Case Report

First Reported Case of Lower Extremity Wound Care with Incidental Myositis Ossificans: Traumatic/Posttraumatic/Circumscripta and an Extensive Literature Review

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Abstract

Myositis ossificans (MO) is a complex disease characterized by heterotopic bone growth, which can be challenging to diagnose as it may mimic other neoplastic abnormalities in its early stages. Its presentation is often obscured by other disease processes, making it a condition that arises from inflammatory processes gone awry and is frequently difficult to treat. The literature suggests supportive therapy and a cautious approach to surgical intervention, including debridements, unless contractures or limitations in range of motion or daily activities are affected beyond acceptable levels. In this paper, we aim to present a case study that provides clinicians with the most current information on MO and its subtypes, including pathological presentations, radiographic findings, and laboratory data to facilitate early diagnosis. We also propose state-of-the-art treatment methods and identify areas for much-needed investigative research. Our hope is that this paper will assist clinicians in making early diagnoses, ultimately helping patients afflicted with this often debilitating disease recover with less costly treatment options.

Keywords: Myositis ossificans, myositis traumatica, myositis workup

Introduction

Myositis ossificans (MO) is defined as a rare pathological, benign ossifying lesion characterized by a focal formation of heterotopic bone and cartilage formation in the extraskeletal soft tissue.[1-12] The World Health Organization (WHO) has reclassified MO as a benign fibroblastic/myofibroblastic tumor.[13] This WHO classification aims to set major precedent for improved standardization and cancer diagnostics leading to greater diagnostic accuracy and more rational and effective treatment modalities for patients.[14]

This article will present a lower extremity wound care case presentation where MO was the underlying pathological causes of the wounds. Subsequently, it will discuss MO's definition, types, incidence, etiology, pathophysiology, histopathology, radiographic characteristics, differential diagnoses, laboratory presentation, and treatment. The goal is to help clinicians avoid surgical intervention that may worsen outcomes for the patient with MO. Furthermore, this paper aims to facilitate early detection and distinction of MO from neoplastic malignancies (like osteosarcoma) which it can mimic, especially in its early phases. Ultimately, this work seeks to help clinicians avoid misdiagnosis, promote early recognition, and prevent unnecessary high cost-initiated medical/surgical care plans, thereby preventing further harm from being done to the patient's that present with this benign, often debilitating, and yet often-times self-limiting disease.[7,11]

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Case Report

The initial clinical presentation

An 85-year-old white female was referred to our hyperbaric and wound center due to worsening cellulitis in her right lower extremity, specifically the lower calf. A wound with associated calcifications was present on the lateral aspect of her right lower leg [Figure 1]. The referral indicated a consideration for surgical interventions to assist in wound, closure, including options such as surgical debridement, biopsy, muscular flap with full-thickness skin graft, or an application of a full-thickness skin graft/skin substitute.

On the initial presentation, the wound measured 2.7 cm (length) × 2.1 cm (width) × 0.2 cm (depth). It was a full-thickness wound extending into the subcutaneous fat and facial layers. Severe reactive cellulitis with prominent erythema was noted in the periwound tissue of the right lower leg [Figure 1]. Additional objective findings included increased local skin temperature (calor) and mild serosanguinous drainage with slight malodor. The patient reported experiencing increased fatigue, higher pain levels, decreased ability to walk, reduced range of motion (ROM) in the lower extremity joints (including the ankle, knee, and hip). She relied on a walker and wheelchair for mobility [Figure 1].

On the initial presentation, she had the following:

Past medical history

A past medical history included the following: abnormality of gait, anxiety, atherosclerotic disease of native arteries, breast cancer in right breast, bony exostosis in the lower extremity, bunions, cataracts bilaterally in her eyes, chronic obstructive pulmonary disease, chronic fatigue, chronic pain, chronic right lower leg wound of 3 years duration, constipation, dementia, dental difficulties with missing teeth and fillings, difficulty walking (for which walker and wheel chair were used), dry eyes, gastric ulcers, hammer toes, hearing loss (with hearing aid usage), hiatal hernia, hyperlipidemia, hypertension, insomnia, muscle weakness, onychomycosis, osteoarthritis, peripheral vascular disease, history of an old right fibula spiral fracture after having slipped and fallen on ice 65 years prior, unsteadiness on her feet, and varicose veins of the lower extremity.

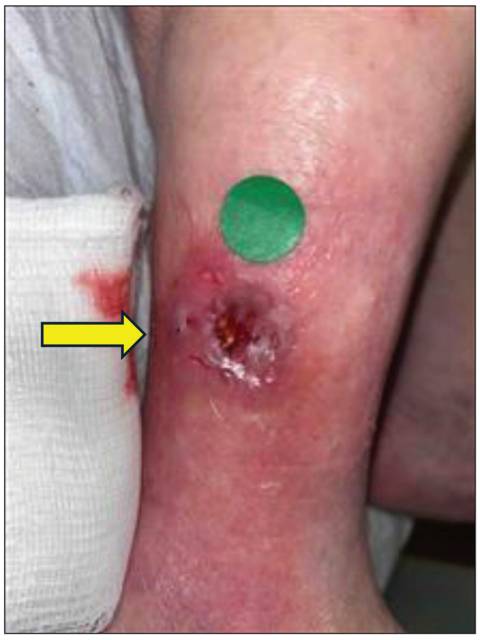

Figure 1: The initial clinical presentation with calcification present and extruding at the 9-O'clock position indicated by the yellow arrow

Past surgical history

A past surgical history which included: a double mastectomy, hernia repair x2, bilateral cataracts, and cholecystectomy.

Social history

Her social history included denial of smoking, alcohol use/abuse, and illicit drug use/abuse. She was widowed and retired and resided at a local rehabilitation facility/skilled nursing facility.

Medications

Her current medications list included: acetaminophen 325 mg tabs every 4 h as needed for pain, albuterol sulfate nebulizer 2.5 mg/3 mL 0.083% inhalation solution to be inhaled once daily, artificial tears 1% ophthalmic solution once daily, Biofreeze 10% external cream applied as needed, Breo-Ellipta 100-25 mcg/ACT inhalation aerosol powder breath activated once daily, cepacol sore throat 5.4 mg mouth throat lozenges one every 4 h, Dulcolax 10 mg rectal suppository once daily, fleet enema 7–19 g/197 mL rectal enema once daily, Guaifenesin ER 600 mg tabs extended release 12 h one tablet every 12 h, loperamide HCl 2 mg one capsule 4 times a day, lorazepam 0.5 mg tabs one tablet daily, melatonin 3 mg oral tablet once daily half hour before bedtime, milk of magnesium 400 mg/5 mL oral suspension 15 mL once daily, Ricola Honey Lozenges 2 mg one every 2–4 h, Senna S 8.6–50 mg oral tablet once tablet twice daily, and Zyrtec 10 mg tablet once daily.

Allergies

Her current allergies included adverse reactions to: penicillin, Dilantin, sulfa antibiotics, sulfa containing products, nuts, and lavender.

Review of systems (ROS)

The ROS was negative with exceptions of findings above and those found in the physical examination listed later below.

Vitals

Height/length 63 in (160.02 cm); weight 150 lbs. (68.18 kg); body mass index (BMI) 26.6, temperature 94.6°F; (35.78°C); pulse 72 bpm; respiratory rate 20 breaths/min; blood pressure 147/70 mm Hg; capillary blood glucose levels: N/A mg/dL; and pulse oximetry: 96% O2 with oxygen supplement at rest.

Physical examination/findings

Lower extremity assessment:

Homans sign: Negative bilateral.

Edema assessment:

- Left extremity: Edema is not present
  Compression device in use: no.
  Calf measurement 24 cm from medial malleolus with left measurement of 37 cm.
  Ankle measurement 3 cm from medial malleolus with left measurement of 23 cm.
  Foot measurement 6 cm from medial malleolus with left measurement of 24.5 cm.
- Right extremity: Edema is present

  Compression device in use: no.
  Calf measurement 24 cm from medial malleolus with right measurement of 36 cm.
  Ankle measurement 3 cm from medial malleolus with right measurement of 23 cm.
  Foot measurement 6 cm from medial malleolus with right measurement of 25 cm.

Vascular assessment

- Left extremity pulses: 2+/4
  Posterior: biphasic.
  Dorsalis pedis: biphasic.
- Right extremity pulses: 2+/4
  Posterior: biphasic.
  Dorsalis pedis: biphasic.
- Left extremity colors, hair growth, and conditions:
  Extremity color: WNL.
  Hair growth on extremity: yes.
  Temperature of extremity: warm.
  Capillary refill: <3 s.
  Erythema: no.
- Right extremity colors, hair growth, and conditions:

  Extremity color: WNL.
  Hair growth on extremity: yes.
  Temperature of extremity: warm.
  Capillary refill: <3 s.
  Erythema: yes.

Additional information

- Left heel to posterior knee (cm): 43.
- Right heel to posterior knee (cm): 42.

Neurological assessment

DTR 1+ Achilles bilateral.

Epicritic sensation: decreased bilateral.

Semm's Weinstein Monofilament test: right side 9/10 with focal deficit noted on heel. The left side is 10/10.

Babinski sign: negative bilateral.

Dermatological assessment

Onychomycotic nails with yellow thickening subungual debris with greater than 1 mm height to the nails.

Peripheral vascular changes to the legs with lack of hair growth noted bilateral, edema of the right leg, and no edema to the left leg.

Erythema to the lower right leg with shiny atrophic skin noted.

Skin texture and turgor decreased bilaterally.

Varicose veins are presented bilateral on the lower extremity.

Musculoskeletal assessment

ROM decreased bilaterally for toes, midtarsal, sinus tarsi joint, ankle, and knee bilateral.

Muscle power 3+/5 for extrinsic and flexor muscle groups.

Deformity

Bunions moderate bilateral.
Hammertoes bilateral.
Flat foot deformity bilateral.

Gait: Use of wheelchair observed. No gait analysis performed.

Shoe gear: Sneakers.

Assistive devices: wheelchair.

Wound assessment(s)

The wound on the right lateral lower leg is classified as a full-thickness wound with an indeterminate origin, acquired on May 15, 2022. It has been identified as a nonhealing wound and was referred by a previous wound care center for surgical evaluation and potential intervention. The initial wound measurements are: length 2.7 cm, width 2.1 cm, depth 0.2 cm, with an area of 5.67 cm^2, and a volume of 1.134 cm^3. On examination, necrotic muscle, bone, and adipose tissue are exposed. There are no tunneling, sinus tracts, or undermining observed.

Moderate serous drainage with some odor is present. The patient reports a wound pain level of 4/10. The wound margin is thickened and rolled under. The wound bed contains 26%–50% adherent yellow slough and 26%–50%

epithelialization. The periwound skin exhibits edema and erythema but does not show signs of brawny induration, excoriation, callus, crepitus, fluctuance, rash, maceration, atrophie blanche, cyanosis, ecchymosis, hemosiderosis, pallor, or rubor. The periwound skin is friable, moist, and warm to the touch. There are no signs or symptoms of infection. The local pulse remains biphasic, as previously documented during physical examination.

Additional clinical information

The patient has a risk for falls. She was advised to wear nonskid socks or well-fitting flat shoes, use adequate lighting to prevent falls, make bathtubs, showers, kitchen and bathroom floors nonslip, take breaks and move slowly while walking, and use assistive devices such as a walker. The patient confirmed understanding of the instructions provided.

Initial treatment provided

A wound culture and tissue biopsy were performed in accordance with the established care protocol. Radiographic imaging of the foot, ankle, and lower leg was ordered. However, an ultrasound Doppler was not indicated, as biphasic palpable pulses were present on physical examination. During debridement, calcifications were removed from the wound were sent for biopsy. The wound was debrided to petechial bleeding, and hemostasis was successfully achieved through direct pressure. Following this, mupirocin 2% mixed with gentamicin sulfate and 1% ointment was applied to the wound bed. A Prisma dressing with silver was placed, calamine lotion applied to the surrounding skin. The wound was further secured with dry sterile dressing (DSD), kerlix, ace bandage, and tube gauze. The patient was scheduled for a follow-up next week. Orders were placed for skilled nursing visits twice per week to perform dressing changes until the next appointment.

The second visit "one week" later and clinical reassessment

The patient was evaluated with no changes in her medical history or physical examination findings, apart from updates to her current vital signs and clinical wound assessment. As per standard protocol in our hyperbaric wound center, photographic imaging of the patient's leg wound was obtained during this visit. This imaging is routinely performed at each encounter for proof of payment documentation, risk management purposes, and to assist in clinical assessment and wound supply management [Figure 2].

The patient's recorded vitals on her second visitation were as follows:

Vitals

Height/length 63 in (160.02 cm); weight 150 lbs. (68.18 kg); BMI 26.6, temperature 97.3°F; (36.28°C); pulse 73 bpm; respiratory rate 20 breaths/min; blood pressure 139/54 mm Hg; capillary blood glucose levels: N/A mg/dL; and pulse oximetry: 96% O2 with oxygen supplement at rest.

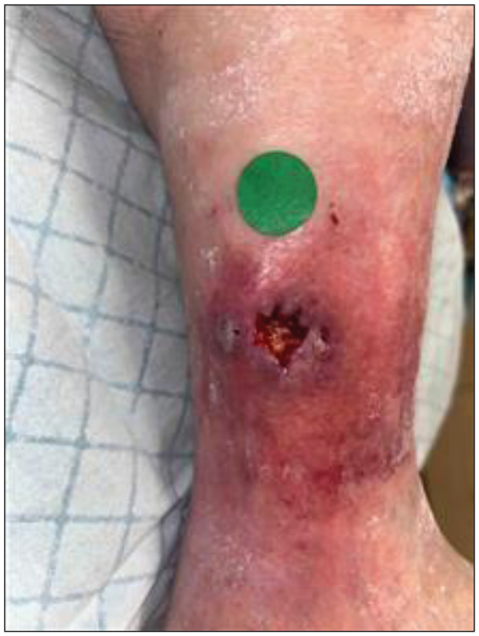

Figure 2: The photograph of the wound at the second clinical visit. Decreased periwound erythema and cellulitis and atrophic skin changes

Her wound care assessment was performed and recorded.

Wound assessment(s)

The wound on the right lateral lower leg is classified as full-thickness wound of indeterminate cause and was acquired on May 15, 2022. It remains nonhealing and was referred by a previous wound care center for surgical evaluation and potential intervention. The wound has the following measurements: 1.4 cm in length, 2.5 cm in width, and 0.2 cm in depth, with an area of 3.5 cm^2 and a volume of 0.7 cm^3. On examination, necrotic muscle, bone fragments, and adipose tissue are exposed. No tunneling, sinus tracts, or undermining are present. The wound characteristics were moderate serous drainage, with no odor. The patient reports wound pain level of 4/10. The wound margins are thickened and rolled under. The wound bed composition is 26%–50% bright red, spongy granulation tissue, and 26%–50% adherent yellow slough. No significant changes were observed.

The periwound skin exhibited edema and erythema consistent with exam done 1 week prior. No evidence of brawny induration, excoriation, callus, crepitus, fluctuance, rash, maceration, atrophy blanche, cyanosis, ecchymosis, hemosiderosis, pallor, or rubor. The periwound skin was friable and moist but not dry/scaly. The temperature of the periwound skin was cool to touch. There were no signs or symptoms of infection. Local pulse remains biphasic.

Return results of her ordered radiographic imaging studies (X-rays), microbiological tissue cultures, and tissue pathology of calcific tissue removed during debridement

The diagnostic imaging, laboratory microbiology, and pathology specimens ordered for the patient have been reviewed. While most findings did not contribute meaningfully to the diagnostic algorithm, the radiographic findings on X-rays provided clinically relevant information.

Radiographic images of the tibia and fibula (anterior posterior [AP] and lateral views) [Figure 3], the ankle (AP and lateral views) [Figure 4], and the foot (AP and lateral views) [Figure 5] were analyzed by an external radiology group near the patient's residence. The radiology report indicated diffuse calcifications in the soft tissue.

The initial tissue culture obtained during the first visit confirmed a polymicrobial infection. The wound was colonized by: *Klebsiella pneumoniae* subspecies pneumoniae, *Providencia stuartii*, and methicillin-resistant *Staphylococcus aureus*. Antibiotic susceptibilities for these organisms were determined and are detailed in the microbiology report [Chart 1]. The

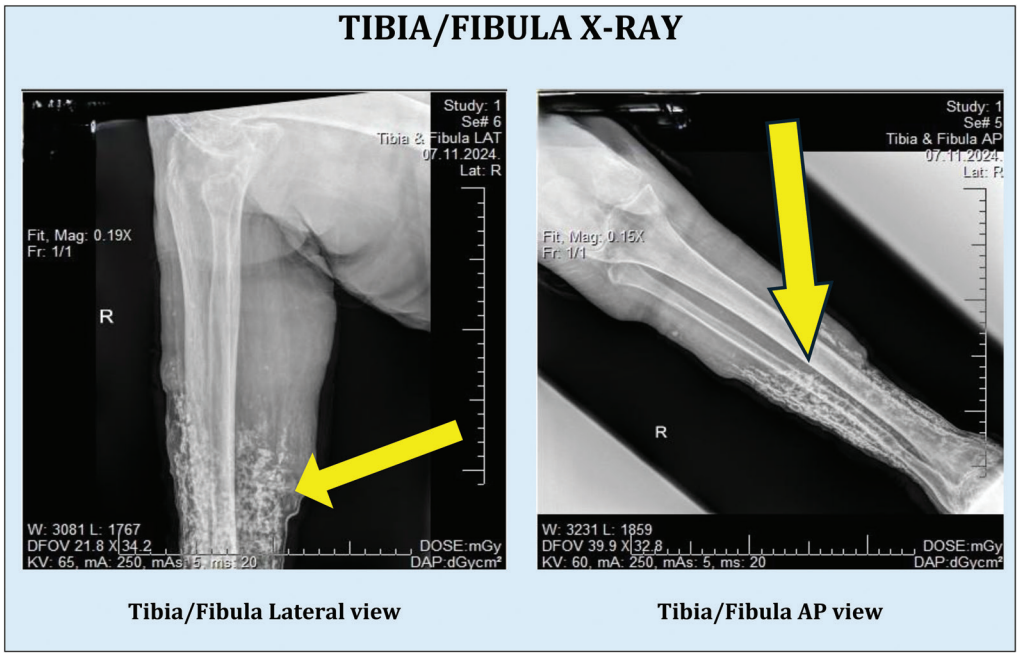

Figure 3: X-ray diagnostic of the right tibia and fibula lateral (LAT) and anterior posterior views. Yellow arrow showing diffuse soft tissue calcifications embedded within muscles of the soft tissue

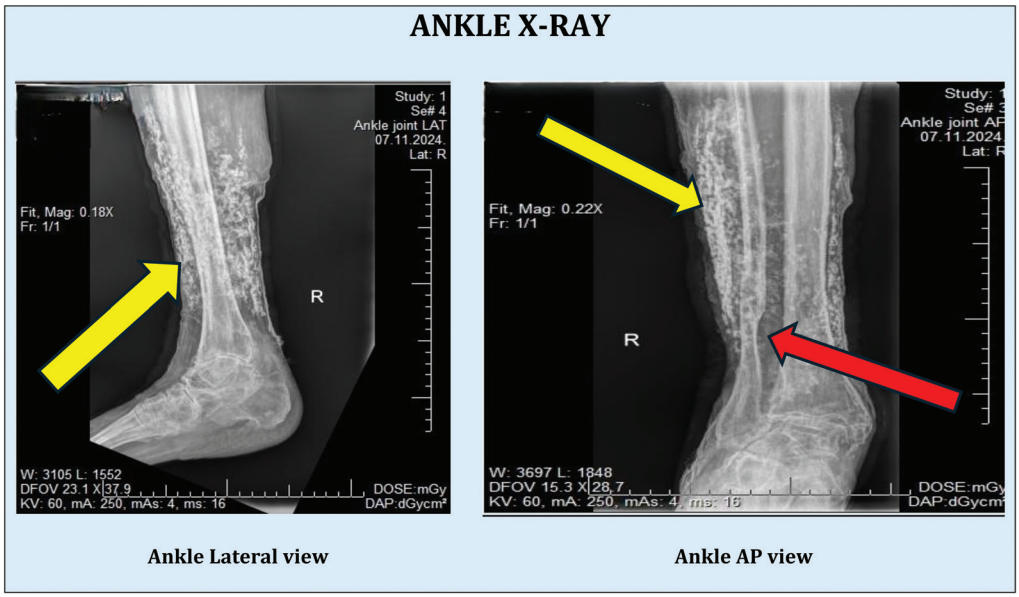

Figure 4: X-ray diagnostic of the right ankle lateral (LAT) and anterior posterior views. Yellow arrow showing diffuse soft tissue calcifications embedded within muscles of the soft tissue. The red arrow indicates old spiral fracture of the ankle

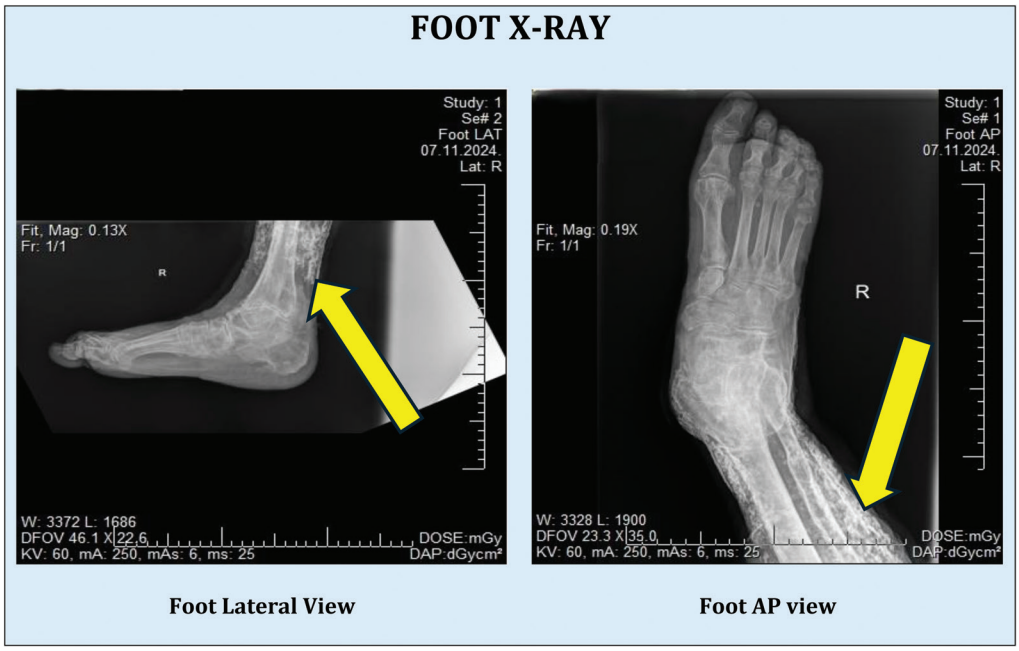

Figure 5: X-ray diagnostic of the right foot lateral (LAT) and anterior posterior views. Yellow arrow showing diffuse soft tissue calcifications embedded within muscles of the soft tissue

	A	B	C
1	Klebsiella pneumoniae subsp pneumoniae		
2		MIC Dilutn	MIC Interp
3	Ampicillin	>=32	R
4	Ampicillin/Sulbactam	16	I
5	Cefepime	<=1	S
6	Ceftriaxone	<=1	S
7	Ciprofloxacin	0.5	S
8	Extended -spectrum beta-lactamase	Neg	Neg
9	Gentamicin	<=1	S
10	Levofloxacin	1	S
11	Meropenem	<=0.25	S
12	Piperacillin/Tazobactam	16	S
13	Tobramycin	<=1	S
14	Trimethoprim/Sulfa	>=320	R
15			
16	Providencia stuartii		
17		MIC Dilutn	MIC Interp
18	Amikacin	<=2	S
19	Ampicillin	>=32	R
20	Ampicillin/Sulbactam	>=32	R
21	Cefepime	<=1	S
22	Ceftriaxone	<=1	S
23	Ciprofloxacin	>=4	R
24	Gentamicin	<=1	R
25	Piperacillin/Tazobactam	<=4	S
26	Tobramycin	2	R
27	Trimethoprim/Sulfa	<=20	S
28			
29	Methicillin-Resistant Staphylococcus aureus		
30		MIC Dilutn	MIC Interp
31	Benzylpenicillin	>=0.5	R
32	Clindamycin	<=0.25	S
33	Erythromycin	>=8	R
34	Oxacillin	>=4	R
35	Trimethoprim/Sulfa	<=10	S
36	Tetracycline	<=1	S
37	Vancomycin	1	S

Chart 1: Microbiology susceptibilities received

treatment plan addressed these infections with topical and/or oral antibiotics, alongside wound dressings containing silver to aid in antimicrobial management.

In addition, the pathological specimen of calcific material removed during the initial debridement was analyzed. However, the findings were inconclusive. The outcome of this analysis is noted below:

Pathology report received

Specimen (verified)

RIGHT LOWER LEG, BONE BIOPSY.

Diagnosis (Verified).

Bone, Right Lower Leg; Biopsy

-Bone tissue with necrotic changes and no evidence of acute osteomyelitis identified. -Superficial ulcerated skin tissue with acute and chronic inflammation, granulation tissue, and fibrin deposition is noted.

Gross description (verified)
Received in formalin, labeled with the patient's name and designated "right lower leg, bone biopsy." It consists of fragments of hard yellow bony tissue measuring 1.5 cm in aggregate. The specimen is submitted entirely in one cassette, after a brief decalcification. Final diagnosis determined by microscopic examination.

Laboratory testing

No blood testing was performed on the patient at this time.

Second treatment provided

Minimal debridement was performed, with careful removal of additional calcifications to preserve the integrity of the underlying tissue. The procedure continued until petechial bleeding was observed, at which point hemostasis was successfully achieved using direct pressure.

The wound was then treated with mupirocin 2% ointment combined with gentamicin sulfate 1% ointment, followed by coverage with Prisma dressing containing silver. The surrounding skin was treated with calamine lotion to maintain integrity and minimize irritation. The Prisma dressing was further secured with a DSD, Kerlix, an ACE bandage extending from knee to toe, and tube gauze.

Treatment orders were placed: for IV antibiotics ceftriaxone (Rocephin) and oral clindamycin to be initiated, and daily skilled nursing visits were ordered for IV antibiotic infusion and twice-weekly dressing changes. In addition, a referral was placed for a community-based infectious disease specialist to assess further management and to determine potential PICC line placement, contingent on the specialist's recommendation.

The diagnosis was made

The X-ray findings confirmed the clinical suspicion, leading to a diagnosis of MO. The condition is consistent with traumatic MO, attributed to an injury sustained 65 years ago. The initial trauma resulted in a spiral fracture following a fall on ice.

Third and final visit "1 week" later with clinical reassessment

The patient's history and physical examinations remained unchanged, except for updated vitals and the latest clinical wound assessment. The wound demonstrated significant improvement with a reduction in periwound erythema and cellulitis. As per standard protocol at our Hyperbaric Wound Center, the leg wound was photographed for documentation and risk management [Figure 6]. In addition, MolecuLight Imaging was conducted and recorded [Figure 7].

The patient's recorded vitals on her *Third* visitation were as follows:

Vitals

Height/length 63 in (160.02 cm); weight 150 lbs. (68.18 kg); BMI 26.6, temperature 96.7°F; (35.94°C); pulse 74 bpm; respiratory rate 17 breaths/min; blood pressure 110/62 mm Hg; capillary blood glucose levels: N/A mg/dL; and pulse oximetry: 98% O2 with oxygen supplement at rest.

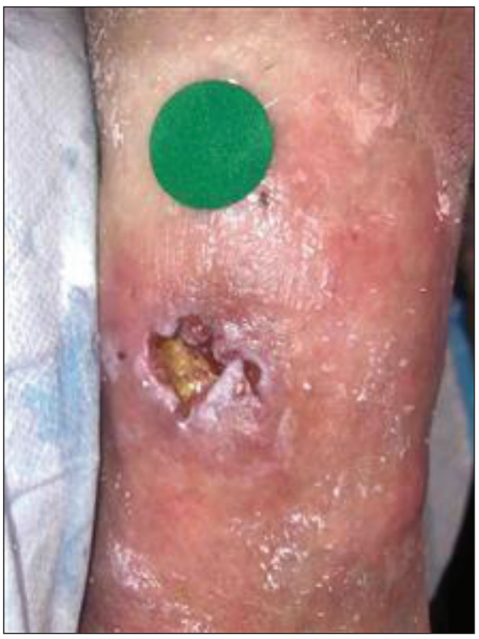

Figure 6: The photograph of the wound at the third clinical visit. Decreased resolving periwound erythema and cellulitis and atrophic skin changes

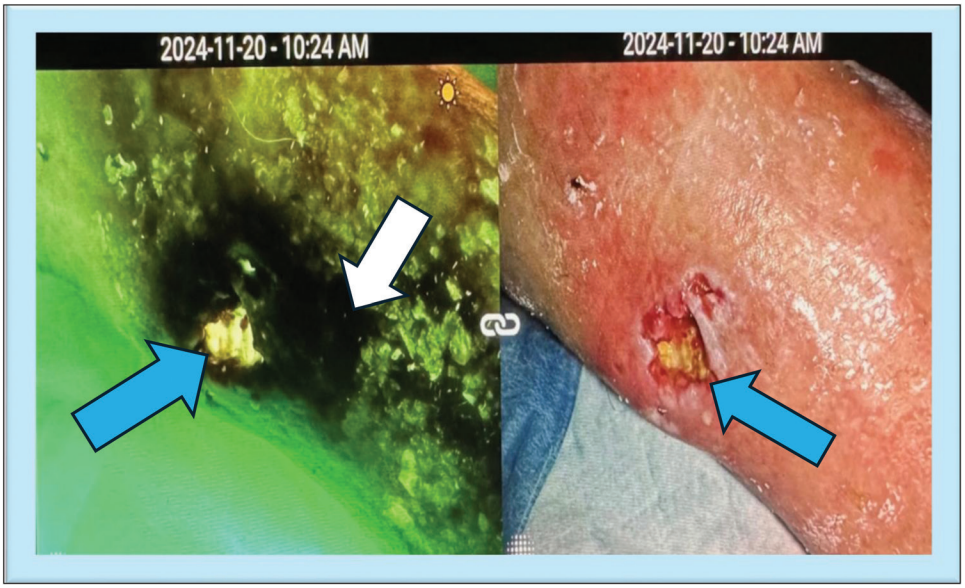

Figure 7: The photograph of the wound at the third clinical visit using MolecuLight Imaging device. The MolecuLight imaging also shows no signs of clinical infection within the wound itself, but the dark discoloration shows the inconsistent vascularity within the wound itself depicted by the white arrow. The light blue arrow indicates the presence of calcific deposits embedded within the soft tissue

Her wound care assessment was performed and recorded.

Wound assessment(s)

The wound on the right lateral lower leg is classified as a full-thickness wound of indeterminate etiology, acquired on May 15, 2022, and remains nonhealing. It was referred from a previous wound care center for surgical evaluation and potential intervention. The measurements of the wound are: 1.2 cm length × 1.2 cm width × 0.3 cm depth, with an area of 1.44 cm^2, and a volume of 0.432 cm^3. On examination, necrotic muscle, bone, or adipose tissue are not present. No tunneling, sinus tract, or undermining were identified within the wound or surrounding tissue. There is a moderate amount of serous drainage, odor not detected, patient reports pain level of 4/10, wound margins are thickened, and rolled under. The wound bed composition: 26%–50% bright red, spongy granulation tissue, and 26%–50% adherent yellow slough. No significant changes were observed in the wound's progression.

The periwound skin continues to exhibit edema and erythema, consistent with findings from the initial assessment 1 week ago. However, there are no indications of: brawny induration, excoriation, induration, callus formation, crepitus, fluctuance, rash, maceration, atrophie blanche, cyanosis, ecchymosis, hemosiderosis, pallor, or rubor. The skin remains friable and moist without signs of dryness or scaling. Its temperature is cool to the touch, and there are no signs or symptoms of infection. The local pulse remains biphasic.

The third treatment provided

The wound underwent minimal debridement utilizing Santyl, an enzymatic collagenase debriding agent. Following debridement, mupirocin 2% ointment was combined with gentamicin sulfate 1% ointment and applied to the wound bed. A Prisma dressing containing silver was then placed for additional antimicrobial protection. The surrounding skin was treated with calamine lotion to maintain integrity and minimize irritation. The Prisma dressing was further secured with ah a DSD, Kerlix, and an ACE bandage extending from the knee to the toe, with tube gauze providing additional stabilization.

The patient and her family have elected to transition to Hospice care, prioritizing comfort measures to be administered exclusively at home moving forward. Consequently, she will discontinue follow-up appointments with our facility and will receive palliative care under home-based management.

Case Discussion

A discussion of the long-term treatment provided in this case must be had, in the fact that, such previous wound debridement's over time may have been contra-indicated as a treatment modality on this patient's behalf and may have exacerbated the potential for doing greater harm and accelerated her degenerative condition by worsening it. When we look at literature concerning MO they are consistent in their recommendations and approaches to the treatments that are being offered, especially surgical debridement or in this case wound debridement's which are considered surgical treatments in nature, should not have be undertaken unless there is severe pain a decrease in mobility or if the lesions must be differentiated from lesions that are malignant and neoplastic in nature, which

it often mimics early on in its onset and thus the coinage of this medical condition being referred to the "*do not touch*" lesion.[4,10] Because of the existential potential in doing greater harm and its potential as a life-threatening disease, these patient's pose a severe diagnostic and therapeutic challenge to the medical practitioner.[15-17] This case is no exception, in that the clinical parameters invoked in the diagnostic work up of the patient (though limited) in conjunction with the resultant findings which were offered in the patient work up did not help to provide a definitive diagnosis of MO, and it was an outright incidental finding that was made and supported based on clinical diagnostic radiographic features and through history obtained from the patient. The radiological X-ray findings showing diffuse calcific heterotrophic bone growths within the soft tissue of the lower extremity and the clinical interrogation of the patient through her history obtained indicating a history of trauma that occurred as result of slipping on ice 65 years prior; the two only facts and clues that allowed us as her practitioner's to connect the dots and gave us the opportunity to elucidate her underlying cause of her wounds as an incidental pathological result of being afflicted with MO traumatica that she presented with.

It is because of this potential for error and misdiagnosis that a knowledge-based discussion of what constitutes this medical condition, and a thorough review must be had on how a diagnosis of this disease can be made correctly to avoid such mishaps in the future, with patients that may present to us for examination and treatment. In addition, it will allow us as practitioners to develop treatment plans that are patient specific, less invasive, less costly, and less risky for the patient over time. Finally, current treatments for this medical condition must also be discussed to aid medical practitioners in their armament in giving patient's afflicted with this medical condition: hope and options to their care, limited though they may be. Empowering practitioners and patient's with the correct knowledge so that patients can make informed decisions concerning their health and their bodies, and to which treatment options practitioners must consider often multidisciplinary and to which patient's must ultimately consent and commit too.

What we "do know" about myositis ossificans

MO, although a debilitating disease is often considered a self-limiting disease characterized by non-neoplastic benign solitary lesions of heterotrophic bone formation and cartilage within the muscle(s) itself but can also affect ligaments, fascia, and surrounding soft tissue.[1-5,7-10,13,17-20] Most frequently affecting individuals in their second and third decades of life[6,21] and affecting males more so than their female counterparts.[6,18] These lesions occur most frequently in larger skeletal muscles such as the brachialis, quadriceps, and the adductor muscle groups. The muscles typically affected most commonly are areas of the arms and the extensors of the thigh.[1,19] More specifically the brachialis of the upper extremity is most affected and the quadriceps femoris and gluteus are the most common lower extremity muscles being affected and typically present more in the anterior compartments than the posterior ones.[6] They have also been found in lesser common anatomical areas such as the neck, scapula, axillary region, hand, foot, chest, and abdominal wall.[6] In addition, they have also been associated with masticatory muscles such as: the masseter muscle, temporalis muscle, and the medial pterygoid muscle.[3] Consequentially, in theory, no muscle, tendon, or fascia is immune to such formations if the cellular conditions are ripe for its development despite not being well understood as to how this cellular mechanism and processes transpires and can be area of further investigation for future research.

MO has been described as early as 1620's into the 1700's and in 1905 by Jones and Morgan who questioned whether a benign ossifying tumor following trauma was a true inflammatory neoplastic entity.[22] Later in the century three classified types were published in 1923 by Lewis[17,23]. Lewis[23] described them as MO nontraumatica, traumatica, and neuritis.[17] A year later (MO) was described by Noble in 1924,[4] who categorized the subtypes as myositis(fibrous) ossificans progressive, traumatic MO circumscripta, and MO circumscripta without history of trauma.[17] These two long lasting categorizations of MO were recently redefined once again and updated by the WHO which now recognizes four types of MO. These types of MO are: 1) MO traumatic/post traumatica/circumscripta; 2) MO associated with paraplegia; 3) nontraumatic/pseudomalignant MO; and 4) progressive MO (also known as fibrodysplasia ossificans progressive (FOP) – which is hereditary and more severe generalized form).[17]

Etiology

Traumatic MO typically results from a direct blow or repeated minor trauma to an area and almost never reported after strain injuries.[2] The etiological cause being attributed to mechanical injury to the soft tissue, ischemia resulting in the soft tissue from the trauma experienced and inflammatory cascade that has been initiated after the onslaught of the initial injury.[9] This type occurs most frequently in 60%–75% of the cases reported of all MO types and can occur at any age but most commonly is seen in adolescents and young adults, usually as result of sporting injuries.[2] Of the remaining cases 25%–40% resulted from nontrauma associated incidences and paraplegia, and even less of those were the progressive MO type. Nontraumatic MO (MO associated with paraplegia and nontruamtic/pseudomalignant MO) often-times are associated with burns, hemophilia, other clotting disorders, and neurological disorders such as paraplegia and poliomyelitis and sometimes even infections.[2,4,5,17,24] They can also occur after surgical operative procedures

such as total hip or total knee arthroplasties or any other minor invasive surgical procedure.

Progressive MO or FOP is a hereditary autosomal dominant condition caused by activating mutation of bone morphogenic protein signaling known as activin receptor A, type I (ACVR1) a bone morphogenetic protein (BMP), and type 1 receptor in all affected individuals.[25-30] These FOP affected individuals appear normal at birth with the exception of characteristic malformations of their great toes/hallux's that are present in all individuals afflicted, such malformations can include but are not limited to hallux valgus deformity bilaterally, lack of toe creases at the metatarsal phalangeal joints, and in some cases macrodactyly.[26,31] This inherited disorder has an incidence in the population of around 1:10,000,000 annually and irrespective of race, gender, ethnicity, or geographic location.[31,32] In 2006, the University of Pennsylvania School of Medicine, identified the exact molecular basis of FOP. The root cause was activating mutations in the activin receptor A type 1 gene (ACVR1, also referred to as the activin receptor-like kinase 2, ALK2), which codes for a BMP type 1 receptor and occurs in every individual afflicted with this disease and is without a doubt the proximate cause. The *ACVR1*/*ALK2* gene has been mapped to chromosome region 2q23q24 by linkage analysis[33,34] and by fluorescence *in situ* hybridization.[33,35] The penetrance of the *ACVR1*/*ALK2* gene is complete and usually arises *de novo*.[31] It should be noted, however, that most patients presenting with toe malformations and heterotrophic ossification (HO) share the same heterozygous mutation in the *ACVR1*/*ALK2* gene (c.617G>A; R206H); this mutation is identified in more than 97% of affected individuals.[31] Recently, other pathogenic variants have been identified within the *ACVR1*/*ALK2* gene complex and involve the glycine-serine-rich domain or in the protein kinase domains of the gene itself.[31] Both the *ACVR1*^{R206H} mutation and all the variants reportedly show mild constitutive activity and *in vitro* enhanced ligand-dependent activity of BMP signaling processes.[31] This allows for the dysregulation of the BMP signaling pathway and is known to be responsible for modification of osteochondrogenesis, that is, believed to cause musculoskeletal phenotype of FOP that we as clinicians see.[31,35] A possible model of BMP signaling pathway disruption in FOP proposes that BMPs bind to complexes of type I and type II serine/threonine kinase BMP receptors (such as ACVR1) on the cell surface to activate intracellular signal transduction through R-SMADs SMAD1/5/9(8).[31] Phosphorylated R-SMADs form a complex with the comediator SMAD4, which translocates into the nucleus of cells and thus regulates transcription that drives endochondral ossification processes and potential over growth seen in the soft tissue radiographically.[31] Interestingly, recent studies established the role of inflammation in HO genesis and propagation in FOP patients. Specifically, it has been shown that activin A, which is expressed by innate immune system cells, plays an important role in both promoting and resolving inflammation, particularly by blocking ACVR1^{WT} signaling. Activin A is effectively perceived as a BMP ligand by ACVR1^{R206H} leading to downstream BMP signaling through SMAD1/5/9(8), thus responding to activins A, AB, AC, and B, to which the wild-type ACVR1 is unresponsive[31,36] giving us possible credence to the notion of inflammation being an underlying pathological cause for MO.[9,11]

Histologic phases

No matter the type of MO encountered, there are three histological phases or changes that occur and are recognized as occurring cellularly and a understanding of them may give us an insight to this mysterious process which could help us understood what transpires histochemically in this disease process and could potentially shed light on some potential areas for further investigative research that could lead to more treatment modalities that could potentially target such cellular mechanistic changes that seem to be occurring in MO.

These stages are known to be the early stage/phase, the intermediate stage/phase, and the late stage/phase.[6,10] In the *Early Stage*/*Phase:* this occurs usually in the first 4 weeks and is characterized by active mesenchymal proliferation of fibroblasts.[2,6,10,37] These fibroblasts are SOX9, SOX10 an alpha smooth muscle actin (SMA) positive which conforms to their ability to migrate, and possibly allow for these cells to line the bone lamellae before differentiating into osteoblasts.[38,39] These cells have significant mitotic activity along with cellular hemorrhaging and necrosis.[6,37] This process often is characterized by the inflammatory cascade and cytokine release that occurs without evidence of calcification.[10,40,41] It has also been suggested that stromal cells may also be recruited from the bone marrow vessels. These cells which are known to be of vascular origin can exhibit a potential to differentiate themselves as an endochondral ossification pathway, highlighting the plausibility of endothelial-mesenchymal transition that occurs to allow for the development of heterotopic bone formation.[42]

In the *Intermediate Stage*/*Phase:* the heterotrophic osteoblasts appear producing the osteoid matrices that form the fibrous capsules that we recognize as pathologic "zone of phenomenon."[2,6,10,40,41,43] This stage consists of three independent zones that are distinctly different in appearance and recognizable. The first is the *central zone*, which consists of mesenchymal tissue, fibroblasts, mitoses, hemorrhage, and necrosis.[6,43] The second zone is known as the *intermediate zone* and consists of osteoblasts and immature bone islands. The third and final zone consists of traces of mature bone.[6,10,40,41,43] This ossification occurs and seems to occur centripetally.[6,43]

Lastly the *Final Stage/Phase:* the final stage begins and typically occurs around the 6th to the 8th week or even earlier and is where peripheral bone formation begins. This continues to occur and in and around the 5th to the 6th month is where these types of lesions begin to completely ossify and become the hallmark of MO presentation that we see radiographically or in other radiological modalities used. These lesions develop cortex and marrow spaces and typically shrink in size about 30% and can resolve spontaneously.[2,6,10,40,41,43]

Clinical presentations

Clinical presentation of these patient may be predicated of having the following risk factors such as: male gender, past history of having formed heterotopic bone, hypertrophic osteoarthritis, ankylosing spondylitis, diffuse idiopathic skeletal hyperostosis, and or any of the cellular stages previously discussed.[1,44] The presence of anyone one of these and the activation of any component of the cellular cascade of probable events mentioned already or the presence of the gene itself (which has been mapped) provides the impetus for the mechanisms in question and the resultant findings made in the presentation of MO patients seen by the to the medical practitioner to who they have chosen or been referred too.

The clinical presentation is highly variable.[8] Typically, in MO traumatica/post traumatica/circumscripta they are found through incidental findings on radiological imaging studies conducted as was in our case presented. It may also rely on relevant patient history, such as trauma or overuse of soft tissue, clinical symptoms such as hematoma, soft tissue masses, acute pain, swelling with restricted motion, histological examination, biopsy, or laboratory tests that indicate its presence.[9,22]

In MO non traumatica or pseudomalignant types the presentation too may also be variable. These patients will not have an interrogative history of trauma associated with it. They may present with the clinical symptoms of localized pain and swelling, functional limitations *without a history of trauma*, occupational difficulties due to lack of mobility, limb length discrepancies which cause ossificans that limit mobility[45] or may have a history of malaise and fever and soft tissue masses. They can have a history of nerve impingement or even surgical procedures such as total hip or total knee replacements. In these patients radiological results or histological examination, biopsy, or adjunctive laboratory testing may afford some type of clue to its presence.[9]

In patients with MO in paralysis/paraplegia they *may or may not have history of trauma associated*. They may have a flaccid appearance or not, experience worsening pain and swelling over time, they may develop restriction of motion due to lack of innervation, developing soft tissue masses and thus a resultant loss of motion with contracture of extremities and joints and may experience increased pressure from their immobility and when combined with the pervious history of trauma which may have been the underlying causative factor of their neuronal damage or not. These neurological sequelae of trauma damages caused may continue to persist on the cellular levels; in addition the causative agents of their neuronal disease processes may also predicate the development of MO in these patients.[46] It was recognized in 1918 by Dejerine and Gillier who noted that 48% of paraplegic and quadriplegic patients had in fact, heterotopic bone formation in their spinal cord injuries.[46,47] These patients like all other MO patients may also be suffering from fever with unknown origin, malaise, abnormal: radiological findings, biopsy, and/or laboratory findings as well.

Finally in those patients with FOP or progressive MO, a hereditary autosomal dominant condition caused by activating mutations in the activin receptor A type 1 gene (ACVR1, also referred to as the activin receptor-like kinase 2, ALK2), which codes for a BMP type 1 receptor and occurs in every individual afflicted. The ACVR1/ALK2 gene has been mapped through linkage analysis to chromosome region 2q23q24.[3,33] These FOP affected individuals appear normal at birth with the exception of characteristic malformations of their great toes/hallux's that are present in all individuals afflicted, such malformations can include but are not limited to hallux valgus deformity bilaterally, lack of toe creases at the metatarsal phalangeal joints and in some cases macrodactyly. In 50% of cases even the pollicis (thumbs) can be affected along with the deformity within their feet.[26,31] They may exhibit difficulty walking, unsteadiness on their feet, frequent falls, and/or abnormalities of gait and mobility accentuating the condition. In addition, they may exhibit clinical flare ups which occur randomly or even after bumps and falls that may occur. These flare ups can last weeks and often are associated with pain and swelling with decreased mobility of the joints. In decreased mobility scooting rather than crawling may be exhibited along with decreased ROM of joints with pain and even complete immobility with locking of the joints themselves because of fusion (ankylosis). Patients may also exhibit decreased in eating and speaking with associated weight loss due to joints of the oral cavity being affected. They can experience hearing loss due to the bones of the ear and inner ear being affected by heterotopic bone formation. Finally, they can experience secondary complications due to respiratory infections resulting from thoracic insufficiency syndrome which causes problems with the rib cage over constricting and thus decreasing tidal lung capacity and thus lung volume capacity which enhances the risk of respiratory infections overall. Finally, other symptomology clinically can present such as: proximal tibial osteochondromas, cervical spine malformations, hypercalcemia, nephrolithiasis risk, alopecia (decrease in hair and eyebrows), cognitive impairment, Marfan

phenotype, childhood glaucoma, cryptorchism, diffuse scalp thinning, short broad, and femoral necks.[31] They may also be subjected to any of the clinical findings found in the other types of MO presented thus far.

How to Make a Diagnosis

Complete patient history

Due to the complexity of diagnosing MO and its subtypes, the diagnosis is largely dependent on the practitioner's expertise. It requires a comprehensive evaluation of the patient's personal and familial history, along with any other clinically assessed investigations and treatments. In addition, any prior trauma, regardless of its perceived insignificance, must be considered.

Radiographic imaging studies

Radiographic imaging is important in patient diagnostic work up, such as the use of ultrasound (US) images and X-rays, which in the initial work up of the patient may be a good low-cost alternative. We can progress to more expense modalities later such as the use of bone scans, computed tomography (CT), magnetic resonance imaging (MRI), and even positron emission tomography (PET) scans when indicated or when the diagnosis of MO is more difficult to elucidate or when a differential diagnosis must be made to avoid misdiagnosis or confusion with more serious neoplastic disorders such as malignancies. Bone scans and PET scans can help to distinguish between infectious abscesses versus malignancy.

Early in the disease the use of US or X-ray's may be a good prognostic indicator helping in distinguishing the difference between cystic and solid soft tissue masses, that patients may be afflicted with.[10] It is also more sensitive for use in early detection of peripheral calcifications that seen in MO.[48] The US can also be used to see the zonal pattern seen in its histological presentation discussed in the intermediate stage/phase previously discussed.[10] CT imaging can also be helpful in the early stages/phases than in the later stage of MO whereby MRI may be more efficacious.[9,49,50] In the early stages of MO, the MRI may be confusing to the practitioner interpretating the images,

MO Imaging Modality vs Histologic Features/Phases

Phases:	Early Phase	Intermediate Phase	Later Phase
Imaging Types:			
X-rays	Soft tissue opacity Nothing	Calcifications are fluffy Calcified rims Separated from bone	Complete mineralization Rim calcified
Ultrasound (US)	Nonspecific Soft tissue mass	Alternating hypointense and hyperechoic zones* Increased Doppler Signal in hyperintense region	Hyperechoic lesion with thick acoustic shadows[51] Decreased Doppler Signal as go out further
Computed Tomography (CT)	Nonspecific hypointense soft tissue mass	Calcified Rim String Sign Clear separation from bone	Calcified Soft Tissue Mass
Magnetic Resonance Imaging (MRI)	Nonspecific Soft tissue mass Striated muscle Edema	Peripheral Calcifications (Decreased Signal IntensityT1/T2 weight images) Edema seen (Increased T1 weight images) in adjacent muscles	Thick Calcifications noted Thick Ossifications Noted Edema of the adjacent muscle subsides
3 PHASE BONE SCANS	Hypervascularity without arteriovenous shunting or puddling	Not applicable or useful Decreasing uptake	Not applicable or useful Decreased uptake
PET SCAN	Using [18F]/[68Ga] or combo Hyperintense illumination	Using [18F]/[68Ga] or combo Hyperintense illumination decreases	Using [18F]/[68Ga] or combo Hyperintense illumination decreases

Chart 2: Imaging modality features found in myositis ossificans in the corresponding histologic phases[10,51]

in early MO on MRI there seems to be a consistent *"striate pattern"* or *"checkerboard-like pattern,"* that is, seen [Chart 2].[7,9]

If one understands the corresponding stage of MO, then imaging can be appropriately ordered. For example, in the early stages/phases (<4 weeks), the presence of fibroblasts and myofibroblasts is present and more amenable to US, X-ray, and biopsies. MRI would be difficult at this stage/phase because it's nonspecific and mineralization that needs to occur is not present now in the disease process.[10] In the later stage/phase or middle stages/phases (4–8 weeks), MO is characterized by more osteoblastic activity and zones become more mature bone these now are more visible in X-rays and in MRI's. But in the later phase of (>8 weeks), cells mature further becoming more mature bone and are better visualized on X-ray and CT imaging.[9] It should also be noted that another distinguishing radiological feature that occurs in MO is edema that surrounds the main lesion in acute and intermediate states of the disease and is not found particularly in sarcomas which it can mimic [Chart 2].[10]

Three phase bone scans can also be used with ^{99m}Tc-hydroxymethylene diphosphonate and can show hyperemia in soft tissue.[52] The bone scan test is both a combination of radio nucleotide angiogram and immediate postinjection blood pooling image and a 2–3 h delayed image.[53] These images help in distinguishing and in differentiation between osteomyelitis, cellulitis, septic arthritis, thrombophlebitis, deep vein thrombosis, and early MO as in case report by Drane W.E of 28-year-old female paraplegic diagnosed with MO after having shot herself in the abdomen.[53,54] Hyperemia seen in MO is not uncommon finding. Arteriography has been a useful tool in distinguishing MO from malignant tumors.[53,55,56] During the active phase of MO, a hypervascularity can be seen and is seen without arteriovenous shunting or puddling.[53] This hypervascularity, that is, seen will regress as the disease progresses and thus the need for serial three phase bone scans done weekly has been advocated.[53,54] However, it must also be noted that arteriography is not as useful as the radionucleotide imaging in the staging of MO disease activity.[53,55,56] Further noted there has been no report of arteriography as useful tool in the early diagnosis of MO and has not been reported [Chart 2].[53]

PET scans/CT using 18F-fluorodexoyglucose ([18F]-FDG) is becoming widely adopted imaging modality to detect hypermetabolic lesions because of due to their increased glycolytic metabolic activity.[57,58] More so, with the advent of new PET tracers such as [18F] or [68Ga] can feature fibroblastic activation protein (FAP) inhibitors (FAPI) that are distinctly enhanced in the early phases of MO (due to their fibroblastic activity that occurs in the early stages/phases). FAPI compounds demonstrate an affinity to binding FAP, a transmembrane serine protease exhibiting heightened expression in activated fibroblasts, which occurs histologically in early phase MO.[57,59] This may be an indication that uses although limited in PET scan technology combined with CT/MRI/X-rays as new tracers such as [68Ga] combined with older tracers [18F] may help potentiate diagnosis of MO especially when histories of trauma exist. They may also help illuminate differential diagnosis's where other inflammatory processes are occurring such as osteomyelitis, abscess, other myopathies, ankylosing spondylitis, and especially when differentiating from neoplastic malignancies which should always be done in conjunction with either needle biopsy or surgical biopsy (the gold standard). Working through such differential diagnosis of lesions such as these which can be encountered will help to distinguish them allowing for a diagnosis of MO and its subtypes to be made [Chart 2].

Lab tests

Although, there are no specific tests for MO except for genetic identification of FOP localized to the gene which has been mapped to chromosome region 2q23q24. The other clinical laboratory tests can be helpful at times to diagnosis MO especially when trying to differentiate it from other pathological causes. Such laboratory tests that become important are complete blood count (CBC), creatine phosphokinase (CPK), creatine kinase (CK), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), alkaline phosphatase (ALP), antinuclear antibodies (ANA), prostaglandin-E2 serum levels (PGE2), and aldolase (ALD).

CBC although not specific for MO can be used to help differentiate it from infectious or inflammatory causes.

CPK is an enzyme found in the brain, muscles, and heart tissue. It is especially important when considering muscle damage.

CPK is extruded from muscle when the muscle tissue is damaged and thus gets released into surrounding soft tissue and into the blood stream. Increased levels are found in myopathies and in MO and at levels above 200 U/L are often found. In active MO these levels may be higher.[60]

CK like CPK is a muscle enzyme, that is, released when muscles become damaged and are released into the surrounding soft tissue and then the blood stream. This enzyme is indicative of the type of muscle damage that has occurred and is more significant with damage which is more extreme and can exceed normal limits dramatically. This enzyme is also a good prognostic indicator of the activity of disease when MO is present. It is also affected by gender, age, recent physical activity, and other conditions that may be affecting the individual and may vary with

other myopathies seen in those patients. It should also be noted that these CK levels can also be normal, and MO can still be present.[61]

CRP is a substance produced by the liver in response to inflammation present. It is a traditional marker for infections, autoimmune disease and inflammatory disease processes, of which MO is one of them. It is characteristically elevated in MO patients and has been repeatedly used as biomarkers for MO patients being treated and whether they in are in active early stages/phases or in later stages/phases where by bone deposition and maturation is occurring. It must be noted that this is not specific for MO but rather incidental finding.[61]

ESR is often used as marker of inflammation and can be used to help distinguish between osteomyelitis, malignancy, and other inflammatory disease processes. In MO patient's, the ESR will be elevated when patients are in active flare-up or in inflammatory stages such as early staged MO and often used as indicator of response to treatment.

ALP is an important indicator of liver and bone health in people and is often affected and elevated in pregnancy, liver disease, bone disease, dietary choice, inflammatory disease, and bone fractures. They are decreased in thyroid disease and malnutrition. In early MO serum, ALP may remain low and thus not helpful. In post onset, the ALP levels may begin to rise at about 3 weeks as the inflammatory process begins and as osteoblastic activity in MO starts to take place.[61] At about the 10th week as MO progresses, the ALP levels peak. Again, this is not a specific test for MO but can be used as an indicator. In the later phases of MO, ALP begins to fall as mature ectopic bone is deposited.

ANA are present in autoimmune diseases that include idiopathic inflammatory myopathies such as polymyositis and dermatomyositis. The ANA can be used as screening tool of these conditions more specifically for autoimmune processes, of which MO is one of them with >95% sensitivity. However, more specific MO antibodies do exist and are expensive tests to run. Errors can occur and you can have MO positive patients that do not exhibit ANA presence and are falsely negative and for this reason they are nonspecific for MO.

PGE2 can be measured in both the urine and the serum unlike all the test discussed thus far which are found in serum only. PEG2 is an indicator of the inflammatory cascade as it is released in tissue injury which is hallmark in MO. It is involved with mediating vascular responses that occur in tissue injury and assists in bone formation, more specifically ectopic bone formation through osteoblastic activity as seen in MO.

ALD is present in muscle tissue and plays a significant role in glycolysis. This enzyme again is released into the tissue when muscle cells are damaged. They represent the extent of muscle damage and inflammation. Combined with all the other tests above, a better picture can be obtained in difficult to diagnose patients affected by MO.

Other tests less utilized for MO include alanine aminotransferase, anti-PM/Scl-100 antibody EIA, aspartate aminotransferase, cytosolic 5'-nucleotidase 1A (cN-1A) antibody IgG, fibrillarin (U3 RNP) antibody IgG, interstitial lung disease panel, Jo-1 antibody, lactate dehydrogenase, myositis specific 11 antibody panel, Sjogren's antibody (SS-A), and Sm/RNP antibody.

Histochemical markers can also be helpful such as osteoblastic markers such as SMA and special AT-rich binding proteins 2 (SAB2). Markers that identify progenitor cells can also be used such as bone morphogenic protein 4, RUNX2, OCT-3/4 SOX9, SOX 10, and transforming growth factor-beta.

Finally, aspiration or tissue biopsy, or surgical excision biopsy may be warranted but may not be conclusive. It may help in differentiating MO from neoplastic malignancy or other discernable diagnostic entities. However, great care must be had early in MO whereby biopsy may afford the wrong diagnosis when trying to ascertain it from its malignant counterparts which MO may mimic early on such as in the case of Osteosarcoma or potentiate the possibility of worsening the disease by those afflicted.

Differential diagnosis possible

Differential diagnosis must be considered promptly because MO can resemble other conditions, such as neoplastic malignancy, in its early stages [Chart 3]. Conducting a biopsy at this stage may lead to an incorrect diagnosis favoring neoplastic malignancy. Consequently, clinicians must exercise thoroughness and maintain a comprehensive understanding of differential diagnosis and testing. This approach helps in eliminating and narrowing down possibilities through detailed patient interviews and objective findings from physical examinations. A chart summarizing diagnostic possibilities have been provided to aid in identifying conditions that need review, and a personal algorithm should be developed by clinicians to help them narrow down the possibilities early on with appropriate testing which aims for an accurate diagnosis of MO early on [Chart 3].

Treatment and management options

Treatments for MO patients range from conservative methods such as immobilization, physical therapy, and medication to surgical management through excision of the masses. Surgery is considered a last resort as it can potentially exacerbate MO over time. Initially, simple measures are most effective. In the absence of fractures, patients should adhere to rest, icing, compression, and elevation. The avoidance of contact sports or work,

MO POTENTIAL DIFFERENTIAL DIAGNOSISES	
NON-MALIGNANT	**MALIGNANT**
Tophaceous Gout Vascular lesions: Phleboliths, DVT Hemangioma Calcium hydroxyapatite disease Periosteal Chondroma/ Juxtacortical Chondroma Synovial Chondromatosis Hoffa's Disease Tumoral Calcinosis Lipoma with metaplasia Calcifying aponeurotic fibroma Calcific myonecrosis Ancient schwannoma Castleman's disease Infectious osteomyelitis Abscess	Sarcomas Extra skeletal osteosarcoma (EO) Parosteal osteosarcoma (PAO) Periosteal sarcoma (PEO) Rhabdomyosarcoma (RS) Ewings Sarcoma (ES) Osteosarcoma Synovial Sarcoma (SS) Malignant Fibrous Histiocytoma or undifferentiated Pleomorphic Sarcoma (UPS) Chondrosarcoma Osteochondroma Nodular fasciitis Metastatic disease Lymphoma

Chart 3: Summary of potential differential diagnoses for myositis ossificans

overstretching of soft tissue and muscle-induced fatigue activities should be avoided. Immobilization can be achieved using casts or modern bracing systems, including orthotics or prosthetic devices, to reduce flare ups, pain, and swelling.

Pharmacotherapy includes the use of magnesium, acetic acid,[8,44,62,63] Nonsteroidal anti-inflammatory drugs such as ibuprofen, indomethacin, meloxicam, and naproxen. These medications work by affecting and inhibiting the inflammatory cascade through the inhibition of prostaglandin production, which is responsible for pain, fever, and inflammation attributes observed in MO patients. In addition, corticosteroids, including Kenalog and dexamethasone, as well as bisphosphonates such as etidronate disodium[8,62,63] and diphosphonates such as ethane-1-hydroxy-1,1-diphosphate, are employed. Oral medications can be complemented by injectable versions but should be avoided because injections may further activate the inflammatory cascade associated with MO, exacerbating the condition.[54] These pharmacotherapeutic agents may be employed throughout the progression of the disease, especially during exacerbations. Where patients with FOP experience significant steroid resultant bone loss due to therapy, aminobisphosphonates are indicated. A new class of pharmacotherapeutic agents, such as tyrosine kinase inhibitors used in myeloid leukemia patients, including imatinib, is significant for inhibiting mast cell responses that may play a role in MO patients and should be considered in practitioner related treatment armamentarium.[31,64]

Physical therapy may include interventions such as stretching exercises, passive stretching exercises, muscle strengthening exercises, ROM exercises and balance exercises along with or combined with US, electrical shockwave therapy, transcutaneous electrical nerve stimulation, and iontophoresis using magnesium or acetic acid may be indicated and help MO patients.[8,62,63]

Surgical biopsies (the gold standard) or surgical needle aspirations should be avoided unless necessary to ascertain a diagnosis or to exclude neoplastic malignancy. Surgical interventions beyond biopsy or aspiration should be considered only as a last resort due to the potential risk of aggravating the condition and should be conducted when bone is fully matured as judged by and supported by the presence of cortex on radiographic imaging, 6–12 months after the onset of the inciting event.[4,8,65-67] Furthermore, surgery should be pursued exclusively if the patient's life is at risk or if the contracture or decreased mobility of affected joints significantly impairs their activities of daily living. In such cases, minimally invasive techniques or robotic-assisted surgery are preferred. It is crucial to minimize extensive excision of masses and tissue manipulation, including procedures such as flaps, skin grafting, and wound debridement. Careful handling and preservation of surrounding and underlying tissues during the procedure are essential to reduce the risk of further harm to the patient. It has also been suggested if surgical intervention is done too early the reoccurrence rates are high.[8,68,69] Finally, it has been recommended that following surgery short doses of radiotherapy be conducted to help in minimizing postoperative pain and help to restore mobility much sooner.[8,70,71]

Conclusion

This article presents an unprecedented case of wound care involving the incidental finding of MO traumatica/post traumatic/circumscripta. It details a lower extremity wound care case where MO was identified as the underlying pathological cause of the clinical wounds. The remainder of the article includes an extensive literature review with concurrent discussions that offer a definition of MO, its types, incidence, etiology, pathophysiology and histopathology, radiographic diagnostic characteristics, differential diagnoses, laboratory presentation, and concludes with a discussion on current treatment options available.

Through this discussion, it is demonstrated that MO poses significant long-term challenges in its diagnosis from a clinical perspective. These challenges impact not only the quality of life but also the functional abilities of those afflicted. Functional impairments may include, but are not limited to, restrictions on the ROM, work performance, social interactions, and psychological well-being, with increased anxiety and depression. This condition also has occupational impacts, such as decreased work efficacy and financial return for patients suffering from the disease.[6]

Furthermore, the article highlights the overall costs associated with managing MO, encompassing medication, laboratory tests, and rarely invasive surgical interventions, when necessary, as well as emphasizing a multidisciplinary approach to care.

Through the discussion of MO and its presentation herein, it is evident that more studies are needed to understand this disease in areas for target therapies. Such therapies requiring further investigation include ALK2 inhibitors. One such drug is saracatinib, a kinase inhibitor that targets scr-family kinases initially developed for solid tumors but also known as potent ALK2 inhibitors. In addition, ALK2 ligand prevention and mammalian target of rapamycin (mTOR) have been identified as key factors in hypoxic and inflammatory hypertrophic ossification (HO) found in MO. Moreover, mTOR signaling and BMP HO in FOP represent another area requiring study. Another drug, palovarotene, a retinoic acid receptor-gamma (RAR-ϒ) agonist, inhibits HO in FOP in mouse models and is yet another candidate for investigative work. Finally, other promising therapies include VEGF inhibitors, ligand traps, phosphoinositide 3 kinases inhibitors, siRNA'S, HIF1-α blockers, and transforming growth factor-β activated kinase (TAK1) inhibitors, which have shown success in preventing HO in FOP.[72]

We are currently in the initial stages of understanding this complex process occurring in MO. Having mapped FOP, it may be feasible to map other subtypes. It is evident that further collaborative studies must be conducted internationally. Clinicians should understand what constitutes MO, how to properly assess a patient, and consider it for a clinical diagnosis when encountering such patients. This approach can help reduce the risk of causing additional harm in clinical practice to the patients under our care and to achieve ultimately a clinical early diagnosis of MO.

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Data availability statement

The original contributions presented in this paper are included in this article, further inquiries can be made to the author of this article.

Ethical policy and Institutional Review Board statement

Written consent was obtained by the patient to participate in this publication with all the associated data and images used.

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