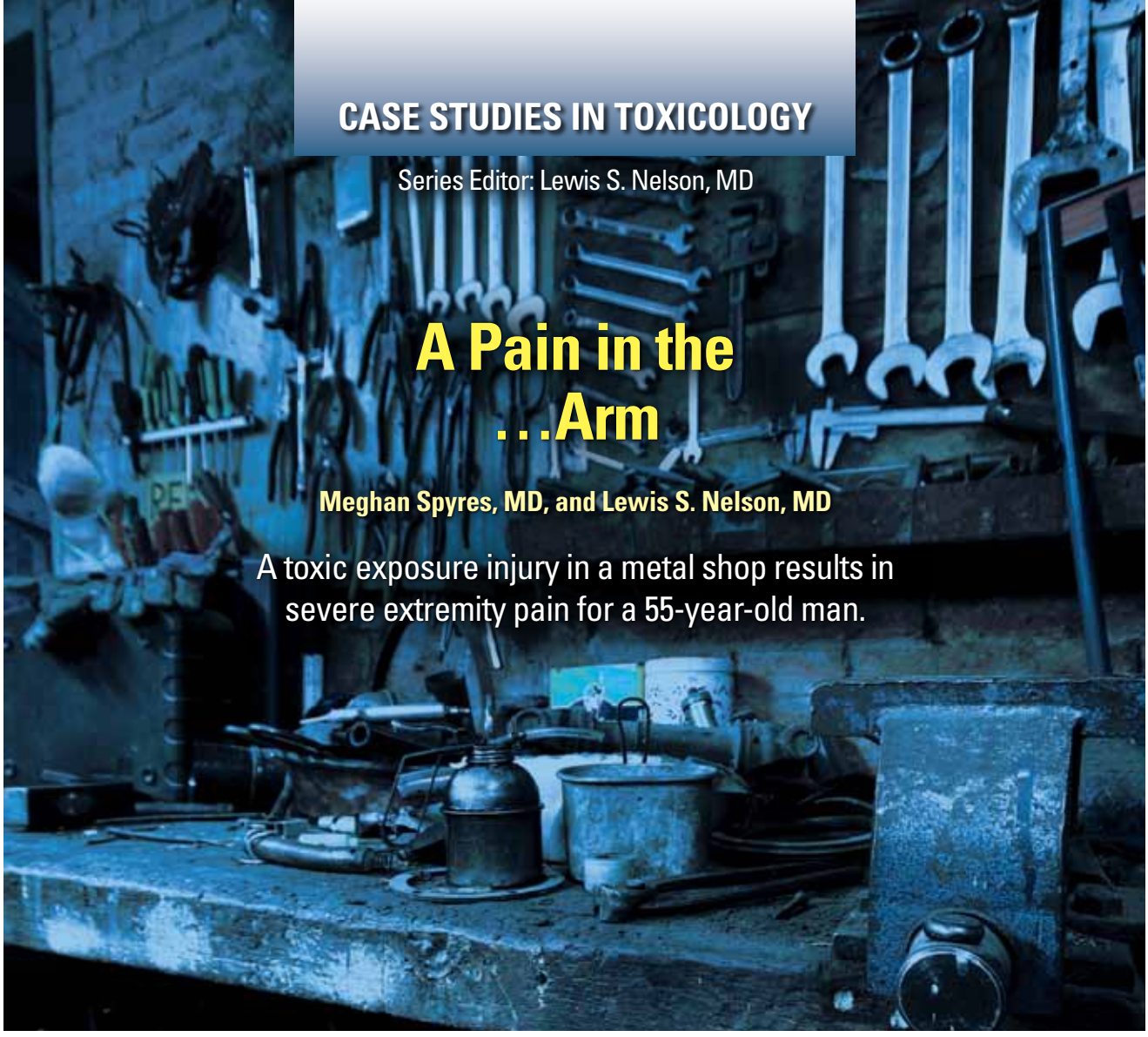

CASE STUDIES IN TOXICOLOGY

Series Editor: Lewis S. Nelson, MD

A Pain in the . . .Arm

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A toxic exposure injury in a metal shop results in severe extremity pain for a 55-year-old man.

Case

A 55-year-old man with an unremarkable medical history presents to the ED complaining of pain in his left forearm and hand**.** Patient acknowledges drinking an excessive volume of ethanol at his friend's metal shop the previous evening and, later, passing out there. He noted extremity pain immediately upon awakening and noticed that his arm was resting in a shallow puddle that had presumably leaked from a nearby container. Pain continued to increase over the next 2 hours.

Vital signs are: blood pressure, 155/85 mm Hg; heart rate, 73 beats/min; respiratory rate, 14 breaths/min; temperature, 98.0˚F. Finger-stick glucose reading is 99 mg/dL and oxygen saturation is 100% on room air. On physical examination, the patient is in no acute distress but appears to be in moderate pain; he is cradling his left arm and is reluctant to move the hand or wrist. Cardiac, pulmonary, and abdominal examinations are normal. The skin is warm and dry, with trace edema on the dorsum of the hand, but no external signs of trauma (Figure, page 10). Close inspection of the arm reveals scant white flakes on the dorsum of the hand and forearm. There is significant tenderness to light palpation along the left upper extremity from fingertip to proximal elbow. Range of motion of the fingers and wrist is limited by pain. Motor function and sensation to light touch of radial, median, and ulnar

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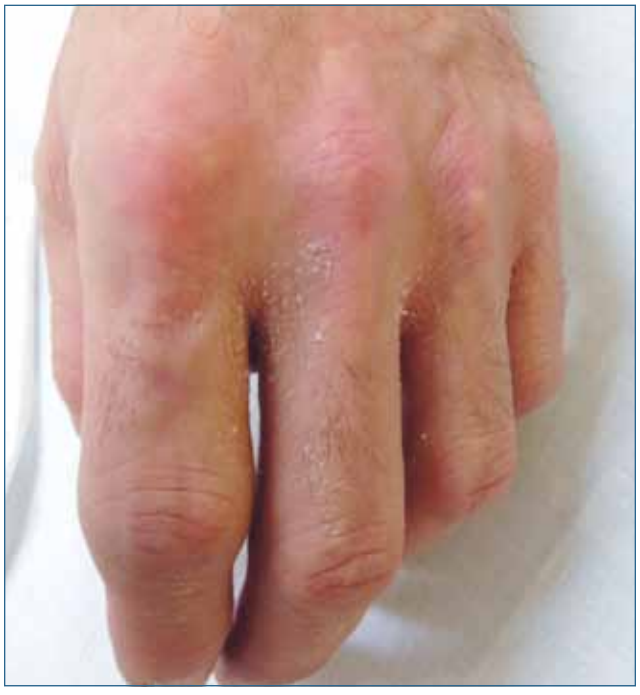

FIGURE Trace edema and scant white flakes on dorsum of hand.

nerves are intact. Radial pulses are normal bilaterally, and capillary refill is brisk.

What historical and examination findings should be sought in a patient with severe extremity pain following an exposure?

As with most clinical diagnoses, a well-performed history and physical examination will provide nearly all of the data needed to make a diagnosis. Common causes of severe extremity pain from exposure include envenomation, high-pressure injection injury (HPII), freezing cold, radioactive materials, hydrocarbons, and acid or alkali.

Envenomation. Although snakebite can cause severe pain, it is almost always accompanied by dermatologic findings such as puncture wounds and signs of inflammation. For example, rattlesnakes, copperheads, and water moccasins (members of the Crotalinae subfamily of Viperidae), indigenous to the United States, have venom containing both hyaluronidase and metalloproteases. These substances cause local tissue destruction and pain upon injection, and produce characteristic skin findings that range from mild edema and ecchymosis to blistering and necrosis. An absence of overt skin abnormalities in the presence of intense extremity pain is atypical, though possible. While certain types of marine envenomation can present with severe pain but limited cutaneous findings, site of toxin entry (eg, puncture wound) is generally visible. Cnidaria (commonly referred to as jellyfish), sea urchin, and members of the Scorpaenidae family, including scorpionfish, stonefish, and lionfish, are common offenders[1] (See *Emergency Medicine.* 2013;45[2]:9,10,20,21 for additional information on marine envenomation).

High-pressure injection injury. HPII often occurs in the nondominant hand while cleaning or testing the spray nozzle of a high-pressure industrial tool. HPII can result in significant pain, with physical findings initially limited to a small puncture wound. Common HPII substances include paint, grease, fuel, hydraulic fluid, and water. HPII causes damage through physical distension of tissue and chemical injury. In addition to high pressure (eg, 2,000 to 10,000 psi), site of injection, and duration of exposure, the chemical characteristics of the substance injected determine extent of injury and associated toxicity. Less dense substances are able to penetrate more deeply, resulting in greater tissue destruction. Paint solvent is particularly dangerous given its low viscosity and irritant nature. An initial HPII can appear deceptively minimal, leading to a delay in presentation for care. Although early findings may be unimpressive, injury may progress to compartment syndrome or extensive tissue necrosis, highlighting the need for early recognition.[2]

Freezing cold. Freezing cold exposure injuries, which can range from frostnip and frostbite to grossly frozen limbs, present with a painful extremity and variable—albeit initially few—abnormal physical findings. Frostbite results in both direct and indirect tissue damage. Ice-crystal formation in the extracellular space increases oncotic pressure, leading to diffusion of water from cells and intracellular dehydration and electrolyte disturbance. As the ice crystals melt, extracellular edema worsens, and endothelial damage creates microthrombi, occluding capillaries and causing ischemia. Rewarming induces an inflammatory and prothrombotic environment, thereby worsening ischemia. In addition to pain, patients may

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complain of cold, numbness, and paresthesias to affected areas. The full extent of injury is not often immediately apparent and may be limited to blanched skin.[3]

Radioactive materials. Direct handling of highly radioactive materials can result in localized radiation exposure. These exposures most commonly occur in industrial settings where radioisotopes are used to assess welds in metal structures (eg, bridges). Clinical manifestation of localized radiation exposure occurs in a step-wise, dose-dependent fashion and includes erythema, blistering, and pain at the site of exposure. At first, symptoms are mild or absent and consist of transient erythema in exposure greater than 6 gray (Gy). Initial erythema and edema as a result of capillary leak may not lead to prominent findings for several weeks until the effects of decreased mitotic activity in the germinal epidermis become evident. Exposures greater than 25 Gy may cause delayed vascular injury, resulting in ulceration and necrosis for several years post-exposure.[4,5]

Hydrocarbons. A variety of household and industrial products contain hydrocarbons, including paint thinners, gasoline, degreasers, dry-cleaning solution, and furniture polish. The lipophilicity of hydrocarbons results in defatting of the lipid-containing stratum corneum. This causes nonspecific dermal irritation, such as skin dryness and dermatitis. The severity of reaction varies by the chemical properties of the specific hydrocarbon and is proportional to duration of exposure; extended contact can result in what is the equivalent of partial- or full-thickness burns.[6]

Acid or alkali. Although dermal exposure to acid or alkali typically results in early skin findings due to tissue destruction by protons (H+) or hydroxyl anions (OH-), respectively, there is at least one important exception: hydrofluoric acid (HF). HF is a unique acid with widespread use, including metal cleaning and glass etching. Dermal exposure manifests in a range of clinical effects that depend on the concentration and duration of exposure. Concentrations of HF greater than 50% cause significant pain and tissue destruction immediately after contact. Exposure to a concentration less than 12%—typical of household rust removers—results in a delayed onset of pain and is usually not accompanied by objective skin changes. However, intradermal precipitation of calcium complexes, including fluorapatite, can cause white discoloration of the skin.[7,8]

Similar to HF, ammonium bifluoride (ABF) is a fluoride-containing acid also used for metal cleaning and glass etching; it is commonly employed to clean metallic automotive parts. Dermal and mucosal effects of ABF are similar to those of HF, but the onset of symptoms can be even more protracted. ABF is a crystalline salt that forms when ammonium hydroxide is mixed with HF. Upon contact with water or bodily fluids, ABF converts to HF. (Despite this effect, manufacturers often consider ABF safer than HF.) ABF can contain over 15% available fluoride, and there have been reports of serious injury and death after ingestion of even small quantities.[9]

Case continued

Details of the history, location of exposure, and physical examination facilitated rapid narrowing of the differential diagnosis. The indoor location, delayed clinical presentation, and absence of significant skin damage, along with site of the incident, implicated HF or ABF as the most likely cause of injury.

How does hydrofluoric acid cause clinical toxicity?

A weak acid, HF remains poorly dissociated in aqueous solution, and thus penetrates the lipophilic cell membrane of dermal cells before dissociating into hydrogen and fluoride ions in the dermis. Deep within the layers of the skin, highly electronegative fluoride ions bind to calcium and magnesium ions, altering their physiologically active concentrations. This leads to vasospasm and excitation of small unmyelinated nerve fibers, manifesting in neuropathic pain. Pain is further exacerbated by deposition of calcium complexes such as calcium fluoride and fluorapatite into tissues, which results in pain out of proportion to the abnormalities noted in dermatologic examination.[8]

HF's unique ability to penetrate deeply into tissues raises the potential for significant systemic toxicity. Following systemic absorption, hypocalcemia and resultant hyperkalemia may lead to life-threatening metabolic abnormalities. Coagulopathy may result from hypocalcemia as calcium is a required cofactor in the coagulation cascade. Ingestion of HF also causes significant irritation

of gastrointestinal mucosa, leading to ulceration or perforation. Chemical pneumonitis and hemorrhagic pulmonary edema may also occur. Fatalities are primarily caused by electrolyte-related dysrhythmias, including ventricular fibrillation.[8]

Dermal HF exposure remains a clinical diagnosis. Finding the original source of the exposure is optimal but it is not possible to chemically identify HF in a timely fashion in the ED. Response to appropriate therapy, however, can confirm the diagnosis.

What is the treatment for hydrofluoric-acid poisoning?

Exposures to small-volume and low-concentration HF carry a low risk for systemic toxicity. Dermal decontamination with copious amounts of water should be performed, but should be limited in cases of ocular exposure. Local application of calcium ions to the exposed area is a simple and effective first-line treatment. If a commercial preparation is not available, one may be prepared by mixing 25 mL of 10% calcium gluconate or 10 mL of 10% calcium chloride with 75 mL of sterile water-soluble surgical lubricant. It is important to monitor evolution or resolution of pain to assess effectiveness of treatment. If topical calcium proves ineffective, intradermal injection of up to 0.5 mL/cm of 5% calcium gluconate solution can be performed. Intradermal administration of calcium chloride is contraindicated based on the high risk of local tissue damage. For areas too large or not conducive to intradermal injection (eg, fingertips), intra-arterial calcium gluconate can be used at a dose of 10 mL of 10% calcium gluconate in 40 mL dextrose 5% in water or normal saline over 4 hours. Arterial access should be ipsilateral and proximal to the area of injury, typically in the radial or brachial artery. Care should be taken to confirm correct arterial line placement to avoid complications of extravasation of calcium into tissues.[8]

In cases in which concern for systemic toxicity arises (eg, when greater than 2% of body surface area is exposed to highly concentrated HF), close monitoring and normalization of the aforementioned electrolytes are paramount. Continuous electrocardiographic monitoring for electrolyte disturbances such as QT prolongation and peaked T waves is essential, as these can lead to dysrhythmia. Vigilance for systemic toxicity is indicated for exposures to concentrated formulas. Dermal exposures to the face and neck, along with oral and inhalational ingestions of any concentration, are potentially fatal. Pain immediately after contact raises concern for exposure to high-concentration HF and should be treated aggressively. When there is clinical suspicion of systemic toxicity, intravenous calcium and magnesium should be administered to prevent hypocalcemia and associated life-threatening hyperkalemia and dysrhythmias. Hemodialysis to remove fluoride ions may be necessary for critically ill patients.[10]

Case conclusion

A preparation of 10 mL of 10% calcium chloride combined with sterile surgical lubricant was mixed and applied to the left hand and forearm. An additional calcium-containing lubricant was added to a surgical glove and placed over the hand, and the forearm was lightly wrapped with an occlusive dressing for 30 minutes. After the dressing and glove were removed and the skin was washed, the patient reported complete resolution of pain and had full range of motion in his hand and wrist. As the dermatologic and neurologic examinations of the extremity were unremarkable and electrolyte levels remained normal, the patient was discharged without report of sequelae.

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