form have been received or will be received related directly or indirectly to the subject of this article.

Corresponding author: Rex W. Hung, MD, Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, 3800 Reservoir Road, NW, Washington, DC 20007.

E-mail address: rexhung123@gmail.com (R.W. Hung).

<https://doi.org/10.1016/j.jhsg.2021.12.002>

2589-5141/Copyright © 2021, THE AUTHORS. Published by Elsevier Inc. on behalf of The American Society for Surgery of the Hand. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

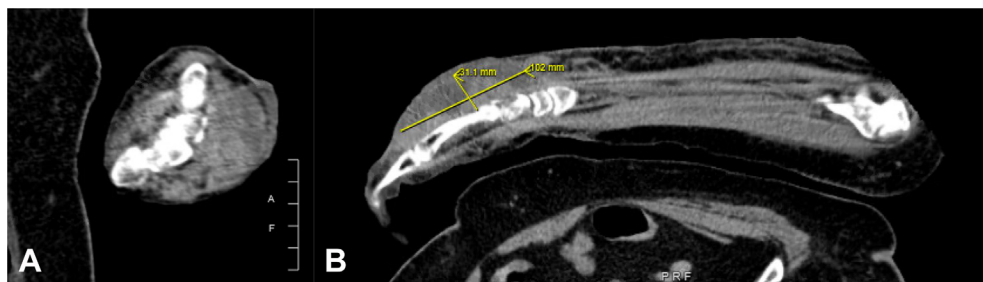


Figure 1. Computed tomography **A** axial and **B** sagittal views of the left hand displaying dorsal hematoma.

saline infiltrated a peripheral intravenous catheter placed in the left dorsal hand, causing mild swelling and pain. On HD 4, worsening respiratory failure required endotracheal intubation and transfer to the intensive care unit. She was started on norepinephrine because of hypotension and prone periodically with a gradual improvement of her respiratory status. Medication administration and blood draws were performed via a triple lumen central catheter; no peripheral intravenous catheters were placed in the left hand or arm because of poor peripheral venous access for the remainder of her hospitalization.

On HD 18, the patient's left hand displayed considerably worsened swelling with a large dorsal purplish bulla. The patient, although intubated, was responsive and was able to answer yes or no questions. She reported pain in her hand and distal forearm and was unable to flex her fingers, but she denied numbness. Vascular surgery was consulted and found no signs of arterial insufficiency on arterial duplex ultrasound and Doppler examination. Computed tomography demonstrated a hematoma of the dorsal wrist (Fig. 1). The venous duplex ultrasound did not find any evidence of venous thrombosis. Nonsurgical management and local wound care were recommended. Hand surgery was consulted on HD 21 for hematoma evacuation after her symptoms continued to worsen. On examination, the left hand had faint ulnar and radial Doppler signals, cool fingers, considerable blistering, mottling, and intrinsic minus posturing (Fig. 2A, B). She had worsened pain with the passive extension of the interphalangeal (IP) and metacarpophalangeal (MCP) joints of the digits and thumb and limited active range of motion. Compartment pressures of 52 and 54 mm Hg in the hypothenar eminence and 40 and 42 mm Hg in the thenar eminence were measured using the Stryker Intra-Compartmental Pressure Monitor System (Fig. 2C). Delta pressures ranged between -2 and 30 mm Hg, indicating compartment syndrome.

An emergent decompressive fasciotomy of the left hand was performed. The thenar and hypothenar muscle groups were severely edematous and immediately herniated through the volar incisions. Two radial incisions on the dorsal surface over the second and fourth metacarpals were also made, releasing the interosseous and adductor compartments and evacuating the dorsal hematoma. All compartments were released, and the dorsal fasciotomies were closed loosely. On postoperative day 2, the patient was extubated and reported improved pain. Range of motion of all digits was limited, although it improved from prior to surgery, with flexion and extension at the MCP and IP joints to $<10^\circ$ of all digits, including the thumb, and improvement in swelling (Fig. 3). By postoperative day 9, she had improved flexion and extension of all digits to $>10^\circ$ at the

MCP and IP joints and could oppose her thumb as far as her middle finger. The dorsal wound displayed an area of superficial necrosis and eschar ulnarly (Fig. 4). She was discharged on HD 31.

The patient continued to recover function through physical therapy, progressing to form a composite fist and fully extend fingers by 3 weeks after surgery. A necrotic eschar on the dorsal hand was debrided serially at 3, 4, and 6 weeks after surgery (Fig. 5). The wound was fully healed at 7 months after surgery, with mild scar contracture and some limitation of wrist flexion to 60° but full wrist extension (Fig. 6). She had a full range of motion in the digit IP and MCP joints, forearm supination and pronation, and wrist radial and ulnar deviation (Fig. 6). Her Disabilities of the Arm, Shoulder, and Hand score, a self-administered questionnaire that assesses the upper extremity disability, was 60 of 100, although her baseline score was unknown. Overall, she was "very satisfied" with her outcome, particularly her range of motion, ability to perform activities of daily living, and resolution of neuropathic pain symptoms. A written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Discussion

Rapid diagnosis of compartment syndrome of the hand, although rare, is paramount to prevent muscle loss and permanent deficits in patients. It should be considered a differential diagnosis in any patient with signs of hand swelling, pain, and bullae after intravenous infiltration. Based on our experience, the development of compartment syndrome after infiltration injury may be insidious, and heightened suspicion must be maintained in patients with complex comorbidities and high resuscitative requirements that may cause progressive tissue edema and decreased tolerance to tissue ischemia over a prolonged period. The management of patients with hand compartment syndrome requires immediate fasciotomies to release all the intrinsic hand compartments to prevent considerable morbidity.¹

Diagnosing compartment syndrome of the hand is primarily clinical and relies on the early identification of signs and symptoms. Patients commonly present with pain with active motion and passive stretching, localized swelling, muscle paresis, and paresthesia.¹ However, not all of these symptoms may develop initially.¹ Bullous edema and intrinsic minus positioning may also be early indicators of underlying soft tissue injury precluding compartment syndrome. Braunlich et al³ described the case of a 60-year-old man with acute bullous eruption of the hand after colonic sigmoidectomy,



Figure 2. A Presentation of compartment syndrome of the left hand 16 days after intravenous doxycycline infiltration injury with bullous eruption. B Intrinsic minus positioning. C Elevated intracompartmental pressure.



Figure 3. Immediate improvement of swelling and hand position on postoperative day 2 after emergent decompression fasciotomy.



Figure 4. Continued healing with full extension of the digits on postoperative day 9; superficial necrosis and eschar ulnarly of the dorsal wound.

which progressed to swelling, pain, and intrinsic minus positioning; an underlying intracompartmental hematoma and pressures up to 75 mm Hg were found. Thus, acute development of bullae, in conjunction with the previously mentioned

signs, may foreshadow a rise in intracompartmental pressures of the hand. Any patient with symptoms suggestive of compartment syndrome in the hand should have a low threshold to measure compartment pressures.



Figure 5. A Dorsal necrotic eschar that underwent serial debridements at 3, 4, and 6 weeks after surgery. B Significant improvement in wound healing at 9 weeks.

Our case is unique in that compartment syndrome, of any region, has never been described after doxycycline infiltration. A systematic review of cases of intravenous infiltration injuries that led to compartment syndrome found that nearly half occurred in the hand or forearm and most were caused by intravenous contrast or fluid in pressurized systems.⁴ Stavrakakis et al⁵ reported compartment syndrome in a 72-year-old woman after the extravasation of 110 mL of intravenous iopromide contrast that led to pain, swelling, and blistering within 3 hours, necessitating urgent fasciotomy and evacuation of a large hematoma. Although most infiltration injuries are minor and require conservative treatment, many factors can determine whether extravasation can progress to severe injury, including medication osmolality, ionic nature, and volume.² Doxycycline, specifically, is acidic, with a pH between 1.8 and 3.3; hydrogen ion donation and the reductive anionic salt can cause tissue damage, including cellular desiccation, coagulative necrosis, vasoconstriction, and edema.² Further, doxycycline has potential vascular toxicity as its oral form has been shown to cause vascular injury and perivascular edema in the gastrointestinal tract.⁶ These characteristics of doxycycline may have induced vascular degeneration and the subsequent development of a delayed hematoma and compartment syndrome in our patient.

Our patient's case was complicated by her physiologic status, as she was critically ill from COVID-19 pneumonia, which is associated with coagulopathic states, prompting prophylactic, therapeutic anticoagulation. Cases of limb ischemia related to COVID-19–induced arterial thrombi and deep venous thrombosis have been reported.⁷ A case of upper-extremity compartment syndrome, specifically, associated with acute superficial venous thrombosis in the setting of severe COVID-19 infection, highlights the potential of hypercoagulable state–induced compartment syndrome related to infection.⁷ One case of acute compartment syndrome of the hand was reported by Hill et al⁸ in a patient with COVID-19 with acute respiratory distress syndrome on anticoagulation after extravasation around an arterial line site. The cause of

this presentation was unclear, but coagulopathic abnormalities of COVID-19 were suggested to play a role. Other cases of atraumatic compartment syndrome associated with anticoagulation, including enoxaparin, have been reported in the literature because of the increased susceptibility of spontaneous hemorrhage or provoked bleeds with subsequent collection within compartments.⁹ These studies suggest the need to measure compartment pressures with a little suspicion in patients on anticoagulation. Our patient may have had vascular thrombotic complications, either arterial or venous, triggered by her COVID-19 infection, which, combined with therapeutic enoxaparin throughout her hospitalization, could have precipitated and augmented the development of compartment syndrome.

The delayed nature of our patient's presentation by nearly 2 weeks is multifactorial and may be related to her critical illness, communication barriers, and caustic properties of doxycycline. Most reported cases of infiltrative injuries causing compartment syndrome were in patients with communication barriers, either pediatric, intensive care unit, or mentally altered patients.⁴ Our patient had many barriers to communication as she was intubated and intermittently responsive, which may have contributed to the delayed presentation and recognition. Further, the vascular toxicity and caustic nature of doxycycline may have caused progressive tissue degeneration, which, combined with ongoing anticoagulation, may have cultivated a delayed hematoma once the vascular integrity was compromised. It is unlikely that this was a missed compartment syndrome because of the lack of myonecrosis and restored hand function. Rather, the unique characteristics and physiologic status surrounding the doxycycline infiltration caused the delayed, gradual development of a hematoma and resultant compartment syndrome.

Despite the notable elevations in our patient's intracompartmental pressures at the time of diagnosis, immediate surgical intervention satisfactorily restored the hand function without muscle loss or contraction. Although her Disabilities of the Arm, Shoulder, and Hand score was notable,

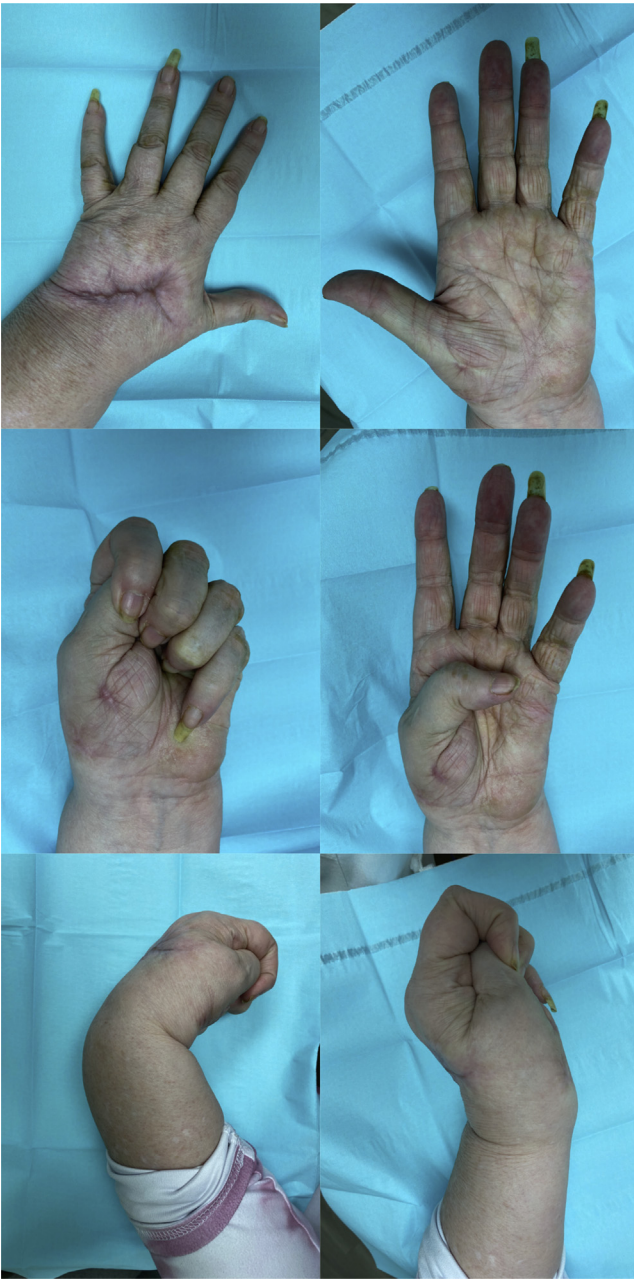


Figure 6. Completely healed dorsal wound at 7 months after surgery, with a full range of motion of interphalangeal and metacarpophalangeal joints of all digits and the thumb, full wrist extension, and mildly limited wrist flexion to 60°.

it is unclear whether her upper extremity function was diminished at baseline because she was aged >50 years or because of obesity comorbidity. Further, reports of impaired physical function and activities of daily living have been reported among patients who survive severe COVID-19 hospitalization in the first 6 months.¹⁰ Nonetheless, our patient reported high subjective satisfaction with the recovery of hand function.

This interesting case highlights the need to consider compartment syndrome of the hand in medically complex patients after infiltration injuries with a low threshold, potentially even more so in patients receiving intravenous doxycycline. Serial examinations should be performed to monitor the progression of symptoms in anesthetized or obtunded patients, as changes may be subtle yet indicative of insidious pathologic progression to compartment syndrome. An improved understanding of patients who develop compartment syndrome after the infiltration of doxycycline will assist providers in early diagnosis and prompt treatment of this condition.

References

- Chandraprakasam T, Kumar RA. Acute compartment syndrome of forearm and hand. *Indian J Plast Surg.* 2011;44(2):212–218.
- Reynolds PM, MacLaren R, Mueller SW, Fish DN, Kiser TH. Management of extravasation injuries: a focused evaluation of noncytotoxic medications. *Pharmacotherapy.* 2014;34(6):617–632.
- Braunlich PR, Braunlich K, Brink R, Ross R, Harker JN. Compartment syndrome of the hand presenting as bullous edema. *Cureus.* 2020;12(3):e7290.
- Bhananker SM, Liau DW, Kooner PK, Posner KL, Caplan RA, Domino KB. Liability related to peripheral venous and arterial catheterization: a closed claims analysis. *Anesth Analg.* 2009;109(1):124–129.
- Stavrakakis IM, Daskalakis II, Detsis EPS, Karagianni CA, Papantonaki SN, Katsafarou MS. Hand compartment syndrome as a result of intravenous contrast extravasation. *Oxf Med Case Reports.* 2018;2018(12):omy098.
- Shih AR, Lauwers GY, Mattia A, Schaefer EAK, Misdraji J. Vascular injury characterizes doxycycline-induced upper gastrointestinal tract mucosal injury. *Am J Surg Pathol.* 2017;41(3):374–381.
- Hembd A, Kim H, Lahsaei P, Haddock NT, Teotia SS. Upper-Extremity Phlegmasia Cerulea Dolens with Compartment Syndrome in Coronavirus Disease 2019 Sepsis [published online ahead of print]. *J Hand Surg Am.* 2021;S0363-5023(21)00269-0. <https://doi.org/10.1016/j.jhssa.2021.04.028>.
- Hill KL, Wu VJ, Kusumoto H, Sherman WF, Savoie FH. Management of orthopaedic emergencies during a pandemic: compartment syndrome of the hand in a patient with COVID-19: a case report. *JBJS Case Connect.* 2020;10(3):e2000377.
- Titolo P, Milani P, Panero B, Ciclamini D, Colzani G, Artiaco S. Acute compartment syndrome of the arm after minor trauma in a patient with optimal range of oral anticoagulant therapy: a case report. *Case Rep Orthop.* 2014;2014:980940.
- Frontera JA, Yang D, Lewis A, et al. A prospective study of long-term outcomes among hospitalized COVID-19 patients with and without neurological complications. *J Neurol Sci.* 2021;426:117486.