Infection

15

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Learning Objectives

- The reader will learn the advantages of various imaging modalities for musculoskeletal infection.
- The reader will review imaging appearances of manifestations of infection on radiologic exams.
- The reader will incorporate current recommendations for terminology regarding musculoskeletal infection.
- The reader will understand mimickers of infection to help generate a differential diagnosis.

15.1 Introduction

Diagnosis of infection can be challenging clinically, based on a number of factors including location, organism, and mode of spread. Other entities can simulate infection clinically or radiologically. Radiologic examinations can improve patient care, if applied appropriately early in the disease process. However, misdiagnosis or delayed diagnosis can lead to poor outcomes. This article discusses the advantages and disadvantages of imaging modalities, the imaging appearance of various types, and manifestations of infection, as well as complicating factors and entities that can simulate infection.

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15.2 General Principles

15.2.1 Routes of Infection

There are three routes for introduction of infection around the body: hematogenous, direct implantation, and contiguous spread [1, 2]. Hematogenous spread is the most common cause of osteomyelitis in most areas of the body, including the spine. Direct implantation is relatively common in the hands and feet (i.e., puncture wounds, penetrating trauma) and in various areas of the body as a result of open surgery and percutaneous procedures. Contiguous spread is related to transmission of infection through the skin or from adjacent tissues. The most common clinical scenarios involving contiguous spread of infection include diabetic pedal infection and pelvic osteomyelitis in paralyzed patients.

Key Points

- Three routes for MSK infection: hematogenous, direct implantation, and direct spread.
- Most common: hematogenous spread.
- In diabetic patients and paralyzed patients, contiguous spread is important.

15.3 Modalities

15.3.1 Radiography

For patients with clinical suspicion of infection, radiographs are typically the initial radiologic examination acquired [3, 4]. Early infection in the extremities is seen as soft tissue swelling, representing cellulitis. However, this finding is nonspecific. In more central locations such as the sacroiliac joints, soft tissue swelling is obviously not as sensitive.

J. Hodler et al. (eds.), *Musculoskeletal Diseases 2021–2024*, IDKD Springer Series,
https://doi.org/10.1007/978-3-030-71281-5_15

Septic arthritis is characterized in the early stages by joint effusion. Depending on location (i.e., deep joints), effusion may not be detected radiographically. As the disease progresses, erosions and joint space narrowing representing chondrolysis are observed. Finally, with onset of osteomyelitis, frank bone destruction is seen. Periosteal reaction may be seen in later stages. Radiographic changes of osteomyelitis can be delayed as much as 2 weeks after onset of infection. Overall, radiographs are insensitive to osteomyelitis in early stages and cannot determine the extent of involvement of osseous or soft tissue disease. Therefore, whether negative or positive, additional imaging is necessary. Despite low utility for diagnosing osteomyelitis, the wide availability and excellent overview of anatomy make radiography excellent for follow-up examinations; evaluation of postoperative changes; identification of soft tissue calcification, gas, and foreign bodies; and characterization of the pattern and distribution of arthritis, including neuropathic osteoarthropathy.

15.3.2 Computed Tomography

CT provides similar findings on radiographs but with more anatomic definition [5]. If intravenous contrast medium is administered, soft tissue enhancement reflecting cellulitis and rim-enhancing fluid collections indicating abscess formation can be detected. In later stages of infection, as osteomyelitis sets in, periostitis and rarefaction of bone will be seen. Eventually, frank bone destruction ensues. Joint effusion, articular narrowing, and marginal erosions indicate septic arthritis. Determining the extent of involvement within the bone as well as in the soft tissues remains limited with CT. Given these limitations as well as associated expense, its use as a clinical tool for this purpose is limited. However, if anatomic information is needed and MRI cannot be obtained, or if there are metal implants, CT may be useful [6].

15.3.3 Ultrasonography

The use of a high-frequency transducer offers excellent depiction of soft tissue anatomic detail, and ultrasonography can be useful for answering specific questions, such as whether there is an infected fluid collection in the subcutaneous tissues [7]. Abscesses and effusions are seen as focal regions of hypoechogenicity often with complex internal characteristics. Joint effusions and tendon sheath fluid can be detected, but these findings are common in the absence of infection. Power Doppler can demonstrate hyperemia of the synovium and surrounding tissues, suggestive of inflammation. Although ultrasonography cannot visualize the marrow compartment, a focused examination can demonstrate cortical breakthrough and periosteal elevation. Owing to availability of other modalities that offer a more comprehensive evaluation, the use of ultrasonography for this purpose is limited.

15.3.4 Magnetic Resonance Imaging

MRI is the imaging modality of choice for evaluation infection [8, 9]. Soft tissue and bone marrow pathology can be detected with high sensitivity. High contrast between different tissue types as well as inflammatory versus non-inflammatory tissue combined with anatomic definition has made this modality useful to surgeons interested in acquiring a "road map" of pathologic tissue before surgery. Additionally, with intravenous contrast administration, it is possible to identify abscesses and extension of phlegmonous tissue and to evaluate areas of devitalization that may require debridement [10, 11].

15.3.5 Nuclear Medicine

Three-phase bone scintigraphy and labeled leukocyte imaging are the most commonly performed radionuclide tests in the evaluation of pedal infection [12, 13]. Although the three-phase bone scan is sensitive for detecting osteomyelitis, many conditions in the diabetic foot demonstrate focal hyperperfusion, hyperemia, and bony uptake, mimicking infection, and, consequently, specificity is low. When there is no increased uptake, the test is excellent for excluding the presence of osteomyelitis, except in the setting of severe vascular disease. Labeled white blood cell examination has higher specificity and is generally interpreted in conjunction with the three-phase bone scintiscan.

The uptake in three-phase bone scintigraphy using 99mTc-labeled methylene diphosphonate is related to blood flow and osteoblastic activity. Localized bone uptake on the delayed third phase is nonspecific, but if all three phases are positive with clinical suspicion of infection, the test is highly sensitive for diagnosis of osteomyelitis. Cellulitis, abscess, and other soft tissue infections show increased uptake on the initial blood flow and second blood pool phases that fail to concentrate in bone on the third phase. Occasionally, and especially, in ischemic feet, there is persistent blood pool activity which can be suspected if there is poorly defined tracer distribution. Residual bony uptake on a fourth phase, acquired after 24 h, can help distinguish osteomyelitis from overlying cellulitis in this setting. Severe ischemia results in photopenia or relative lack of uptake and chronic osteomyelitis, or partially treated infection may not show characteristic uptake on the first two phases resulting in false-negative examinations [12, 13]. Persistent radiotracer uptake may be seen with treated osteomyelitis. Bone turnover and hyperemia caused by neuropathic osteoarthropathy, trauma, recent

surgery, or inflammatory arthropathy can appear similar to infection, leading to a false-positive examination. Specificity is lower as a result of vascular insufficiency and complicating neuroarthropathy. In the setting of underlying complicating conditions, where there is nonspecific uptake on the delayed phase, corresponding uptake on a labeled white blood cell scan increases specificity.

White blood cell scanning is based on accumulation of labeled leukocytes in infected tissue with reported sensitivity and specificity ranging from 75% to 100% and 69% to 100%, respectively. Combined with three-phase bone scintigraphy, specificity increases to 90% to 100%. Focal uptake in the foot, without appreciable amounts of red marrow, is generally indicative of infection. It may be difficult to separate soft tissue from bone infection, both of which will accumulate leukocytes. Corresponding delayed uptake on a three-phase bone scintiscan can make the diagnosis of osteomyelitis. False negatives may be seen with prior antibiotic treatment and ischemia. Noninfectious inflammatory conditions such as rheumatoid arthritis and hyperemic conditions such as acute neuropathic disease can occasionally show increased uptake, a false positive.

15.3.6 Positron Emission Tomography and Cross-sectional Imaging

18-F-FDG positron emission tomography (PET) combined with CT (PET/CT) has shown promise for imaging infection, related to increased metabolism of glucose in areas of inflammation [14]. The high resolution of PET is a significant advantage over bone and labeled leukocyte imaging. However, to date, limited data exist to test its efficacy in the diabetic foot and the jury is still out. Hybridization of PET with MRI (PET/MRI) is emerging as a new tool to provide important diagnostic information, with data predominantly limited as of yet, to oncological applications. Perhaps, in the future hybridization techniques may play a useful role in the evaluation of diabetic foot infection.

Key Points

- Radiographs: inexpensive, widely available; good for initial screening, follow-up.
- Ultrasound: limited use; best for answering specific questions, evaluating for soft tissue pathology such as abscess, tendon involvement.
- CT: usually reserved for bone biopsy localization.
- MRI: generally the test of choice for diagnosis and evaluation of extent for surgical planning.
- Nuclear medicine: limited anatomic information; can be used when MRI is contraindicated.

15.4 Imaging Manifestations of Infection

15.4.1 Cellulitis

Cellulitis is seen as replacement of the normal fat signal in subcutaneous tissues on T1-weighted images, with high signal (though less than fluid) on T2-weighted or STIR images and diffuse enhancement after contrast agent administration, with swelling and loss of fat density on CT [1, 5, 9, 11]. The margins are typically poorly defined. Abscesses appear as a focal collection of signal approximating fluid on T2-weighted or STIR images, with thick rim enhancement on post-contrast T1-weighted images. Sinus tracts are characterized by a thin, discrete line of fluid signal extending through the soft tissues with enhancement of the hyperemic margins. Sinus tracts are visualized as linear tracts of fluid signal or parallel lines of enhancement in a "tram-track" configuration.

15.4.2 Septic Arthritis

Septic arthritis results from seeding of microorganisms, usually bacteria, either with direct inoculation or more commonly hematogenously [15]. The risk for joint infections is related to IV drug use, immunocompromised state, and diagnostic and therapeutic injections. The earlier the diagnosis, the lower is the risk for irreversible destruction of the articular cartilage. The clinical and serologic findings are suggestive of pyogenic septic arthritis which is established with drainage and culture. The role of imaging is secondary and is mainly related to suggest a clinically unsuspected septic arthritis. Absence of joint effusion on US shows a high negative predictive value. Radiographs cannot exclude septic arthritis. The earliest radiographic findings are soft tissue swelling and joint effusion which lack reproducibility and are nonspecific. MRI findings suggesting septic arthritis include joint effusion, synovial thickening, and surrounding soft tissue changes such as fasciitis and myositis (Fig. 15.1). Contrast administration may show diffuse synovitis and soft tissue abscess formation. Limited subchondral bone marrow edema is usually reactive, whereas diffuse marrow edema, particularly if obvious on T1-weighted images, is suggesting osteomyelitis [16]. Although sensitive, MRI lacks specificity as most of the above described findings may be seen in inflammatory joint disease as well [17].

Rapid development of effusion in infected joints can cause intense capsular and pericapsular soft tissue edema on MR imaging ("angry effusion"), which can help differentiate bacterial septic arthritis from chronic arthropathies in which capsular expansion is more gradual.

Tuberculous arthritis has a more chronic course compared to pyogenic arthritis and is common in endemic areas, but in developed countries, it is seen in immunosuppressed

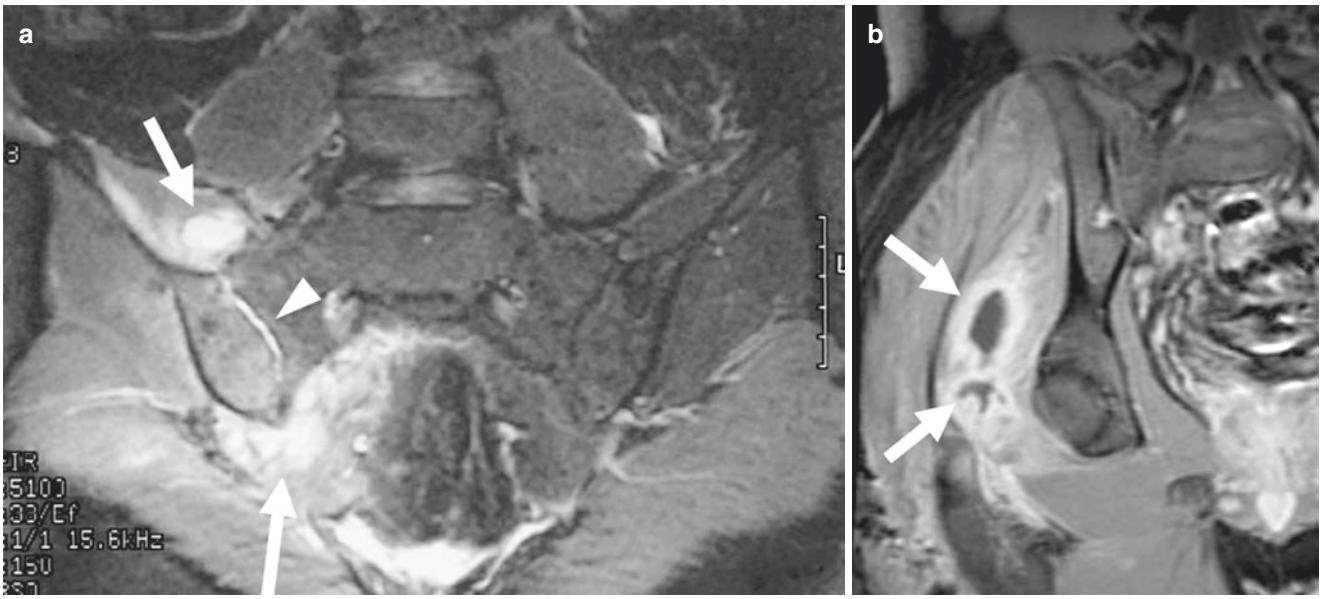

Fig. 15.1 A 35-year-old male patient with right lower back pain for 2 weeks; recent onset of right sciatic pain. Low-grade fever. Aspiration-proven *Staphylococcus aureus* septic sacroiliitis. Coronal STIR image (**a**) shows fluid signal within the joint (arrowhead) with distension of the joint recesses superiorly and inferiorly (arrows), the latter extending into the sciatic notch. Note surrounding soft tissue edema representing inflammation. Coronal T1-weighted fat-suppressed post-contrast image (**b**) shows rim-enhancing abscesses (arrows) in the gluteus musculature

patients, immigrants, and elderly patients. Tuberculous arthritis is considered to occur secondarily to hematogenously induced osteomyelitis, is mostly monoarticular with the hip being involved up to 15%, and if untreated results in joint destruction [18, 19]. Establishment of diagnosis is not possible based on imaging findings alone. The *Phemister triad* refers to the presence of *periarticular osteopenia*, *peripheral erosions*, and *gradual joint space narrowing* on radiographs. Minimal subarticular sclerosis, soft tissue swelling, osteolysis, and minimal periosteal reaction may also be seen [18, 19]. Joint space will be narrowed late in the course of the disease. Effusion and synovial hypertrophy are seen on MRI and are indistinguishable from those seen in other arthropathies. Sacroiliac joint involvement may show abscesses, often calcified, and are best appreciated with CT.

Patients with joint effusion and clinical suspicion of septic arthritis should undergo image-guided aspiration of the fluid with fluoroscopy, ultrasonography, or CT, depending upon the individual joint involvement and the body habitus of the patient.

15.4.3 Osteomyelitis

Osteomyelitis is characterized by altered bone marrow signal, with low signal (loss of the normal fat signal) on T1-weighted images, edema signal on T2-weighted or STIR images, and enhancement on postgadolinium T1-weighted images (Fig. 15.2). Other MRI findings in cases of osteomyelitis include cortical disruption and periostitis. Periostitis is seen as a thin, linear pattern of edema and enhancement surrounding the outer cortical margin that will appear thickened if the periostitis is chronic [2–5, 8–10].

Recognition of abnormal bone marrow signal in the appropriate clinical setting results in high sensitivity for diagnosis of osteomyelitis. Other entities can mimic this alteration in signal, including fracture, tumor, active inflammatory arthritis or neuropathic disease, infarction, or recent postoperative change. However, these other processes usually have different morphology than osteomyelitis and recognition of these patterns often enables differentiation. For example, identification of a fracture line, a discrete lesion, adjacent arthritis or neuropathic disease, or postoperative metal artifact improves specificity. Correlation with radiographs and clinical history is also important. Additionally, over 90% of the time, osteomyelitis of the foot and ankle is a result of contiguous spread through the skin with the majority of cases demonstrating skin ulceration, cellulitis, soft tissue abscess, or a sinus tract. These findings can be thought of as "secondary signs" of osteomyelitis, recognition of which improves specificity [10, 11].

In a significant proportion of cases, the MR imaging findings are not "classic"; this has been reported in cases of soft tissue ulceration and adjacent bone marrow edema but with absence of fat replacement on T1-weighted images. This appearance has been referred to as "osteitis"—a nebulous term that has been defined differently by different authors (Fig. 15.2). A recent white paper from the Society of Skeletal Radiology (in press) recommends against use of this term, instead describing likelihood or risk of underlying osteomyelitis or progression to frank bone infection. The idea is that "reactive edema" can occur in the bone marrow adjacent to a

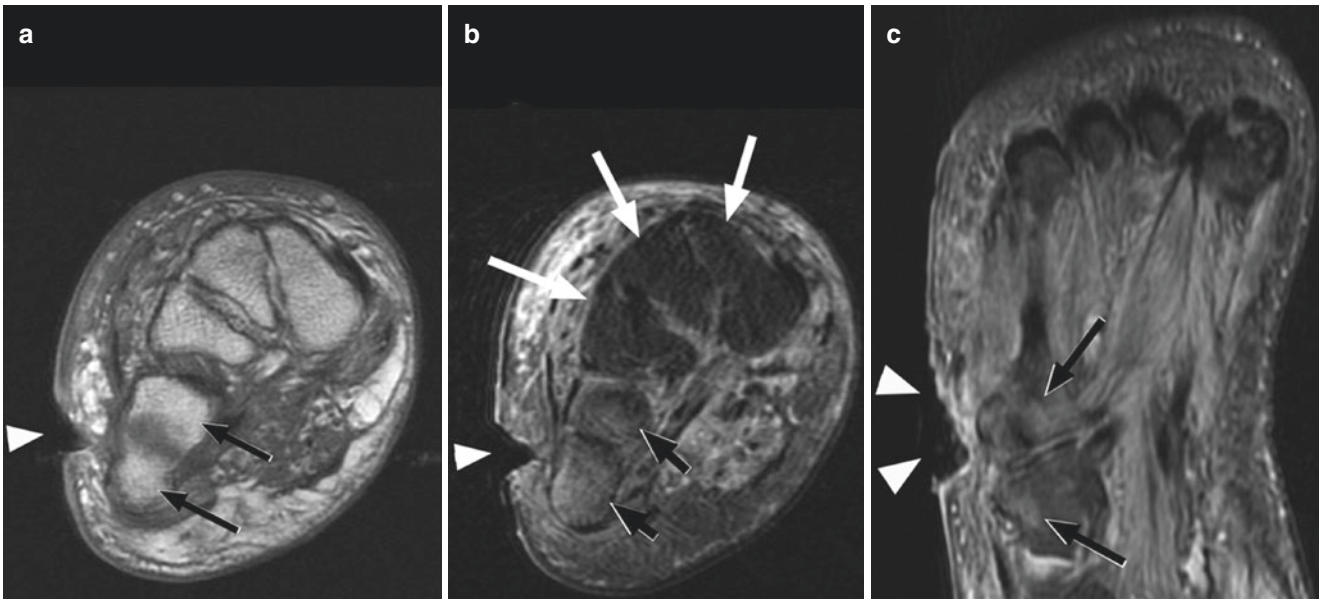

Fig. 15.2 A 58-year-old woman with poorly controlled type 1 diabetes and early osteomyelitis. Coronal T1-weighted MR image (**a**) of the midfoot shows deep ulceration (arrowhead) adjacent to the 4th and 5th metatarsal bases. Underlying bone marrow signal appears normal (arrows) on T1-weighted images. Coronal (**b**) and axial (**c**) T2-weighted fat-suppressed images show the ulcer (arrowheads) with soft tissue edema representing cellulitis. Bone marrow edema is present (black arrows) in the metatarsal bases (compared to normal marrow signal in the cuneiform bones (white arrows)). Considering proximity to soft tissue ulceration and cellulitis, this should be reported as suspicious for early osteomyelitis (i.e., not *osteitis*)

soft tissue infection, and this does not necessarily mean that there is a bone infection. If the T1 signal is normal, there is a lower probability of osteomyelitis than if the fat signal is partially or completely replaced (high probability). In addition, if there is close proximity to a surface ulcer and the ulcer abuts the bone, any T2 marrow signal should be considered suspicious for early osteomyelitis. Expressing findings in terms of probability helps standardize therapeutic algorithms.

15.4.4 Chronic Osteomyelitis

Chronic osteomyelitis can have additional findings. Chronic manifestations of osteomyelitis include bone sclerosis, sinus tracts, abscesses (in soft tissue or bone), and devitalized areas; devitalized bone is called a sequestrum. The importance of a sequestrum (as well as devitalized soft tissue) is that intravenous antibiotics may not reach these areas, leading to persistent infection.

15.4.5 Abscess and Phlegmon

Abscess can occur in acute or chronic infections, often with sinus tracts connecting areas of infection with collections [1–5, 7]. Abscesses are seen as complex fluid collections on MRI with rim enhancement following contrast administration. A "phlegmon" is a mass-like region of infection without liquefaction. Chronic, smoldering intra-osseous abscess in a pediatric population is referred to as a Brodie abscess (Fig. 15.3). This typically occurs at the metaphysis of long bones, especially around the ankle. The classic finding of a Brodie abscess is an ovoid focus of fluid signal on MRI (corresponding to focal lucency and surrounding sclerosis on radiographs) "dripping" to the physeal plate. An appearance of multiple Brodie abscesses (or intermittent lesions in multiple locations) is seen in the condition known as chronic recurrent multifocal osteomyelitis (CRMO, also known as chronic nonbacterial osteomyelitis, CNO), which is of undetermined etiology but appears to be immune-modulated.

15.4.6 Devitalization

Changes related to ischemia should be taken into account in infection, particularly when interpreting MRI of the diabetic foot. Documentation of the presence and extent of ischemic and devitalized areas facilitates surgical planning for debridement and limited, foot-sparing amputations. Pre- and post-contrast MR images can detect ischemia and devitalization of the foot as focal or regional lack of soft tissue contrast enhancement. Devitalization, or foot "infarction," is seen as a focal area of nonenhancement with a sharp cutoff with increased enhancement in the surrounding reactive, hypervascular tissue. Only contrast-enhanced images allow reliable recognition of gangrenous tissue because T2- and T1-weighted images reveal uncharacteristic signal alterations [11].

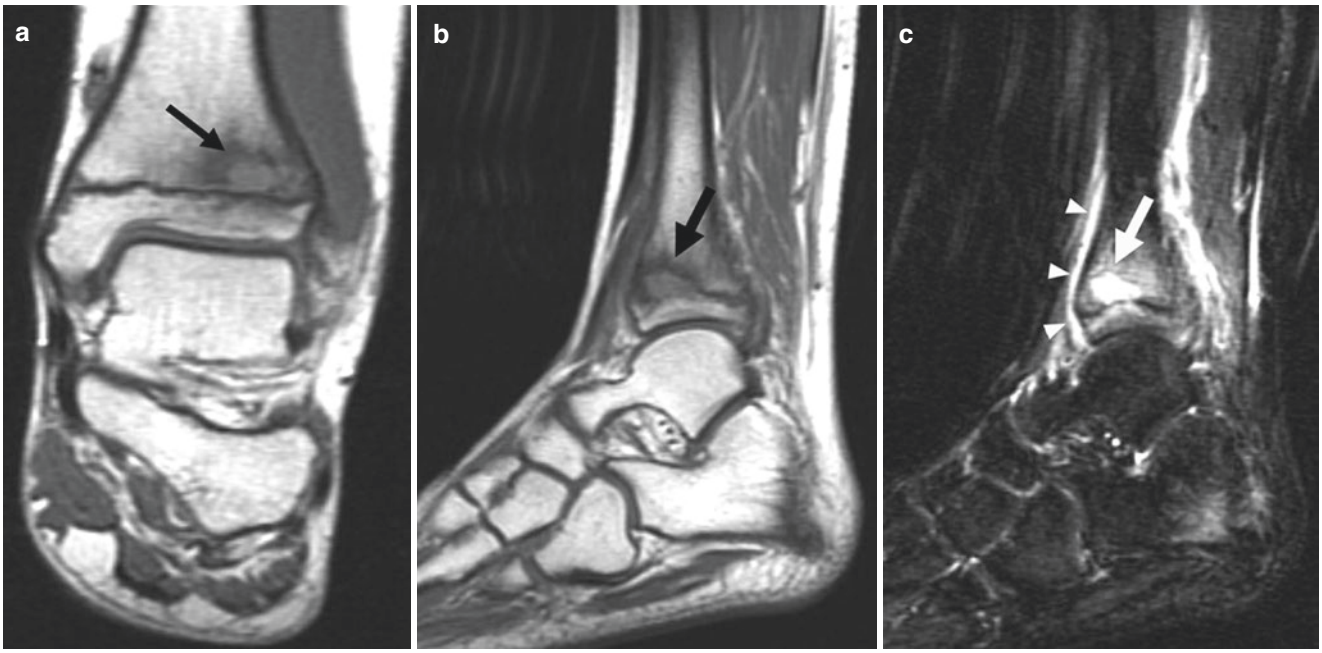

Fig. 15.3 A 10-year-old boy with chronic pain in the lower leg and intermittent fevers. Brodie abscess. Coronal (**a**) and sagittal (**b**) T1-weighted MR images of the ankle show a focal lesion (arrow) in the metaphysis of the distal tibia with slightly ill-defined margins. Sagittal STIR image (**c**) reveals fluid signal within the lesion (arrow) and surrounding bone marrow edema. Note periosteal reaction (arrowheads)

Underlying infection, including osteomyelitis, cellulitis, and abscess, would not be expected to enhance within necrotic areas (Fig. 15.4). In this setting, signal characteristics on T1- and T2-weighted images should be primarily relied on for diagnosis of soft tissue and osseous infection. If intravenous contrast is provided, the radiologist should be familiar with the appearance of devitalized tissue to reduce false-negative readings for infection.

15.4.7 Evaluation of Extent of Involvement

Extent of infection in soft tissue and bone is fairly well delineated on post-contrast MR images. However, infection does not tend to remain confined by fascial planes and spreads centripetally from the inoculation site across fascial compartments, into and across joints, and through tendons. Soft tissue involvement is often more extensive than the osseous disease, requiring careful examination of the soft tissues proximal to the source of infection. Without proper debridement the patient may eventually require more extensive amputation.

15.4.8 Spinal Involvement

Spine infection deserves special consideration; it is a relatively common clinical condition that can result in serious morbidity [20–22]. Recognition of early radiographic and MR manifestations is extremely important to avoid serious complications.

Radiologic diagnosis of spine infection is best made with MR imaging which is very sensitive for early detection of infection and accurate for delineation of extent of involvement and identification of paraspinal abscess for operative planning. However, identification of spine infection using other modalities is important because radiographs, CT, or bone scan is often ordered initially.

Radiographs are typically the first study obtained as part of the radiologic workup of suspected infection. Early manifestations of infectious spondylitis on radiographs include disc narrowing, vertebral endplate osteolysis or irregularity, and paraspinal soft tissue mass. Eventually, gross destruction of the endplates, collapse of the vertebral body, deformity, and sclerosis may occur. Generally, only one disc level is involved, although more severe or chronic cases spread to adjacent vertebral levels can occur along paravertebral ligaments or fascial planes. MRI is the primary modality for the diagnosis of infectious spondylitis. High sensitivity (ranging from 90% to 100%) and specificity (ranging from 80% to 95%), combined with anatomic detail, allow accurate diagnosis as well as delineation of extent of involvement and identification of paraspinal and epidural abscess.

The infected disc demonstrates low signal on T1-weighted images and high signal (approximating fluid) on T2-weighted images (Fig. 15.5). Fat suppression technique is recommended on the T2-weighted images to best demonstrate the associated endplate edema. On T1- and T2-weighted

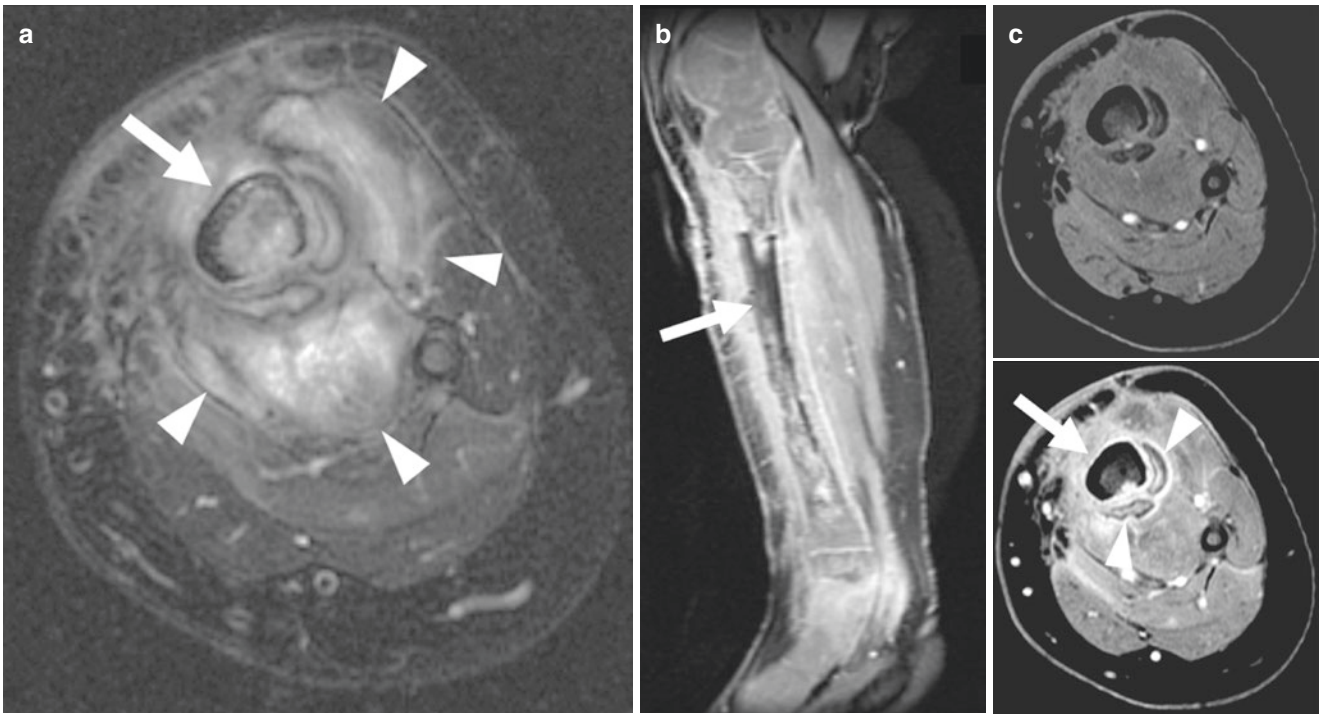

Fig. 15.4 A 6-year-old boy with chronic leg pain and fevers. Biopsy-proven osteomyelitis. Axial T2-weighted fat-suppressed MR image (**a**) of the lower leg demonstrates abnormal signal in the tibia (arrow) representing osteomyelitis. Note surrounding phlegmonous tissue (arrowheads). Sagittal T1-weighted fat-suppressed post-contrast image (**b**) and axial T1-weighted fat-suppressed pre- and post-contrast images (**c**) show nonenhancement of the mid tibial shaft (arrow) consistent with devitalization (a sequestrum). A rim of enhancing new bone formation (involucrum, arrowheads) is present

sagittal images, the endplates may be irregular, with loss of the normal low signal cortical line. Administration of intravenous gadolinium in conjunction with a fat-suppressed T1-weighted imaging sequence can aid diagnostic confidence; the infected disc demonstrates rim enhancement along the margins, with enhancement of the adjacent vertebral endplates. Occasionally, the entire vertebral body above and below the affected disc level enhances diffusely.

T2-weighted images and fat-suppressed T1-weighted gadolinium-enhanced images are particularly useful for identification of paraspinal or epidural abscess. These abscesses are typically longitudinally oriented, extending along paraspinal ligaments or fascial planes, often far from the original site of infection. On T2-weighted images, the abscess shows increased T2 signal intensity, approximating fluid, but often with lobulated margins and internal complexity representing septations, debris, or devitalized tissue. Gadolinium-enhanced images show rim enhancement at the margins of the abscess, which is generally thick and irregular.

Like infection, degenerative disc disease results in disc narrowing with associated endplate irregularity and sclerosis. In addition, Schmorl's nodes (intravertebral disc herniation) cause the appearance of endplate irregularity and in early stages show marrow edema on MRI. Although soft tissue mass is absent (except for disc bulge), this is not a reliable discriminator on radiographs or CT. However, disc degeneration is commonly associated with a vacuum phenomenon, a finding that is nearly 100% specific for absence of infection. As a result, vacuum disc should be sought in cases of suspected infection; lateral radiographs in flexion and extension can aid in identification of a vacuum phenomenon. CT is excellent for detection of small vacuum phenomena at suspected levels. On MRI, Modic type 1 endplate changes can mimic infection, with decreased T1 signal and increased T2 signal. However, the associated disc will show low signal on T1- and T2-weighted images if degenerated compared with the high T2 signal characteristic of infection. MRI can also detect paraspinal edema and mass effect, which are absent in degenerative disc disease.

15.5 Aspiration/Biopsy and Atypical Infections

Most hematogenous musculoskeletal infections are caused by bacteria, with the vast majority being *Staphylococcus aureus*. This and other bacterial infections generally have similar ("classic") imaging characteristics as described above, with diagnosis made by aspiration or biopsy. Culture of infections resulting from transcutaneous spread (i.e., diabetic ulcer) or

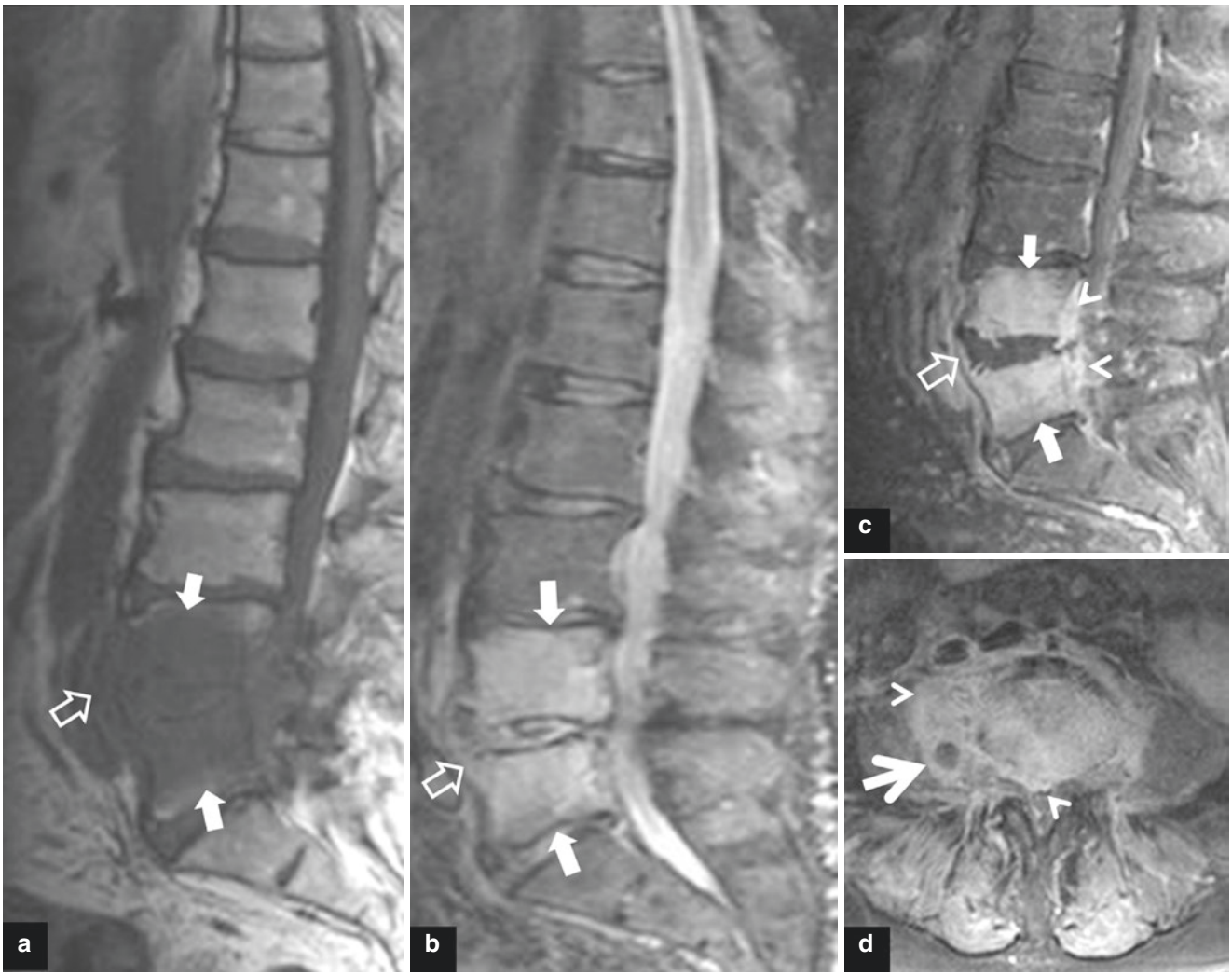

Fig. 15.5 A 70-year-old male patient with a history of 5 months of low back pain and a final diagnosis of tuberculous spondylodiscitis. MRI with sagittal T1-weighted (**a**), STIR (**b**), and contrast-enhanced fat-suppressed T1 on sagittal (**c**) and axial (**d**) planes show bone marrow edema in the L4 and L5 vertebral bodies (arrows), subligamentous spread sparing the disc (open arrows), epidural and paraspinal phlegmon (arrowheads), and paraspinal abscess formation (thick arrow)

inoculation (i.e., stepping on a nail) can exhibit more fastidious organisms and multi-organism involvement. In these situations, a PCR (polymerase chain reaction) assay can be useful to analyze the DNA or RNA of the organism to quickly determine the causative organism rather than waiting for culture results. Additionally, in as many as 75% of cases, culture results are falsely negative [23]. Finally, PCR can be useful in differentiating chronic infection from other pathologies, especially in diagnosis of prosthetic joint complications [24].

In the case of transcutaneous spread, care must be taken not to inadvertently inoculate the bone with the organism infecting the soft tissues. For example, if there is a diabetic foot ulcer with questionable abnormality in the adjacent bone on MRI, a biopsy through the infected soft tissue will virtually guarantee bone infection.

Nontraditional infections (fastidious organisms, nonbacterial infections) can have non-classic imaging features. This can be due to the preferred food source of the organism; where *S. aureus* feasts on standard agar culture medium (and disc material), mycobacterial infection grows poorly on bacterial agar culture plates and in discs. As a result, discs are often involved only later in tuberculous spinal infections, with paraspinal spread predominating. It can also be due to the chronicity of the infectious process; whereas bacterial infections usually exhibit rapid onset and progression, fungal, parasitic, mycobacterial infections and others can grow slowly and insidiously leading to radiological manifestations relating to chronic inflammation. These include bone sclerosis and erosion, bone destruction and deformity, necrosis, "cold" abscesses in soft tissue and bone, and soft tissue calcification. The classic example is tuberculosis of the spine, leading to gibbus deformity and calcified paraspinal abscesses.

Many atypical infections involving the musculoskeletal system are actually manifestations of systemic infection, and

other organ involvement is the primary concern. This can occur in tuberculosis, where musculoskeletal infection is usually a consequence of lung or genitourinary disease [18, 19]. Fungal and parasitic infections are often diffusely disseminated, affecting multiple organ systems [25, 26]. Disseminated or chronic infections are often associated with an underlying immunocompromised state which can be related to HIV infection, steroid treatment, malnutrition, and diabetes as well as other chronic metabolic conditions.

15.6 Mimickers of Infection

15.6.1 Neuropathic Osteoarthropathy

Differentiation of osteomyelitis and neuropathic osteoarthropathy can be difficult, because both can demonstrate marrow abnormality, joint effusion, and surrounding soft tissue edema [27]. Some rules may be used to help differentiate these entities on MR images. First, the vast majority of cases of osteomyelitis of the foot and ankle are due to contiguous spread. Therefore, a bone marrow abnormality without adjacent skin ulceration, sinus tract, or soft tissue inflammation is less likely to represent infection. This concept is particularly useful when there are extensive bone marrow signal abnormalities and lack of subcutaneous tissue involvement. Second, neuropathic osteoarthropathy is predominantly an articular process manifesting as instability, often with multiple regional joints involved (e.g., the Lisfranc, Chopart, or multiple adjacent metatarsophalangeal joints). This and other articular manifestations of neuropathic disease (subluxation, cysts, necrotic debris) are not as common in infection. Associated neuropathic marrow changes can be extensive (especially at the midfoot) but tend to be centered equally about a joint and at the subarticular bone. Osteomyelitis shows more diffuse marrow involvement, and unless there is a primary septic arthritis, the marrow changes are generally greater on one side of the joint. Finally, location of disease is important. Neuropathic osteoarthropathy by far is most common at the Lisfranc and Chopart joints. Osteomyelitis occurs predominantly at the metatarsal heads, toes, calcaneus, and malleoli, a distribution that mirrors that of friction, callus, and ulceration. However, contiguous spread of infection can occur at atypical sites if there is a foot deformity (e.g., the cuboid in cases of rocker-bottom deformity) (Fig. 15.6).

15.6.2 Renal Failure

Chronic renal failure can lead to resorption of bone at the joints and enthesial attachments, as well as the intervertebral discs, leading to an appearance on imaging similar to that of infection [28]. This is also referred to as "dialysis-associated spondyloarthropathy" or "spondylosis of renal failure" due to high incidence in the spine. However, other joints with high stress and bone turnover can be involved, including the sacroiliac joints. The appearance is related to bone resorption, hyperemia, and instability due to secondary hyperparathyroidism. Radiographs show bone resorption that can simulate erosion. Edema and joint effusion are observed. A background of altered bone density typical of secondary hyperparathyroidism can be sought (i.e., "rugger jersey spine"). There may also be amyloid deposition within or around the joints or discs; amyloid is low signal on T1- and T2-weighted images. If there is history of renal failure, this diagnosis can be entertained in the setting of imaging features concerning for infection. However, if the clinical picture is compatible with infection (increased WBCs, fever, positive blood culture), biopsy may be needed. The pathologist should be prompted to look for amyloid and perform a Congo red stain.

15.6.3 Crystalline Disorders

Crystalline diseases can simulate infection on various modalities [29–32].

Gout (monosodium urate crystal deposition) can present in various ways including tophaceous versus non-tophaceous and intra-articular versus extra-articular. Extra-articular involvement can include infiltration of tendons and bursae. Cases with more severe involvement can present with bone destruction and even a mutilans pattern of joint erosion. Intra-articular crystal deposition can simulate infection, with joint effusion and erosions. The inflammatory nature of arthritis also results in subchondral bone marrow edema as well as periarticular edema which can be very difficult to differentiate from osteomyelitis. Demonstration of tophi, which are mass-like foci in or around the joint, can suggest the true diagnosis; tophi demonstrate low signal on T1- and T2-weighted images, unlike infection-related abscess or phlegmon [32]. Additionally, since gout is a systemic disease, involvement of other joints should be sought in the patient's imaging file. Recently dual-energy CT has proven useful for diagnosis and determination of extent of involvement [33].

CPPD (calcium pyrophosphate deposition) and HADD (hydroxyapatite deposition disease) are calcium-based crystal disorders involving joint cartilage (CPPD) and tendons/bursae (HADD). In the case of CPPD, inflammatory involvement can lead to joint effusion and periarticular edema that can simulate gout or infection; the clinical manifestation is often referred to as "pseudogout" due to paroxysmal pain and swelling. Radiographs can be helpful in this circumstance with demonstration of chondrocalcinosis (calcium deposition in fibrocartilage and/or articular cartilage); this appearance is nonspecific and is often incidental in older patients. However, association with soft tissue swelling/joint effusion with the typical clinical presentation can reveal the

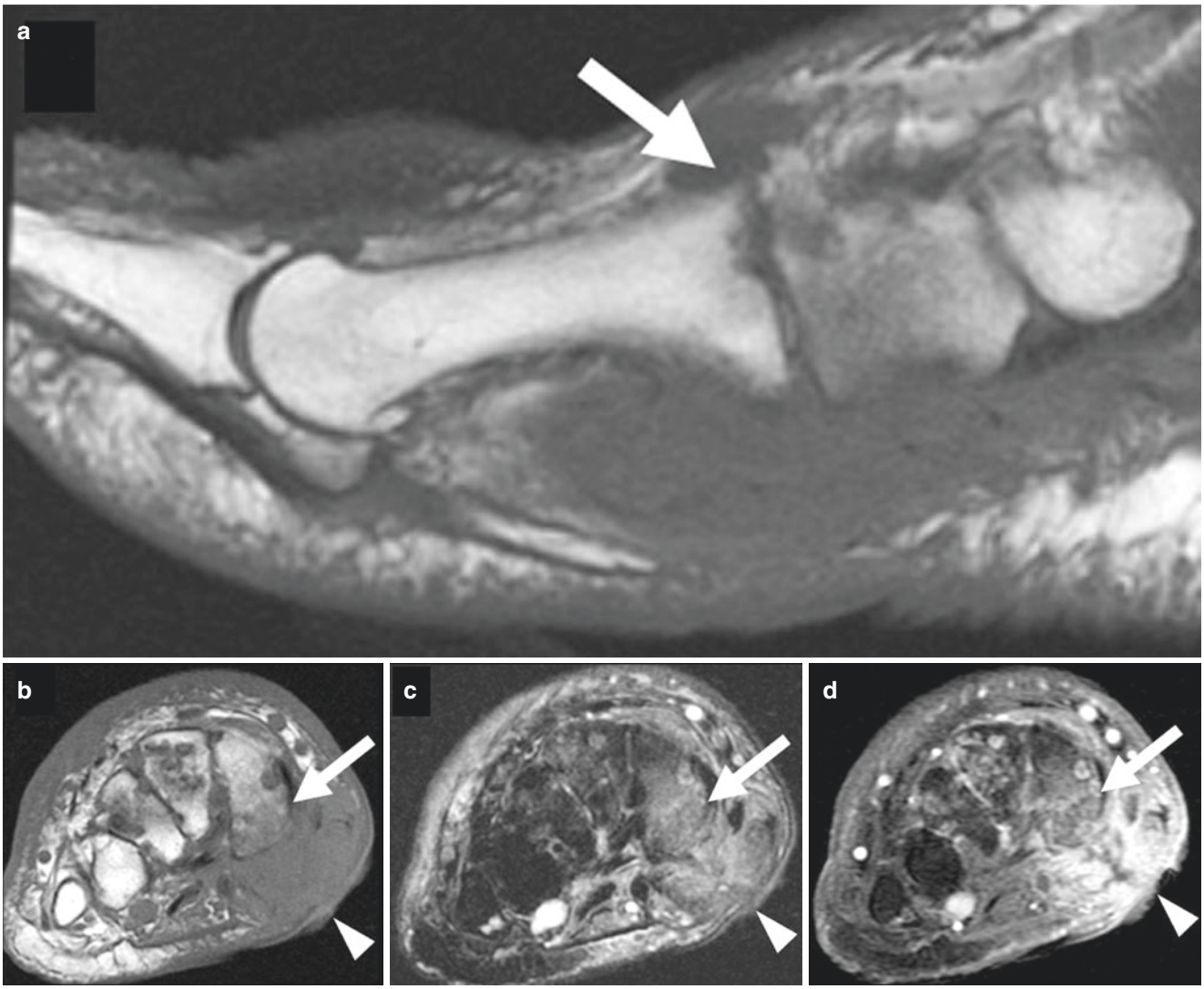

Fig. 15.6 A 56-year-old man with neuropathic osteoarthropathy of the midfoot presents with an ulceration and concern for superimposed osteomyelitis. Sagittal T1-weighted image (**a**) shows Charcot arthropathy involving the Lisfranc joint (arrow). Coronal T1-weighted (**b**), T2-weighted fat-suppressed (**c**), and T1-weighted fat-suppressed post-contrast images (**d**) of the midfoot demonstrate ulceration (arrowheads) with cellulitis and adjacent sinus tract extending to the medial cuneiform (arrows) where marrow signal alteration is consistent with superimposed osteomyelitis

diagnosis. HADD is also characteristic on radiographs, with focal calcification at a tendon attachment or bursa. This most commonly occurs at the rotator cuff; but if the location is atypical (i.e., hand tendon or gluteal attachment), the clinical presentation can mimic infection.

15.6.4 Inflammatory Arthropathies

Rheumatoid arthritis, reactive arthritis, and psoriatic arthritis (as well as less common arthropathies resulting in synovial proliferation) can simulate septic arthritis and osteomyelitis on imaging exams, with joint effusion, joint space narrowing, erosions, and subchondral bone marrow edema [34, 35]. One useful differentiating feature is periarticular edema. Inflammatory arthropathies are generally chronic processes with slow distention of the joint capsule, whereas at least bacterial infection results in marked hyperemia and rapid joint distention resulting in aggressive appearing pericapsular edema ("angry effusion"). This effect is accentuated in smaller, lower capacity joints (i.e., the sacroiliac joint). Additionally, chronic inflammatory arthropathies (especially rheumatoid arthritis) may exhibit synovial proliferation with a mass-like quality, whereas bacterial arthritis progresses rapidly without proliferative synovial hyperplasia, except in later stages or in poorly treated cases. Finally, septic arthritis, except in rare circumstances of disseminated infection, is a monoarticular process. Chronic inflammatory arthropathies listed above are associated with systemic disease and can exhibit similar findings in other joints and locations such as tendon sheaths and enthesial attachments.

15.6.5 Tumor

Certain neoplasms can have characteristics similar to infection on imaging exams. Imaging findings that can be seen in both infection and tumor include bone destruction, periosteal reaction, fluid collections and necrosis, and soft tissue mass effect [36–38]. Tumor is generally easily differentiated from septic arthritis or discitis because neoplasms rarely cross joints. Involvement of both sides of a joint therefore indicates an arthritic process, inflammatory or degenerative. However, tumors involving the shaft of a bone can result in destruction and periosteal reaction similar to osteomyelitis. Tumors at the epiphysis can cause a joint effusion (i.e., osteoid osteoma). Small round cell tumors result in a permeative pattern similar to infection. Classic lesions simulating osteomyelitis include Ewing sarcoma, leukemia and lymphoma, and Langerhans cell histiocytosis. Conversely, atypical infections such as tuberculosis and fungal and parasitic infections can cause focal bone destruction simulating tumor. When biopsy is performed, one should always consider sending samples for both histologic and microbiologic analysis (Fig. 15.7).

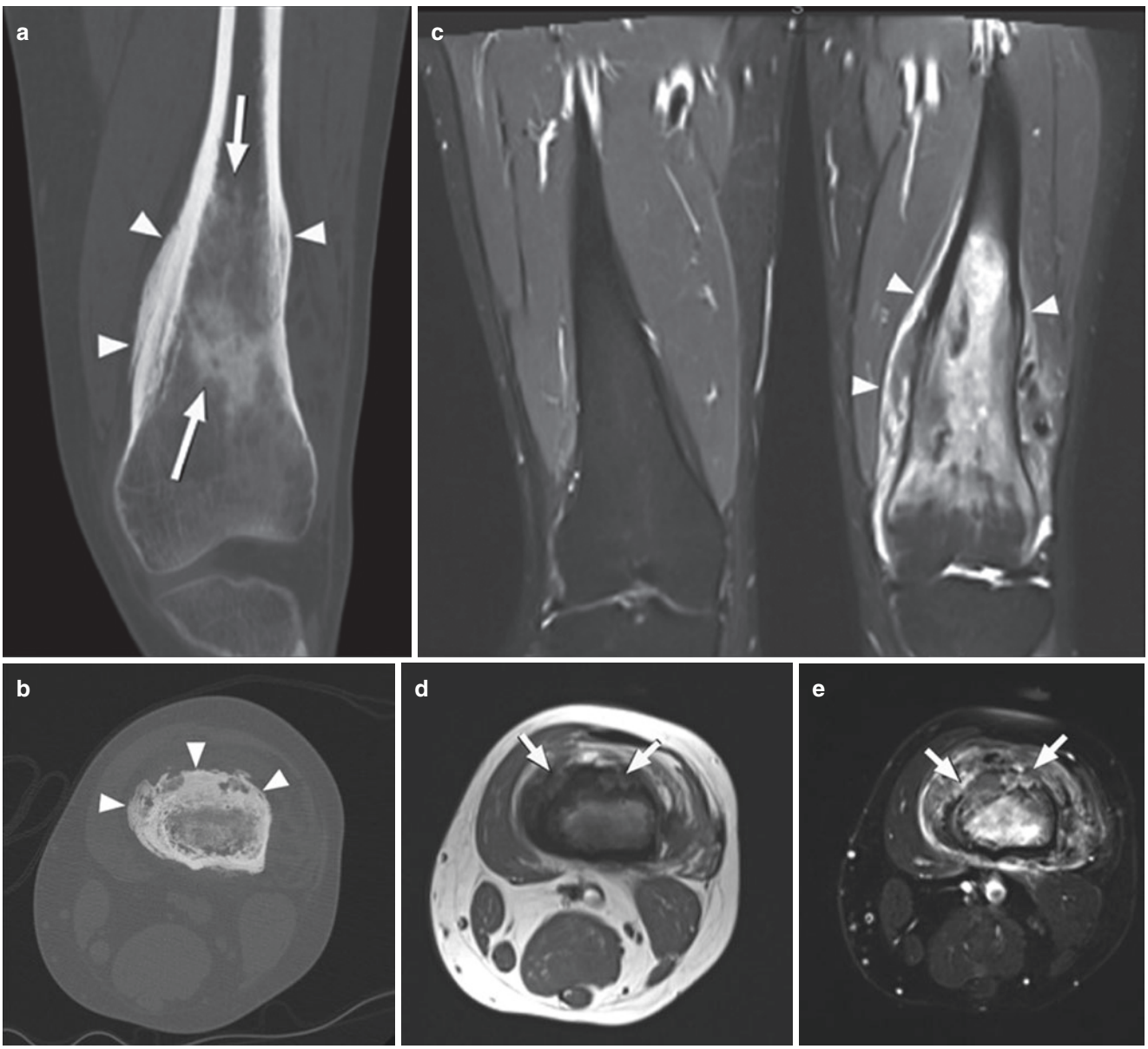

Fig. 15.7 A 38-year-old man with aching leg pain for a year. Chronic osteomyelitis simulating lymphoma. Coronal (**a**) and axial (**b**) CT images show a sclerotic lesion in the distal femoral shaft (arrows) with thick periosteal reaction (arrowheads). Corresponding coronal STIR image (**c**) shows an extensive, ill-defined intramedullary lesion with periosteal reaction and soft tissue mass effect (arrowheads). Based on course of symptoms and imaging features, biopsy was performed with differential diagnosis of chronic osteomyelitis or lymphoma. In retrospect cortical sinus tract formation (arrows) can be seen on axial T1-weighted (**d**) and T2-weighted (**e**) images

Key Points

Mimickers of infection

- Neuropathic osteoarthropathy.
- Manifestations of renal failure.
- Crystalline diseases: i.e., gout.
- Inflammatory arthritis: i.e., rheumatoid arthritis.
- Tumor: i.e., lymphoma, leukemia, Ewing sarcoma.

15.7 Concluding Remarks

Radiologic examinations play an essential role in diagnosis and management of infection. The practitioner should maintain up-to-date knowledge regarding advantages and limitations of the different imaging modalities to provide the most efficacious care.

Take Home Messages

- MRI is the test of choice for diagnosis and management of MSK infection.
- Current terminology guidelines recommend against use of the term "osteitis" for description of early/borderline cases of osteomyelitis.
- Beware of performing percutaneous biopsy in questionable cases that let you iatrogenically introduce infection.
- When performing biopsy, always consider the possibility of alternate etiology such as neoplasia.

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