American Journal of Emergency Medicine 37 (2019) 1601.e3–1601.e5

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Case Report

Barriers to frostbite treatment at an academic medical center☆

Sarah L. Khan, MD [a,*], Raj Parikh, MD [c], Theodore Mooncai, MD [b], Sukhmeet Sandhu, MD [a], Raagini Jawa, MD, MPH [a], Harrison W. Farber, MD [d]

[a] Boston Medical Center, Department of Internal Medicine, United States of America
[b] Boston Medical Center, Department of Emergency Medicine, United States of America
[c] Boston Medical Center, Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, United States of America
[d] Tufts Medical Center, Division of Pulmonary, Critical Care and Sleep Medicine, United States of America

ARTICLE INFO

Article history:
Received 12 April 2019
Accepted 5 May 2019

Keywords:
Frostbite
Cold injury
Epoprostenol
Prostacyclin

ABSTRACT

The treatment of frostbite injuries has undergone a radical change over the past decade with a shift from supportive therapy and observation towards early and aggressive medical intervention with thrombolytics and vasodilators. Institutions that have implemented evidence-based protocols have significantly decreased their amputation rates (Bruen et al., 2007; Lindford et al., 2017a; Twomey et al., 2005). We present the case of a middle-aged male treated for frostbite of multiple fingers on both hands. Because there was no treatment protocol at our institution, there were multiple delays in the patient's care including imaging and initiation of intravenous (IV) prostanoids. This case illustrates the deleterious effects of delays in treatment and strongly suggests that all facilities located in areas of cold exposure should have protocols in place for such an occurrence.

1. Introduction

Frostbite is a tissue injury, typically of the digits, and sometimes the face, which occurs due to cold exposure. Freezing injuries can be sustained in varied environments, from the wilderness where outdoorsmen may be exposed to prolonged cold to urban settings where laborers or homeless individuals may spend extensive time outside in winter weather [4,5].

Treatment begins with rewarming, wound care, and analgesia. Historically, this was the extent of intervention until weeks after the injury when affected digits either recovered or were amputated. Recent advances in understanding of the pathophysiology of frostbite injury have led to a more proactive approach to management. Several hospitals including the University of Utah Health Center, Helsinki University Hospital, and Hennepin County Medical Center in Minnesota pioneered protocols centered around the early administration of intra-arterial (IA) thrombolytic therapy [1-3]. Studies from each institution have demonstrated decreased rates of amputation and improved patient outcomes with such treatment. As a result, early thrombolytic therapy has become the standard of care for severe frostbite injury [1-3]. There is also evidence that prostacyclins such as iloprost have comparable digital salvage rates and should have a role in treating frostbite injuries [2,6].

2. Case presentation

A 47-year old Hispanic male, with a history of opioid use disorder, homelessness, HIV, and untreated hepatitis C, was transported to the emergency department (ED) with cold exposure and frostbite in both hands precipitated by a period of record breaking sustained cold in the northeastern United States.

Initial evaluation demonstrated frostbite injuries to both hands with hemorrhagic bullae extending over the intermediate and proximal phalanges of digits 3–4 on the left hand and digits 2–5 on the right (Fig. 1). There was also a non-hemorrhagic blister over the plantar surface of his right foot. The hand injuries were associated with significant pain and decreased sensation in the affected digits. The foot injury caused no pain, discomfort, or sensory change. The patient received immediate wound care and pain control.

Because there was no established protocol for the treatment of frostbite at the hospital, there were persistent delays in care. On day two, approximately 48 h after admission, the patient underwent a technetium-99 bone scan which demonstrated preserved flow in the digits of the left hand. In contrast, there was absent flow and decreased soft tissue and bone uptake in the majority of the right fifth digit, as well as the middle and distal portions of the fourth digit. Based on these findings, nifedipine and sildenafil were initiated for vasodilation.

On the fourth day of hospitalization, for further vasodilation, IV epoprostenol was initiated in accordance with an established hospital protocol for treatment of severe Raynaud's phenomenon and digital ischemia secondary to scleroderma. Epoprostenol was uptitrated to 6 ng/kg/min, the maximum dose tolerated by the patient. Per that

☆ Declarations of interest: none.Presented at the CHEST meeting, October 9, 2018 in San Antonio, TX.

* Corresponding author at: 72 East Concord Street, Boston, MA 02118 – 2526, United States of America.
E-mail address: Sarah.Khan@bmc.org (S.L. Khan).

https://doi.org/10.1016/j.ajem.2019.05.012
0735-6757/

Fig. 1. Severity of frostbite at time of admission (day 0), at time of epoprostenol initiation (day 4), at time of epoprostenol completion (day 9), and on day of discharge (day 15). Dorsal and palmar views are shown of the right (R) and left (L).

protocol, after five days of treatment, epoprostenol was tapered and discontinued. Despite visual improvement of both hands with epoprostenol treatment, post-intervention bone scan on day 14 demonstrated bone necrosis in the distal phalanx of the left fourth digit, middle and distal phalanges of the right fifth digit, middle and distal phalanges of the right fourth digit, and distal phalanx of the third digit of the right hand.

The patient was discharged after a 15-day hospitalization to a medical respite facility for ongoing wound care, occupational therapy, and further evaluation and care by Orthopedic Surgery.

3. Discussion

This case of severe frostbite highlights the deleterious effects of delays in treatment and lack of an established treatment algorithm reflecting changes in therapeutic approach that have evolved over the past decade. The prior approach to treatment, described by the adage "frostbite in January, amputate in July", was largely supportive and observational [1]. Intervention was delayed until the extent of the injuries became apparent months later, with necrotic areas undergoing amputation. However, there now exists a substantial body of literature supporting early interventions to produce better outcomes for patients affected by frostbite.

Because frostbite injuries are largely due to local thrombosis, the mainstay of modern treatment is thrombolytic therapy [1-4,7-12]. Protocols developed at the University of Utah Health Center and Helsinki University Hospital use invasive digital angiography to determine the extent of injury followed by the administration of IA tPA and heparin within 24 to 48 h of exposure [1,2,13]. A similar protocol from Hennepin County Medical Center in Minnesota uses a technetium-99 bone scan for initial imaging followed by either IA or IV tPA [3]. The duration of thrombolytic therapy is guided by repeat imaging to determine whether perfusion has been successfully restored [1-3]. If there are signs of persistent vascular compromise on repeat imaging, tPA is continued for a maximum of 12 to 48 h, with heparin continued for 2 to 4 h after tPA is discontinued [1-3]. At the University of Utah, frostbite patients treated per the institution's protocol for thrombolytic therapy had a digital amputation rate of only 10% compared to a rate of 41% in patients treated conservatively [1]. The University of Helsinki and Hennepin County Medical Center reported amputations rates of 25% and 19% respectively after the institution of their thrombolytic-based treatment protocols [2,3].

The Helsinki protocol also incorporates the use of IV iloprost, a prostacyclin analog which causes vasodilation, in cases in which there are either contraindications to thrombolysis or incomplete responses to tPA [2]. Several case reports and series have also reported the use of iloprost either alone or following tPA [7,9,14,15]. Cauchy, et al. compared amputation of at-risk digits in patients treated with IV iloprost alone versus iloprost with tPA, and found amputation rates of 0 and 3.1%, respectively [6].

Because IV iloprost is not available in the United States, substituting IV epoprostenol might be a reasonable alternative. Epoprostenol is a prostacyclin currently used intravenously for treatment of pulmonary arterial hypertension [16] and digital ischemia associated with severe Raynaud's phenomenon secondary to scleroderma [17]. To our knowledge, there are no reports of treating frostbite with epoprostenol. Despite some improvement in this patient's digits with this treatment (Fig. 1), the overall outcome was poorer than that reported in the above studies. However, this may have been due to a delay in instituting epoprostenol rather than a failure of the medication.

Increased time from rewarming to thrombolytic therapy has been significantly associated with amputation with a 26.8% decrease in salvage for every hour of delay [18]. However, while patients with delayed treatment do appear to have higher rates of amputation, Pandey et al. recently reported on five patients who received IV iloprost up to 72 h after their initial injury whose tissue loss was less than expected [19,20]. They suggested that iloprost can be beneficial for severe frostbite up to 72 h after injury. It seems likely that a similar relationship would exist between delayed initiation of epoprostenol therapy and tissue loss. Further investigation, using a standardized treatment protocol similar to the Helsinki protocol, is warranted to determine whether epoprostenol is an effective substitute for iloprost.

In conclusion, this case illustrates the importance of early imaging and intervention in order to successfully treat severe frostbite. While the combination of thrombolytics and/or vasodilators that are used may vary between institutions, timely initiation of treatment is crucial regardless of the treatment regimen. Hospitals in cold climates should establish triage and treatment protocols to ensure that they are prepared to quickly identify and treat patients with severe frostbite, prevent amputations, and, ultimately, improve patient outcomes.

Author contributions

Study concept (SLK, RP, TM, SS, RJ, HWF); literature review (SLK, TM, RJ), drafting of the manuscript (SLK, TM, SS); critical revision of the manuscript (SLK, RP, HWF); approval of the manuscript (HWF).

Financial/material support

None.

Disclosures

None.

References

[1] Bruen KJ, Ballard JR, Morris SE, Cochran A, Edelman LS, Saffle JR. Reduction of the incidence of amputation in frostbite with thrombolytic therapy. Arch Surg 2007;142:546–50. https://doi.org/10.1001/archsurg.142.6.546.

[2] Lindford A, Valtonen J, Hult M, Kavola H, Lappalainen K, Lassila R, et al. The evolution of the Helsinki frostbite management protocol. Burns 2017;43:1455–63. https://doi.org/10.1016/j.burns.2017.04.016.

[3] Twomey JA, Pelti GL, Zera RT. An open-label study to evaluate the safety and efficacy of tissues plasminogen activator in treatment of severe frostbite. J Trauma 2005;59:1350–5.

[4] Hutchinson RL, Miller HM, Michalke SK. The use of tPA in the treatment of frostbite: a systematic review. Hand (NY) 2018;14:13–8. https://doi.org/10.1177/1558944718800731.

[5] Petrone P, Kuncir EJ, Asensio JA. Surgical management and strategies in the treatment of hypothermia and cold injury. Emerg Med Clin North Am 2003;21:1165.

[6] Cauchy E, Davis CB, Pasquier M, Meyer EF, Hackett PH. A new proposal for management of severe frostbite in the austere environment. Wilderness Environ Med 2016;27:92–9. https://doi.org/10.1016/j.wem.2015.11.014.

[7] Groechenig E. Treatment of frostbite with iloprost. Lancet 1994;344:1152–3.

[8] Cauchy E, Cheguillaume B, Chetaille E. A controlled trial of a prostacyclin and rt-PA in the treatment of severe frostbite. N Engl J Med 2011;364:189–90. https://doi.org/10.1056/NEJMc1000538.

[9] Handford C, Buxton P, Russell K, Imray CEA, McIntosh SE, Freer L, et al. Frostbite: a practical approach to hospital management. Extreme Physiol Med 2014;3:7. https://doi.org/10.1186/2046-7648-3-7.

[10] Patel N, Srinivasa DR, Srinivasa RN, Gemmete JJ, Krishnamurthy V, Dasika N, et al. Intra-arterial thrombolysis for extremity frostbite decreases digital amputation rates and hospital length of stay. Cardiovasc Intervent Radiol 2017;40(12):1824–31. https://doi.org/10.1007/s00270-017-1729-7.

[11] Sheridan RL, Goldstein MA, Stoddard Jr FJ, Walker TG. Case records of the Massachusetts General Hospital. Case 41 - 2009. A 16-year old boy with hypothermia and frostbite. N Engl J Med 2009;361:2654–62. https://doi.org/10.1056/NEJMcpc0910088.

[12] Wagner C, Pannucci CJ. Thrombolytic therapy in the acute management of frostbite injuries. Air Med J 2011;30:39–44. https://doi.org/10.1016/j.amj.2010.08.006.

[13] Lindford A, Valtonen J, Hult M, Kavola H, Lappalainen K, Lassila R, et al. The evolution of the Helsinki frostbite management protocol. Burns 2017;43(7):1455–63. https://doi.org/10.1016/j.burns.2017.04.016.

[14] Kaller M. BET 2: treatment of frostbite with iloprost. Emerg Med J 2017;34(10):689–90. https://doi.org/10.1136/emermed-2017-207129.2.

[15] Poole A, Gauthier J. Treatment of severe frostbite with iloprost in northern Canada. CMAJ 2016;188(17–18). https://doi.org/10.1503/cmaj.151252.

[16] Sitbon O, Noordegraaf AV. Epoprostenol and pulmonary arterial hypertension: 20 years of clinical experience. Eur Respir Rev 2017;26:265–70. https://doi.org/10.1183/16000617.0055-2016.

[17] Law ST, Farber HW, Simms RW. Use of intravenous epoprostenol as a treatment for the digital vasculopathy associated with the scleroderma spectrum of diseases. J Scleroderma Relat Disord 2017;2:208–12. https://doi.org/10.5301/jsrd.5000255.

[18] Nygaard RM, Lacey AM, Lemere A, Dole M, Gayken JR, Wagner ALL, et al. Time matters in severe frostbite: assessment of limb/digit salvage on the individual patient level. J Burn Care Res 2017;38:53–9. https://doi.org/10.1097/BCR.0000000000000426.

[19] Irarrazaval S, Besa P, Cauchy E, Pandey P, Vergara J. Case report of frostbite with delay in evacuation: field use of iloprost might have improved the outcome. High Alt Med Biol 2018;19(4):382–7. https://doi.org/10.1089/ham.2018.0027.

[20] Pandey P, Vadlamudi R, Pradhan R, Pandey KR, Kumar A, Hackett P. Case report: severe frostbite in extreme altitude climbers – the Kathmandu iloprost experience. Wilderness Environ Med 2018;29(3):366–74. https://doi.org/10.1016/j.wem.2018.03.003.