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REVIEW ARTICLE

The utility of bone scintigraphy with SPECT/CT in the evaluation and management of frostbite injuries

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Objective: Frostbite is a localized cold-thermal injury resulting from prolonged exposure of flesh to freezing and near freezing temperatures. The depth and extent of frostbite injuries are not easily assessed, from a clinical standpoint, at the time of injury making it challenging to plan appropriate management and treatment.

Methods: A review of the literature of management of cold-related injuries and retrospective case review of the imaging and clinical course of frostbite injury.

Results: Bone scintigraphy with single photon emission computed tomography (SPECT)/CT was performed in the acute and subacute course of frostbite injuries,

subsequently leading to earlier definitive management and shorter hospital stay.

Conclusion: Multiphase technetium-99m-methylenediphosphonate (^{99m}Tc-MDP) bone scintigraphy with SPECT/CT can expedite clinical management of frostbite injuries by determining the extent of injury and can accurately predict the level of amputation if needed.

Advances in knowledge: SPECT/CT is underutilized at many facilities but can have a profound and immediate impact on clinical management of patients with frostbite when used in combination with physiological bone scan imaging.

INTRODUCTION

Frostbite is a localized cold-induced tissue injury resulting from prolonged exposure of flesh to freezing (0°C) and near freezing (2°C) temperatures.^{1,2} Frostbite typically affects adults between 30–49 years of age with a strong male predominance (10:1) and most commonly involves the hands and feet (>90% cases), although the face, cheeks, ears and nose may also be affected.^{3–5} Vasospasm and arteriovenous shunting leading to ischemia and infarction is central to the pathogenesis of frostbite and occurs on a spectrum ranging from minor exposure and pernio (chilblains), to necrosis and gangrene. The severity of frostbite is dependent on the duration of exposure. Frostbite has a predilection for those who are unable to protect themselves from adverse environments such as wilderness hikers, alcoholics and substance abusers, psychiatric patients, and the poor.^{1,6,7}

The depth and extent of frostbite injuries are not easily assessed at the time of injury, which makes it difficult to plan appropriate treatment and to determine treatment efficacy.^{1,5–7} Surgeons often recommend waiting and watching for tissue demarcation prior to any proposed amputation, which can take weeks to months after the initial injury.⁸

Multiphase technetium-99m-methylenediphosphonate (^{99m}Tc-MDP) bone scintigraphy with single photon emission CT (SPECT)/CT can expedite clinical management of frostbite injuries by determining the extent of injury and can accurately predict the level of amputation if needed.^{1,7}

CLINICAL PRESENTATION

Presenting signs and symptoms

Education is a vital component for those at risk of frostbite injuries as prevention is much more effective than treatment.^{9,10} Ensuring optimal clothing, nutrition, and adequate hydration are essential primary defenses. Secondary prevention techniques after cold exposure such as shielding from the wind, exchanging wet for dry gloves and socks, warming the affected area in the armpit or groin, generating heat with exercise, and avoiding rubbing the affected area can help reduce the risk of cold injury.^{2,9,10} Frostbite injuries occur on a spectrum and thus have a varied presentation. The affected area (typically the fingers and toes) are usually white or discolored with loss of sensation and proprioception with or without the presence of pain.^{9,11} Once frostbite occurs, it is recommended to avoid rewarming until a constant warm temperature can be

Figure 1. Multiphase [^{99m}Tc]-MDP bone scintigraphy and bilateral extremity angiogram following a severe frostbite injury. Delayed (A) and soft tissue phase (B) images with fingertip markers demonstrate absent radiotracer activity within the majority of the bilateral fingers. These findings mirror the digital subtraction angiogram, which demonstrates diminutive arteries in both the right (C) and left (D) hands with no significant arterial flow to the digits. MDP, methylene diphosphonate.

maintained because repeated episodes of thawing and refreezing will damage the microcirculation and worsen the injury.^{9,10}

Emergency department treatment

The initial evaluation of a frostbite injury includes determining the time since cold exposure, removing jewelry or rings, and photographing the affected area prior to rewarming.^{2,5,6} Eliciting a history of smoking, vascular disease, or past cold injury may help assess underlying small vessel dysfunction and stratify the risk for severe injury.^{2,5,6} Examination includes digit and nail inspection with comparison to the unaffected normal side (if possible). Ulceration, hemorrhagic blisters, skin changes (pallor, hair loss, numbness pain, and non-deforming skin) and gangrene indicate inadequate soft tissue perfusion and possible deep tissue ischemia.¹² Rewarming should occur in a tightly controlled warm bath with antiseptic at 37–39°C and should proceed slowly because higher temperatures can contribute to the injury process.^{13–15}

Following rewarming, the affected areas are once again examined and the injuries are scored using a clinical scoring system with four grades: (1) superficial reversible, (2) superficial dermal, (3) deep dermal, and (4) deep subcutaneous, muscle, nerves, and/or bone.^{2,5} Although this scoring system is useful as a general guide for clinical management, diagnostic imaging is ultimately required to determine the viability of affected soft tissue and/or bone if surgery is planned.

PATHOPHYSIOLOGY

After acute exposure to subzero temperatures, there is a chain of physiologic processes that result in acute cellular death and subsequent tissue loss. The process starts with local vasoconstriction and ischemia leading to the formation of both extracellular and intracellular ice crystals.^{4,7,10} Extracellular ice crystals result in electrolyte shift and intracellular dehydration, while intracellular ice crystals cause direct damage to the cell membrane, with the net effect of cell death.^{3,4}

Immediate cellular injury leads to release of prostaglandins, thromboxanes, bradykinin, and histamine resulting in endothelial injury and loss of dermal blood flow.⁴ To counteract this, the body responds by alternating cycles of vasoconstriction and vasodilatation to reestablish blood flow. However, rewarming results in reperfusion damage with microcirculation blockage by leukocyte and/or platelet microemboli, leading to further stasis of blood flow and worsening ischemia from arteriovenous shunting of flow from superficial to deep sites.^{3,15,16}

IMAGING

Angiography and radiography

Angiography and radiography are used to assess the vasculature and underlying bone, respectively, following a frostbite injury.¹⁶ The usefulness of these modalities vary depending on the time interval since the injury occurred. Digital subtraction angiography is the diagnostic modality of choice within 24 h of a deep frostbite injury for the evaluation of vascular insufficiency and to

Figure 2. Multiphase [^{99m}Tc]-MDP bone scintigraphy with SPECT/CT after a severe frostbite injury of the bilateral feet. Plantar angiographic phase images (A) demonstrate absent uptake in the bilateral forefeet to the level of the metatarsal heads on the left and to the distal metatarsal shafts on the right. Planar soft tissue and delayed phase images in plantar, medial and lateral views (B) show focally increased radiotracer uptake involving the left first-5th metatarsal heads with absent radiotracer uptake at the left first-5th phalanges. There is increased radiotracer uptake involving the right fourth-5th metatarsal heads with absent radiotracer uptake in the right first-5th phalanges and right first-3rd distal metatarsals. Maximum intensity projection fused SPECT (C) and fused SPECT/CT (D) delayed phase images demonstrate absence of radiotracer uptake in the bilateral forefeet confirming these findings. Note that on planar images it is difficult to identify the precise location of tracer absence without markers. The areas of intense uptake represent the demarcation zone between viable and nonviable tissue. A bilateral transmetatarsal amputation was subsequently performed. MDP, methylene diphosphonate; SPECT, single photon emission CT.

initiate urgent thrombolysis if indicated.^{17–20} The use of CTA and MRA has been proposed although their role is not established and they offer no therapeutic potential if arterial thrombosis is identified.^{21–23} Radiography can be used as a general survey of the affected limb immediately after frostbite to identify radiopaque foreign bodies or occult fractures.¹⁶ Radiographs can also show a number of osseous changes weeks to months after deep frostbite injuries.^{24–26}

Bone scintigraphy with SPECT/CT

^{99m}Tc -MDP bone scintigraphy can be obtained 2–4 days after an acute frostbite injury to assess the microcirculation and depth of injury.²⁷ These bone scans are obtained using three phases that include angiographic, soft tissue, and delayed phase images.^{1,3,28,29}

Immediately following intravenous injection, the distribution of the radiopharmaceutical initially reflects the relative regional blood flow during the angiographic (flow) phase. Approximately 5–15 min after injection, the radiopharmaceutical enters

the extracellular space resulting in the soft tissue (blood pool) phase.³⁰ Over the next several hours, the radiopharmaceutical biodistribution shifts to the osseous structures as it binds to hydroxyapatite crystals and calcium salts, which leads to characteristic uptake in the skeleton as well as uptake in other sites of calcium deposition in the body during the delayed phase.^{31,32}

Angiographic and soft tissue phase radiotracer activity is usually coupled in cold-thermal injury as regional blood flow is a prerequisite for ^{99m}Tc -MDP uptake within bone.³³ This accounts for the lack of osseous radiopharmaceutical uptake in pathologic conditions such as deep frostbite.³⁴ The information yielded from multiphase bone scans performed 2–4 and 7–10 days after injury has been shown to be 84% sensitive in accurately predicting the extent of soft tissue injury and bony revitalization months before it is apparent by clinical examination.^{3,35}

The patterns of uptake on each phase after a frostbite injury correlate well with the clinical management, e.g. minor injury

Figure 3. Multi phase [Tc^{99m}]-MDP bone scintigraphy with SPECT/CT of the bilateral hands after a severe frostbite injury. Angiographic (A) and delayed phase images with fingertip markers (B) demonstrate absent radiotracer uptake within the bilateral hands. The SPECT (C) and fused SPECT/CT MIP images (D) demonstrate the precise anatomic location of non-viable tissue at the level of the metacarpal heads. The patient subsequently underwent bilateral transmetacarpal amputation 8 days after initial presentation. MDP, methylene diphosphonate; SPECT, single photon emission computed tomography.

requiring no surgical intervention (hyperperfusion, normal soft tissue and delayed uptake), mild ischemia with superficial tissue infarction and minor debridement (absent angiographic and soft tissue uptake with normal delayed uptake), and deep gangrene and bone infarction requiring amputation (absent uptake on all three phases).⁷ The expedited determination of viable tissue and bone can have major implications for patients and may prevent the formation and potential catastrophic sequel of gangrene.^{3,16}

Delayed phase images are the most important for guiding surgical management, but at times can be limited due to poor anatomic resolution. Markers at the tips of the digits at the time of flow acquisition can aid localization (Figure 1).

The addition of coregistered low-dose non-enhanced CT with images reconstructed at a slice thickness of 5 mm in a 256×256 matrix to bone scintigraphy can help overcome the shortcomings of planar and SPECT imaging in the assessment of frostbite injuries. SPECT/CT is acquired immediately after delayed phase images to precisely localize scintigraphic findings and has been proven to have a higher accuracy, specificity, and sensitivity than planar imaging for oncologic evaluation of osseous metastatic disease.^{36,37} It has also proven value as a problem-solving tool applied to investigating a multitude of other disorders such as bone pain, heterotopic ossification, osteoid osteoma, diabetic foot infections, extraosseous radiotracer uptake, and also in the evaluation of musculotendinous sport injuries and orthopedic conditions.^{38–41}

In frostbite-related injuries the tips of the distal phalanges of the hand and feet are challenging to assess with conventional bone scintigraphy due to limited spatial resolution and overall juxtaposition of the phalanges, metacarpal/metatarsal, and carpal/tarsal bones. SPECT/CT provides important anatomic information allowing the interpreter to precisely distinguish the margin of viable and non-viable bone to aid in surgical planning (Figure 2). Patient positioning during acquisition of the SPECT/CT images is important to perform with the appendages in neutral anatomic position.

Imaging of the hands is typically performed in the “superman position” where the patient is in prone position with arms outstretched above their head and the hands laid out on soft surface such as rolled towels or X-rays-transparent pillow. Due to the prevalent incapacitating shoulder conditions such as osteoarthritis, frozen shoulder, and rotator cuff tears, an alternative positioning for the “superman position” is resting the hands in a pronated position lying on an X-rays-transparent flat pillow situated over the patient's pelvis while the patient is in a supine position. Imaging of the feet is typically performed in supine position with the feet in resting plantar flexion. Immobilization is also advised to prevent misregistration further increasing the specificity of diagnosis.

Localization of areas of increased uptake indicate the healing response and predict viability and clear demarcation of tissue loss well before physical examination allowing for expedited

intervention and therefore shorter hospitalizations, earlier rehabilitation, and decreased risk of superimposed infection.^{16,42} Our experience is that routine use of SPECT/CT for frostbite injuries assists in management decisions with the goal to minimize the amount of tissue loss and maximize functional capacity after recovery.

Treatment

The clinical grading system can be used to guide frostbite injury management: Grade 1 indicates full recovery and discharge, while Grades 2–4 require hospital admission. The treatment of Grades 3 and 4 typically range from surgical debridement to frank amputation.^{2,5,6}

Without imaging, conservative management requires a prolonged hospital stay until the line of demarcation between infarction and viable tissue develops over a period of 1–3 months.^{43,44} In the past, this prolonged hospital stay was crucial to determine the required level of amputation as there was no way to objectively judge the appropriate level of amputation prior to the

development of gangrene.^{4,5,7,8} The watch and wait approach to ensure clear tissue demarcation leads to longer hospitalization, increased risk of hospital acquired infections, and cost for both the health system and the patient. Fortunately, the functional information from multiphase bone scan combined with the anatomic precision of SPECT/CT can lead to shorter hospitalizations by demarcating the margin of viable bone earlier than clinically observable (Figure 3).^{16,42,45}

CONCLUSION

Frostbite injuries can result in amputation due to vascular occlusion and tissue death. Frostbite poses a unique set of diagnostic and therapeutic challenges to the clinician because the severity and extent of disease is often unknown or underestimated on the initial presentation. Multiphase bone scintigraphy can be used to expedite management by reliably evaluating soft tissue and bone viability. When used in combination with SPECT/CT, bone scintigraphy can identify patients that may require surgery and can delineate the appropriate surgical margin long before it is clinically apparent.

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