Radiographic Musculoskeletal Findings Indicating Opioid Misuse: An Overview for Orthopedic Surgeons

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Abstract *Background:* Given the high prevalence of musculoskeletal conditions in the USA, it is important for orthopedic surgeons to promptly identify patients who may be at risk for opioid misuse. *Questions/Purposes:* The aim of this literature review was to elucidate various musculoskeletal pathologies and complications, as seen on imaging, that may indicate opioid misuse or opioid use disorder. *Methods:* A literature search was conducted using the PubMed, Scopus, and Cochrane Library databases for articles related to imaging findings associated with chronic opioid use or misuse in orthopedic patients. Two independent reviewers conducted the search utilizing pertinent Boolean operations. *Results:* We reviewed 36 full-text articles and categorized the radiographic evidence of opioid misuse as follows: soft-tissue

radiologic findings, cellulitis, necrotizing fasciitis, abscess formation, retained needles, discitis, myopathy and rhabdomyolysis, osteomyelitis, septic arthritis, and septic thrombophlebitis. *Conclusion:* Knowledge of the radiologic findings of opioid misuse will assist orthopedic surgeons in making timely diagnoses that may alter therapeutic regimens for their patients.

Keywords opioids · orthopedic · intravenous drug use · imaging · cellulitis · abscess · necrotizing fasciitis · rhabdomyolysis · osteomyelitis · septic arthritis · septic thrombophlebitis

Introduction

In recent years, considerable effort has been undertaken to monitor the use of prescribed opioids and to expand regulations in prescribing for patients with chronic non-cancer pain or acute pain. These efforts are crucial, as deaths from drug overdose continue to rise. In 2016, there were 63,632 drug overdose deaths, of which two thirds involved opioid use; the 10.6% increase in overdose deaths from 2014 to 2015 is attributed to a doubling of the number of deaths from synthetic opioids such as fentanyl [35]. In 2016, 75% of fatal opioid overdoses reported by the Massachusetts Department of Public Health had a positive toxicology screening for fentanyl [25].

Still, prescribed opioids are playing a role in the crisis. A 2009 report showed that orthopedic surgeons were responsible for 8% of the estimated 201.9 million opioid prescriptions dispensed that year in the USA [39]. It has been shown that the probability of long-term opioid use increases sharply after 1 month of opioid use and that about one in seven persons who have received a refill or had a second opioid prescription was on opioids 1 year later [36]. Inadvertently, physicians attempting to control acute pain through prescribing opioids may be contributing to the opioid epidemic.

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Imaging plays a key role in the detection and characterization of substance use, and radiographic findings can visualize the sequelae after consumption of opioids, cocaine, amphetamines, and their derivatives such as 3,4-methylenedioxymethamphetamine (“ecstasy”) [14]. Some complications are related to the injection of drugs with unsterilized and contaminated needles into muscles, veins, arteries, and/or subcutaneous tissue. Broadly, these complications can be categorized as soft-tissue lesions, muscular pathology, and bone and joint pathology and are most commonly caused by pathogenic organisms either locally or distally from the site of drug injection [14]. Infectious complications are responsible for 60 to 80% of hospital admissions of intravenous (IV) drug users [16].

It is important for orthopedic surgeons to be aware of the clinical sequelae of opioid use. Radiographic images remain a foundation for evaluation of orthopedic diagnoses. The goal of the current study is to review clinical pathologies and associated complications, with a specific focus on radiographic and advanced imaging findings, so that the practicing orthopedic surgeon can be better prepared to recognize opioid misuse in their patients.

Methods

A review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [22]. The goal was to identify all studies written in English or with English translations related to radiographic findings associated with opioid misuse in the orthopedic population—considered to be patients seen by an orthopedic surgeon or sports medicine practitioner. Two reviewers independently conducted the search in October 2018 using the following databases: PubMed, Scopus, and Cochrane Library. Each search included the following terms and Boolean operations: (1) (“intravenous drug abuse” OR “intravenous drug use” OR “opioid abuse” OR “opioid use” OR “illicit drug use”) AND (orthopedic OR musculoskeletal) AND (Image OR Imaging OR radiographic OR radiologic); (2) (“intravenous drug abuse” OR “intravenous drug use” OR “opioid abuse” OR “opioid use” OR “illicit drug use”) AND (orthopedic OR musculoskeletal) AND (“xray” OR “x-ray” OR “CT” OR “MRI” OR “ultrasound”); and (3) (“intravenous drug abuse” OR “intravenous drug use” OR “opioid abuse” OR “opioid use” OR “illicit drug use”) AND “complications” AND “radiology.” Both reviewers independently filtered and reviewed returned articles based on title and abstract of all returned articles, and any discrepancies were co-reviewed. The main criterion for selection was radiographic findings of opioid misuse in orthopedic patients.

Results

Following the two independent authors’ search criteria of the databases, 202 articles were considered for initial review. Duplicate articles were excluded. The authors reviewed the 40 articles for full-text evaluation review. All references in

each identified article were cross-referenced to ensure all available articles were evaluated.

Based on the results of our search, we identified several categories of complications that may be present in orthopedic patients misusing opioids: soft-tissue radiologic findings, cellulitis, necrotizing fasciitis, abscess formation, retained needles, discitis, myopathy and rhabdomyolysis, osteomyelitis, septic arthritis, and septic thrombophlebitis.

Soft-Tissue Pathology

Soft-tissue complications are among the most common sequelae of IV drug use resulting in hospital admission [11]. IV drug users may present to the emergency department with complications of using contaminated needles; injection in subcutaneous tissue or muscle results in cellulitis, subcutaneous infection, abscess formation, necrotizing fasciitis, and myositis, among other conditions [11]. These infectious processes are often polymicrobial and require urgent diagnosis to prevent delay in antibiotic administration and possibly surgical intervention.

Cellulitis

Cellulitis is a superficial soft-tissue infection marked by edema and erythema of skin and subcutaneous tissues, often resulting from streptococcal or staphylococcal infection. Cellulitis may appear similar to subcutaneous infection or abscess formation, related and often coexistent infectious processes. Patients with an uncomplicated superficial infection are often treated with oral antibiotics directed at streptococcal and staphylococcal species. If the patient has a history of IV drug use or examination reveals a skin puncture, bedside ultrasound, the first imaging modality used to evaluate a clinical suspicion of cellulitis, should be completed. In early cellulitis, ultrasound demonstrates diffuse thickening and echogenicity of the subcutaneous tissue. Later, fluid accumulates in the subcutaneous tissue, giving it a “cobble-stone appearance” (seen in any subcutaneous edema) (Fig. 1). Although useful as a primary modality, ultrasound has several limitations—most notably, that a patient with painful cellulitis might not be able to tolerate the direct skin contact and pressure from the probe. For that same reason, ultrasound should be avoided with an open wound.

When ultrasound is not feasible, magnetic resonance imaging (MRI) can be considered. MRI findings include dermo-hypodermal thickening and linear areas of high signal intensity that form a network in the hypodermis [34]. These findings are nonspecific but can provide clarity. Caution should be exercised with MRI if there is any concern of retained metallic objects such as needles. For this reason, we suggest first performing an X-ray of the area.

Necrotizing Fasciitis

Necrotizing fasciitis, a rare, life-threatening, rapid-spreading soft-tissue infection often affecting deep adipose layers, fascia, and muscle [15], is associated with 25 to 50% mortality rates [6, 15, 37]. *Clostridium perfringens* is one of the most common infecting organisms, with predisposing injuries including crush

Fig. 1. Ultrasound of a 17-year-old IV drug user with suspected forearm abscess demonstrates cellulitis of the elbow and forearm. **a, b** Long and transverse grayscale ultrasound images of the elbow and forearm demonstrate soft-tissue edema (brackets), which is nonspecific. **c** Power Doppler ultrasound of the forearm demonstrates hyperemia, indicative of cellulitis. **d** Soft-tissue abscess within the upper arm of an IV drug user demonstrates a cavitary complex fluid collection (solid arrows), surrounded by soft-tissue edema (dotted arrows).

injury, open fracture of long bones contaminated with spore-containing soil, and large arterial injury. It is the most common cause of gas gangrene, and symptoms may include blisters, swelling, and jaundice [37]. Infection progresses rapidly, and prompt diagnosis and treatment are crucial. Clinical suspicion should be high in patients with severe pain over the affected area, high fever, and dusky skin discoloration with rapidly spreading borders. Prompt radiographic imaging can aid in diagnosis. Often, soft-tissue gas produced by a polymicrobial infection with gas-producing organisms may be visualized on computed tomography (CT) scan. Nonspecific findings include thickening of one or both of the superficial and deep fascial layers, edema extension into inter-muscular septa and muscle, and asymmetrical fascial thickening with fat stranding [13]. In equivocal CT studies, MRI studies can be of use. Specifically, T1-weighted imaging (T1WI) may show a loss of muscle texture and high signal intensity in the setting of intramuscular hemorrhage, and T2-weighted imaging (T2WI) may demonstrate edema in a reticulated pattern with sub- or inter-fascial crescentic fluid collections [13]. In the absence of soft-tissue gas, no imaging modality can reliably exclude the diagnosis of necrotizing fasciitis; hence, a high clinical suspicion in the absence of positive imaging findings for necrotizing fasciitis should not delay surgical intervention (Fig. 2).

Abscess Formation

An abscess forms through the accumulation of purulent material composed of bacteria, inflammatory proteins, and

necrotic tissue within subcutaneous tissue or muscle. It often forms via direct inoculation through skin penetration and is a common finding in IV drug use with contaminated needles. An abscess can resemble cellulitis, and so advanced imaging such as CT or ultrasound is needed. Ultrasound of an area of soft-tissue edema may demonstrate a well-circumscribed subcutaneous mass with surrounding hyperechoic tissue; a fluid-filled abscess may appear as a well-circumscribed hypoechoic structure with posterior acoustic shadowing deep to the mass. Ultrasound is amenable to image-guided aspiration for microbiologic diagnosis and targeted treatment (Fig. 3).

Retained Needles

Repeated injection may result in a needle fracturing in the user's body [2, 26, 38]. If the needle is retained in soft tissue, an inflammatory capsule may form around it, encapsulating it in scar tissue. Also, bacteria may reproduce, forming an abscess or collection around the needle. While pre-procedural CT and X-ray are often obtained to find or evaluate retained needles, ultrasound has comparable efficacy to CT in locating radiolucent foreign bodies and is more timely, cost-effective, and radiation sparing (Fig. 4) [29].

Discitis

Discitis, an infection in the intervertebral disc space primarily caused by *S. aureus*, should be considered in a patient

Fig. 2. Computed tomographic (CT) imaging of necrotizing fasciitis in an IV drug user to rule out abscess formation. Coronal (a) CT image demonstrates bubbly lucencies with the posterior soft tissues suggestive of necrotizing fasciitis. Subsequent magnetic resonance imaging (MRI) post-gadolinium contrast T1 fat-saturated axial (b) and sagittal (c) images demonstrate enhancement of the fascia (solid arrows) representing necrotizing fasciitis, as well as an anterior skin defect (dotted arrows), related to skin necrosis, at the site of attempted IV injection.

with focal back pain not relieved by rest who also has a fever, chills, or signs of neurologic compromise [1]. It remains a challenging diagnosis to make; a delay of 2 to 4 months in diagnosing an infection can lead to permanent spinal cord injury, a major cause of morbidity [1]. On plain radiographs, bony erosive changes may take up to 6 weeks to manifest, highlighting the importance of obtaining secondary imaging [1]. MRI with contrast is the imaging

modality of choice; it will show end-plate enhancement of the disc, adjacent vertebrae, paravertebral soft tissues, and epidural abscess [1, 10]. The affected disc will appear hypointense on T1WI and hyper-intense on T2WI [10]. Surgeons must keep a high index of suspicion of discitis in febrile patients presenting with back pain in the setting of IV drug use, new neurological deficits, recent bacteremia, or endocarditis [1]. Also important to note is the increase in

Fig. 3. Pulmonary abscess in an IV drug user by hematogenic dissemination. a Lateral radiograph demonstrates a rounded opacity (arrows) in the left lower lobe. b CT of the thorax demonstrates a cavity with an air-fluid level representing an abscess (black dotted arrow).

Fig. 4. **a** Anteroposterior radiograph of the neck demonstrates retained needles (arrows) in the soft tissues in a homeless man who came to the emergency department with chest pain. **b** Lateral radiograph of the forearm shows a retained needle (arrow) within the antecubital region of the arm.

resistance to fluoroquinolones, the best oral bioavailable agent for bone infections, which is not sufficient as monotherapy for staphylococcal spine infections [1, 9].

Repeat MRI is not routinely indicated unless back pain recurs or the C-reactive protein level remains elevated (Fig. 5) [20].

Fig. 5. Magnetic resonance imaging (MRI) of the cervical spine demonstrating discitis/osteomyelitis with epidural abscess in a 25-year-old man, an IV drug user who was found unconscious. **a** Sagittal T1-weighted image demonstrates confluent low T1 signal within C3, representing osteomyelitis. **b** Sagittal T2-weighted image shows an epidural mass extending from the disc space and compressing the cord (arrows). **c** Sagittal inversion recovery image highlights pre-vertebral edema (arrows), as well as edema in the C3 and C4 vertebral bodies. **d** Sagittal post-contrast T1-weighted fat-saturated image shows pre-vertebral, intra-discal, and epidural enhancement. **e** Axial post-contrast T1-weighted fat-saturated image shows the epidural abscess (arrows) compressing the cord with enhancing phlegmonous tissue extending through the neural foramina and into the epidural space.

Fig. 6. Magnetic resonance imaging (MRI) of rhabdomyolysis. **a** Coronal inversion recovery MRI of the thighs shows sheet-like edema (arrows) within the quadriceps musculature. **b** Axial proton-density MRI of the thighs demonstrates hyperintensity within the vastus intermedius bilaterally (arrows), indicative of edema. **c** Axial coronal inversion MRI of the right thigh shows extensive edema.

Muscular Pathology

Myopathy and Rhabdomyolysis

An opiate-induced myopathy can occur through repeated intramuscular injections of opioids such as heroin, which can cause direct myotoxicity and lead to muscle contractures [40]. Although opioid-induced myopathy is rare, cocaine-induced myopathy is much more common and related to an increase in sympathomimetic activity resulting in severe vasoconstriction that causes muscle ischemia and infarction [41]. Cocaine-induced myopathy can occur within hours of IV use or after smoking the alkaloid-freebase (crack cocaine) [32]. The creatine kinase (CK) elevation range correlates to the risk for acute myoglobinuric renal failure. MRI is the modality of choice [7]. For patients whose renal function is already compromised, special care should be taken to avoid the use of gadolinium-based contrast due to its potential renal toxicity. A bone scan may be indicated to assess widespread muscle injury and will show diffuse accumulation of the radioisotope in the affected muscles [33]. Adequate assessment of muscle involvement is warranted, given the additional risk factors associated with cocaine-induced rhabdomyolysis, including hypotension, seizures, and coma. It is crucial to ask patients about their use of heroin or other drugs that can cause rhabdomyolysis and subsequent renal failure (Fig. 6) [4].

Bone and Joint Pathology

Osteomyelitis

Hematogenous spread of infection, with contiguous or direct inoculation of infective organisms deep to the periosteum, may result in gradual inflammatory damage to the underlying bone and result in acute, subacute, or chronic

osteomyelitis or in inflammation of the medullary cavity of the bone. Often, radiographic images show no evidence of

Fig. 7. Radiograph of osteomyelitis of the radius. **(a, b)** Lateral and anteroposterior radiographs of the forearm in a 45-year-old IV drug user show retained needle (arrow) in the soft tissues and a soft tissue defect (dotted arrows), with destruction of the radial cortex (arrowhead).

Fig. 8. Septic arthritis. **a** Anteroposterior radiograph of the shoulder in an IV drug user shows focal lucency (arrow) at the humerus. **b** Radiograph 1 month later shows erosions of the humerus and glenoid. **c** Axial computed tomography shows humeral lucency and diffuse glenoid bone loss (dotted arrow). **d** Axial T1-weighted fat-saturated magnetic resonance imaging (MRI) shows joint effusion with extensive intra-articular debris and synovial thickening (arrows). **e** Sagittal T1-weighted MRI shows large articular erosions of the bare area of the humeral head with confluent low T1 signal (arrows), indicative of osteomyelitis.

bone abnormality, as 30 to 40% of bone destruction is necessary for visualization. Plain radiography findings may include nonspecific periosteal reaction and osteolysis, which can complement findings from other modalities. The role of CT is limited but can be used to determine the extent of bony destruction in biopsies or in patients with contraindications to MRI [27]. MRI is the most accurate modality to assess osteomyelitis, with sensitivity and specificity of 0.90 and 0.79, respectively [23, 24]. MRI is also useful to distinguish soft-tissue from bone infection and to determine the extent of infection, but its use is limited in patients with surgical hardware present [19]. Overlying soft-tissue infection with fluid-sensitive sequencing can alert the clinician of the etiology of a direct inoculation via soft-tissue infection (Fig. 7). For patients with absolute or relative contraindications to MRI, nuclear imaging with tagged white blood cells can be considered. Nuclear imaging has been shown to detect osteomyelitis 10 to 14 days before changes can be seen on plain films; however, this comes at the cost of low specificity [28].

Septic Arthritis

A painful, infectious condition, septic arthritis is most commonly caused by hematogenous spread from a distant source (e.g., pneumonia, endocarditis), direct seeding, spread from

contiguous infection (e.g., osteomyelitis), pyogenic infection, and IV drug use [31]. In both children and adults, the knee is the most involved joint [17]. IV drug users usually have infections with unusual organisms, including *Mycobacterium avium*, *Pseudomonas aeruginosa*, and *Enterobacter* species [31]. Septic arthritis is typically monoarticular and presents with a warm and swollen joint with decreased range of motion [31]. While joint aspiration is required for diagnosis, radiographs may show signs of effusion and destruction. MRI with post-contrast sequences may demonstrate nonspecific abnormalities but is useful if the diagnosis is uncertain. Post-contrast sequences can help demonstrate the type of synovitis and whether it is acute or chronic. For example, frond-like hypertrophy of the synovium can be indicative of acute synovitis, whereas lamellated synovium is more often associated with chronic processes [21]. Additionally, post-contrast sequences may help a practitioner with the septic arthritis diagnosis identify other signs of infection or inflammation, such as periarticular soft-tissue edema and enhancement or fluid collections and lymphadenopathy. To prevent a delay in diagnosis and progressive joint destruction, surgeons must assess the patient's use of IV drugs to target the infectious organisms. Empiric therapy is not recommended in IV drug users; the antibiotic choice should be based on the results of

Fig. 9. Ultrasound of septic thrombophlebitis. **a** Grayscale ultrasound of the basilic vein shows heterogeneous echotexture within the vein (arrows), indicating clot. **b** Color Doppler ultrasound shows loss of color flow within the vein.

joint aspirate and antimicrobial susceptibility of the offending organism (Fig. 8) [18].

Septic Thrombophlebitis

An inflammatory process involving the superficial veins, thrombophlebitis is associated with micro-thrombotic events [5]. With IV opioid use, inflammation is generally secondary to infection; hence, the term *septic thrombophlebitis* is used [8]. The pathophysiology involves Virchow's triad, which consists of impaired blood flow at the injection site, endothelial damage due to vessel perforation, and hypercoagulability related to the underlying infection [8]. The vessel most commonly involved is the right common femoral artery, with *S. aureus* the most common causative agent.

This condition involves local hyperemia, edema, proximal venous distension, and a tender, palpable mass that might extend the length of the vessel, with skin pigmentation and varices in chronic cases [5]. Ultrasound and duplex scanning of veins may detect vessel wall thickening, air within the vein, or echogenic or echolucent thrombi [5, 14, 30]. The deep veins should be imaged because of the high risk of deep vein thrombosis [5]. Management involves early treatment with non-steroidal anti-inflammatory drugs, mobilization of the affected limb, IV antimicrobials, anticoagulants, and thrombus removal (Fig. 9) [3, 5].

Conclusions

Patients with opioid use disorder, because of fear of stigma, often are seen only after they have advanced complications. Therefore, a radiologist or orthopedic surgeon may be one of the first physicians to definitively diagnose a patient suffering from substance use disorder. Knowledge of the imaging findings associated with opioid use and misuse is important for radiologists, physicians in general, and orthopedic

surgeons in particular. Prompt recognition of substance use disorder may alter therapeutic regimens and accelerate recovery for vulnerable patients on a potentially complicated perioperative course.

Healthcare providers can encourage patients with substance use disorders in several ways, as eloquently stated by emergency radiologist Efren J. Flores, MD [12]:

[We] can encourage patients with substance use disorders to use sterile needles, inform them about needle exchange programs, and advise them to use alcohol at the injection site to decrease the risk of developing infections. We can also collaborate with other members of the care team, in particular mental health professionals, to develop outreach efforts and help steer patients into recovery programs or connect them with coaches, both in the hospital and community settings, to help them with their illness. . . . Most importantly, we need to have compassion in our interactions with these patients. It's the first step to getting them on the path to recovery.

Compliance with Ethical Standards

Conflict of Interest: Harry G. Greditzer IV, MD, Dustin H. Massel, MD, Carlos M. Barrera, BS, Christopher P. Emerson, MS, Michael G. Rizzo, MD, Nisreen Ezuddin, MD, Camila Brasil, MD, Ane Ugarte Nuno MD, and Jean Jose, DO, MS, declare that they have no conflicts of interest.

Human and Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

Informed Consent: Informed consent was waived from all patients included in this study.

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