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REVIEW ARTICLE

Lower limb complications of diabetes mellitus: a comprehensive review with clinicopathological insights from a dedicated high-risk diabetic foot multidisciplinary team

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ABSTRACT

Diabetic complications in the lower extremity are associated with significant morbidity and mortality, and impact heavily upon the public health system. Early and accurate recognition of these abnormalities is crucial, enabling the early initiation of treatments and thus avoiding or minimizing deformity, dysfunction and amputation. Following careful clinical assessment, radiological imaging is central to the diagnostic and follow-up process. We aim to provide a comprehensive review of diabetic lower limb complications designed to assist radiologists and to contribute to better outcomes for these patients.

INTRODUCTION

Diabetic complications in the lower extremity are common and diverse. They are associated with significant morbidity and mortality and impact heavily upon the public health system. These complications result from complex interactions between diabetic vasculopathy, neuropathy, structural deformity and decreased immunity. Early and accurate recognition of these abnormalities is crucial, enabling the early initiation of treatments and thus avoiding or minimizing later complications. Following careful clinical assessment, radiological imaging is central to the diagnostic process. Unfortunately, most radiologists are relatively unfamiliar with the complex interplay of disease processes in this patient cohort. Furthermore, most do not have the opportunity to work closely with a dedicated team of clinical specialists (podiatrists, endocrinologists and vascular surgeons) in a multidisciplinary forum (at Monash Health, this is called the High Risk Diabetic Foot Unit) where valuable feedback, follow-up and clinical insights are provided. As a consequence, radiographs, CT and MRI of abnormal diabetic lower limbs are not infrequently misinterpreted, and sometimes, important findings are simply missed. We aim to provide a comprehensive review of lower limb complications in diabetes mellitus designed to assist radiologists and to

contribute to better outcomes for these patients. Topics are grouped anatomically rather than pathologically owing to the multifactorial nature of their aetiologies.

PERIPHERAL ARTERIES

Diabetes mellitus contributes significantly and independently to the development of peripheral arterial disease and is associated with a 4–5 times increased likelihood of critical limb ischaemia and lower limb amputation.^{1–3} Peripheral artery disease delays ulcer healing and predisposes to gangrene formation, as the diminished arterial supply is incapable of meeting the increased metabolic demand of an infected foot.^{4,5} Lower limb atherosclerosis in patients with diabetes tends to occur more distally.^{3,6,7} Arteries below the knee are preferentially affected, particularly the peroneal and posterior tibial arteries. Aortoiliac disease is usually less severe.⁶ Common to all imaging modalities, appearances of atherosclerotic lesions include calcific or non-calcific plaques, stenoses and occlusions.⁸ Diabetes-related peripheral artery disease may also display characteristic microaneurysms and tortuosity in distal arteries.⁶

Digital subtraction angiography (DSA) is the gold standard in diagnosing the extent and severity of peripheral artery

disease and provides potential for angiographic interventions (Figure 1). Relative disadvantages include it being invasive and relatively poor characterization of focal lesions with complex morphology when compared with cross-sectional imaging techniques such as multiple detector CT.^{9,10}

Non-invasive techniques such as duplex ultrasound, CT angiography and MR angiography are increasingly used to assess diabetic peripheral artery disease and guide the choice of subsequent intervention (*e.g.* endovascular *vs* surgery). Duplex ultrasound is now in many places the first-line imaging modality for investigation of peripheral artery disease with reported sensitivity and specificity of 87.6% and 94.7%, respectively.¹¹ The accuracy of this modality does however remain variable as there is significant operator dependence. MR angiography and CT angiography have also been compared reasonably with conventional DSA, but both techniques suffer from reduced spatial resolution and accuracy in the smaller, peripheral arteries.^{11–16}

Other than clinical assessment and ankle–brachial index measurement, duplex ultrasound is routinely used as the first-line modality at our institution. The standard of arterial ultrasound

in our Diagnostic Imaging Department is high, and the results are consistent with findings at DSA, if performed. Not infrequently, dense arterial calcification or excessive subcutaneous fat in the lower abdominal area preclude accurate duplex ultrasound assessment of the crural arteries and iliac arteries, respectively. In these instances, CT angiography or DSA is used, the latter especially if endovascular treatment is being contemplated.

NERVES

Playing a pivotal role in the pathogenesis of diabetic foot complications, diabetic neuropathy is usually diagnosed on clinical grounds, augmented by electrophysiological studies. Diffuse symmetrical sensorimotor polyneuropathy is the commonest presentation, followed by focal or multifocal neuropathies.¹⁷ Diabetic amyotrophy results from lumbosacral plexopathy and manifests as thigh pain and progressive weakness. Muscular atrophy may be evident on cross-sectional imaging.^{17–19} MR neurography has been increasingly tested in experimental studies to diagnose peripheral neuropathy. Using 3.0-T MRI systems, diseased nerves may display the following features: (1) fusiform enlargement, (2) increased signal on fluid sensitive sequences (T2 signal), (3) abnormal fascicular pattern, (4) deviated course and (5) enhancement with contrast.^{20–22}

Figure 1. Lower limb angiography and angioplasty. Unsubtracted images (a, c) from a selective right lower limb digital subtraction angiogram in a 54-year-old male with ischaemic tissue loss of the great toe. Figure (a) reveals diffuse disease with multiple moderate- to high-grade stenoses of the anterior tibial artery (arrow), proximal occlusion of the peroneal artery (right-pointing arrow head) and multifocal stenosis and distal occlusion of the posterior tibial artery (left-pointing arrow head), a typical distribution of peripheral vascular disease in diabetes. Digital subtraction image of angioplasty to treat the diseased anterior tibial artery (b), and post-angioplasty result showing improved vessel calibre and flow (c).

Figure 2. MRI of the foot. Sagittal T_1 of the forefoot in a 49-year-old male with Type 1 diabetes mellitus showing marked thinning of the protective “fat pad” overlying the first metatarsal head (arrow). In an ambulating patient, this predisposes to ulceration, infection and osteomyelitis, especially in the context of peripheral neuropathy.

Symmetrical multifocal intraneural lesions in proximal nerves of lower limb have been recently described using MR neurography, correlating with more severe neuropathic symptoms.²³

SOFT TISSUES

Fat atrophy

Fatty involution is common (Figure 2). Ultrasound studies of long-term patients with diabetes have demonstrated thinned plantar soft tissue in the region of the metatarsal heads, and correlative MRI has confirmed the fibrous replacement of fat in this area.²⁴ Atrophied and displaced plantar fat pads provide less protection against microtrauma, leading to ulcerations.^{25,26}

Callus and ulceration

Callus formation and skin ulceration are seen in a significant number of patients with diabetes in predictable locations vulnerable to increased pressure and friction. The typical sites are

over the distal great toe, heads of first and fifth metatarsals, posterior calcaneus, medial and lateral malleoli.²⁷ The plantar soft tissues superficial to the cuboid are particularly susceptible in patients with the “rocker-bottom” deformity as part of Charcot neuropathic osteoarthropathy (CN).^{28,29} Callus predisposes to ulceration, which predisposes to cellulitis and osteomyelitis.^{30,31}

On MRI, calluses appear as well-defined focal prominence overlying skin and subcutaneous tissue. They can demonstrate T_1 hypointense, T_2 hypointense or isointense signal, with significant gadolinium contrast enhancement except where there is devitalized soft tissue.³² Ulcerations are seen on MRI as defects of skin and/or subcutaneous tissue and, if formed on previous calluses, surrounded by “heaped-up” edges (Figure 3). The base of the ulcer contains granulation tissue.²⁷

Sinus tracts

Sinus tract allows a portal for dermal organisms to enter and infect deep soft tissue or bone. The course of the sinus tract, if able to be traced on MRI may point to site(s) of osteomyelitis. Sinus tracts most often appear as thin linear soft-tissue T_2 hyperintense signal with enhancing margins on post-gadolinium chelate fat-suppressed T_1 imaging, giving the typical “tram-track” appearance (Figure 3).^{33,34}

Cellulitis

Soft-tissue infection often results from contiguous spread of microorganisms via skin ulcerations and sinus tracts. Plain radiograph and CT might show swelling, loss of fascial planes and occasionally gas within soft tissues.³⁵ Gas is encountered in cellulitis secondary to gas-forming organisms or, more commonly, air tracking from skin ulceration to deeper tissues.⁸ MRI features of cellulitis include thickened skin, subcutaneous oedema, increased fat reticulation and alteration of the normal fat signal. Cellulitic fat appears hypointense relative to normal fat on T_1 weighted images and hyperintense to muscle on fat-suppressed T_2 weighted images (Figure 4).³² The presence of

Figure 3. MRI of the foot. Axial T_2 fat-suppressed (a) and sagittal T_1 (b) weighted images demonstrate a deep penetrating skin ulcer on the plantar medial aspect of the calcaneum and sinus tract (arrows) with a “tram-track” appearance. The presence of a deep infected ulcer and sinus tract, and associated adjacent bone marrow oedema (asterisk) is highly specific for established osteomyelitis.

Figure 4. MRI of the forefoot. Axial images demonstrating soft-tissue oedema on the lateral second toe with T1 hypointensity (a, asterisk), T2 hyperintensity (b, arrow) and contrast enhancement (c, arrow head), consistent with cellulitis.

intense contrast enhancement is useful in differentiating true cellulitis from benign soft-tissue oedema, also seen commonly in the diabetic foot.³² It is important to note, however, that neither sterile devitalized tissue nor the centre of a soft-tissue abscess will enhance even in the context of regional cellulitis.⁸

Abscess

Prolonged foot infection is often associated with abscess formation, the prevalence on MRI having been reported from 10% to 50% in patients with diabetes.³⁶ The majority of abscesses form near skin ulcerations or sinus tracts; however, some can be seen more remotely as infection spreads to deeper tissues.³⁷ They are found more frequently in patients with established osteomyelitis, reflecting the fact that both entities represent advanced stages of infection.³⁶ The necrotic centre may show gas and air-fluid levels on plain radiography, hypoattenuation on contrast-enhanced CT with rim enhancement, and well-defined hypoechoic fluid collection on ultrasound, within which hyperechoic foci of debris/gas may be seen.³⁸ Colour Doppler ultrasound demonstrates peripheral hypervascularity but no flow within the necrotic centre.³⁸ MRI features of an established soft-tissue abscess are (1) isointensity or hypointensity relative to muscle on T_1 weighted images, (2) fluid-like signal on T_2 weighted images and (3) rim enhancement after intravenous gadolinium on T_1 images.⁴

Necrotizing fasciitis

Necrotizing fasciitis is a life-threatening infection of the superficial and deep fascia diagnosed clinically. Imaging shows gas tracking along fascial planes with occasional muscle involvement.³⁸ Rarely, the process involves adjacent bone (Figure 5).³⁹

Soft-tissue hypoperfusion/ischaemia/gangrene

Microvascular disease and its associated pedal ischaemia or gangrene can be qualitatively assessed using contrast-enhanced MR angiography. Normal soft-tissue perfusion should result in contrast enhancement with at least 10% increase in signal.⁸

Mild ischaemia without devitalization shows subtle decrease in enhancement compared with adjacent tissue, whereas necrotic or gangrenous region shows no contrast enhancement, being sharply demarcated from surrounding rim of enhancing hyperaemic soft tissue.⁸ Although not utilized at our institution, dynamic MRI can also be used to quantify loss of tissue perfusion.⁴⁰ Gas gangrene, caused by gas-forming bacterial infection of necrotic tissue, shows gas within soft tissue appearing as signal void on MRI.^{4,41} Gas gangrene is an emergency and needs to be differentiated from gas tracking from superficial ulcers to deeper tissues via sinus tracts.⁴¹

Figure 5. CT of the foot. Axial CT of the foot shows extensive subcutaneous emphysema (arrows) consistent with necrotizing fasciitis. In this rare case, gas extends to the mid-foot bones, indicating emphysematous osteomyelitis.

Figure 6. Soft tissue ultrasound and foot plain X-ray. (a) A foreign body shown on ultrasound as a hyperechoic focus with ring of hypoechoic granulation tissue (arrow). (b) The same nail was seen on plain X-ray.

Bursitis

Immunocompromise resulting from diabetes predisposes to septic bursitis often with preceding repetitive trauma.^{42,43} Prepatellar bursitis is the commonest in the lower limb.^{44,45} Plantar ulcers or cellulitis can lead to intermetatarsal bursitis, although fluid in the first three intermetatarsal bursae can be physiological up to 3 mm in transverse diameter, as well as being seen in the development of Morton's neuroma.⁴⁶ Adventitial bursitis frequently accompanies a callus as an elongated fluid collection in the adjacent subcutaneous tissue.⁸ Pes anserine bursitis has also been linked to diabetes, and imaging appearances are similar between infectious and inflammatory types.^{47–49} Ultrasound demonstrates increased synovial fluid with thickening and distension of the synovial membrane and synovial hyperaemia on colour Doppler. Bursal fluid shows heterogeneous echogenicity, often containing echogenic debris.⁵⁰ MRI shows increased synovial fluid with contrast enhancement of synovial membrane but not the bursal fluid.³⁸

Foreign bodies

Foreign bodies are commonly found in neuropathic foot owing to sensory loss and diminished protective reflexes. Impacted foreign bodies in the diabetic foot predispose to infection.^{32,51} Plain radiography and/or ultrasound performed with high frequency linear probes are commonly used to detect and assist with removal of foreign bodies (Figure 6). These are usually hyperechoic on ultrasound with a surrounding rim of hypoechoic inflammatory and granulomatous tissue.^{52,53} MRI can demonstrate low signal intensity foci, sometimes with susceptibility artefact.³²

BONES

Osteomyelitis

Osteomyelitis in a diabetic foot or ankle is nearly always owing to contiguous spread from an adjacent ulcer or soft-tissue infection; therefore rarely found in a foot with intact skin.⁸ Early diagnosis is challenging, but crucial to avoid late complications such as lower limb amputation.⁴¹

Plain radiographs can demonstrate periosteal reaction, cortical destruction, loss of normal trabecular pattern and bone lysis with or without osteosclerosis (Figure 7). However, these classical signs typically do not appear until at least 7–10 days after onset of infection, when the affected bone has undergone demineralization to the order of 30–50%; enough to manifest as

focal lucency.⁵⁴ In early stages of infection, soft-tissue swelling and blurred fascial planes may be the only visible radiographic abnormalities likely to be detectable on plain films.⁵⁴ These plain radiographic changes reflect cellulitis and should not be regarded as adequate in the exclusion of complicating osteomyelitis.

CT is significantly more sensitive in demonstrating early changes of osteomyelitis compared with plain radiography. Early, in the

Figure 7. Plain X-ray of the foot. Plain radiograph shows marked reduction of density and ill-defined margins in the third toe (asterisk), indicating osteomyelitis. Abnormality in the fourth toe (arrow) was longstanding and more consistent with chronic microtrauma and remodelling in the context of profound sensory neuropathy. Note previous amputation of the second metatarsal head.

Figure 8. CT of the foot. Axial (a) and sagittal (b) views demonstrate marked osteolysis and periarticular erosive changes at the talonavicular joint with sequestrum (arrows) within the navicular, consistent with septic arthritis/osteomyelitis. Advanced Charcot foot with rocker-bottom deformity is seen, with the cuboid (b, asterisk) descended from the collapsed longitudinal arch.

acute phase, CT may demonstrate patchy medullary lucency, cortical destruction and periosteal reaction. In chronic osteomyelitis, sequestra and cloacae are reliably depicted by CT (Figure 8). CT contrast resolution of soft tissue detail is only modest in the detection of associated soft-tissue processes, such as cellulitis, ulcers and sinus tracts.⁵⁴

Technetium triple phase bone scan has excellent sensitivity (100% in some studies) in detecting osteomyelitis, but poor specificity, particularly in patients with pre-existing Charcot foot or concomitant fractures.⁵⁵ In established osteomyelitis, increased uptake is present in all three phases. Labelled leukocyte scintigraphy has been shown to improve diagnostic accuracy,^{55,56} particularly when combined with technetium bone scan (sensitivity, 92.6%; specificity, 97.6%).⁵⁷ Concordance of positive findings on both studies indicate true osteomyelitis, while positive leukocyte scan with negative bone scan suggests possible soft-tissue infection without osseous involvement.⁵⁸

MRI provides excellent detection and characterization of soft-tissue abnormalities (such as sinus tract, cellulitis and abscess) in cases of suspected osteomyelitis, with sensitivity and specificity

of 90% and 79.0–82.5%, respectively.^{55,56} Primary signs of osteomyelitis on MRI include hypointensity of involved bone marrow on T_1 weighted, hyperintensity on T_2 weighted and enhancement on post-gadolinium images (Figure 9). Increased marrow signal seen on fluid sensitive or post-contrast images represents non-specific oedema and increased vascularity, therefore, can also be seen in other conditions causing local inflammation, such as CN, septic arthritis, and occasionally, intense adjacent cellulitis without established osteomyelitis. Low marrow signal on T_1 weighted images reflects true alteration of normal marrow fat content; hence, it is more specific for osteomyelitis.^{54,55}

Bone infarction

Avascular necrosis (AVN) of pedal bones is a well-recognized complication in diabetes mellitus, with the talus, navicular, first and second metatarsals being the commonest sites.⁵⁹ Diabetes has been linked as a risk factor for Freiberg's disease, *i.e.* AVN of the second metatarsal head (Figure 10).⁶⁰ Radiographic signs occur late, classically showing mixed lucencies and sclerosis with the late characteristic "crescent sign", *i.e.* a thin linear lucency in the subchondral area, reflecting fractured and collapsed

Figure 9. MRI of the foot. Axial views demonstrating extensive low T_1 signal (a) and (b) high signal on fat-suppressed (FS) T_2 weighted images. Gadolinium enhancement on axial FS T_1 image (c) within the marrow of the fifth metatarsal (arrows), representing osteomyelitis, and surrounding cellulitis.

Figure 10. X-ray of the foot. Previous partial amputation of the proximal phalanx of the left (L) great toe. Flattening of the heads of the left second and third metatarsals consistent with Freiberg's avascular necrosis. In addition, there are stress fractures involving the shaft of the second and third metatarsals, likely related to osteonecrosis of the metatarsal heads and amputation of the proximal phalanx of the first toe with resultant alteration in biomechanics.

subchondral trabeculae.⁶¹ Depending on the phase of osteonecrosis, plain radiograph and CT may be normal (acute phase) or may reveal variable amounts of osteopenia, focal bony sclerosis, mixed sclerosis and lucency (mottling), and subsequent articular collapse and fragmentation (subacute and chronic phases).⁶² MRI can identify early AVN prior to CT/radiographic changes or indeed clinical symptoms, particularly in the neuropathic diabetic foot.⁶³ The infarcted medullary bone of inhomogeneous signal intensity is classically surrounded by an inner hyperintense and outer hypointense “double-line” on T_2 weighted images, representing vascular granulomatous tissue underneath sclerotic bone (Figure 11).^{63–66} The “double-line” sign is, however, frequently absent in small pedal bones, in which poorly defined areas of T_1 hypointensity may be seen without contrast enhancement.⁶⁷

Pathological fractures

Pathological fractures occur in diabetes owing to the combined effects of neuropathy, vasculopathy and reduced bone quality.^{68,69} Bone bruises and bone oedema are visible on MRI as areas of regional altered marrow signal (dark on T_1 and bright on T_2 weighted images relative to normal fatty marrow). Subtle fractures that may be radiographically occult are often well seen on CT or MRI (Figure 12).⁷⁰ Cuboid fractures are common and contribute to the loss of lateral pedal arch and subsequent rocker-bottom deformity.⁷¹ Atraumatic calcaneal avulsion fractures are characteristically seen in the diabetic foot. These present in three different patterns: (1) superiorly displaced posterior calcaneal avulsion, (2) impaction of mid-calcaneus, (3) “wedge type” fracture with the fracture line extending from the posterior tubercle towards the talocalcaneal joint.⁷² The third type is typical in patients with heel ulcer and possible underlying osteomyelitis, resulting from increased Achilles traction on the weakened calcaneum (Figure 13).⁷³

Skeletal deformities

Common structural deformities in diabetics include hammer/claw toes, hallux valgus, pes planus and rocker-bottom deformity detectable on plain radiographs or CT.⁷⁴ Hammer toe deformity (Figure 14), *i.e.* fixed hyperextension of metatarsophalangeal joints is thought to result from intrinsic muscle atrophy. This deformity is associated with an increased incidence of plantar skin ulceration.^{24,75,76}

JOINTS

Charcot neuropathic osteoarthropathy

CN or Charcot foot is a progressive disease affecting the joints, bones and soft tissue, especially of the foot and ankle. It is seen in up to 13% of patients with diabetes.⁷⁷ Its pathogenesis is thought to stem from a combination of peripheral sensory (especially proprioceptive and pain) and autonomic neuropathy. The sensory deficits contribute to repetitive minor trauma to relatively insensitive feet whilst the autonomic deficit results in peripheral vasodilation and increased regional blood flow, which in turn results in increased osteoclastic activity. Consequent osteolysis and osteopenia predispose patients to injury thus forming a vicious cycle, leading to severe deformity.^{78,79} CN may

Figure 11. MRI of the lower limb. T_2 fat-saturated sagittal view (a) demonstrates a serpiginous rim of T_2 hyperintensity (short white arrow) in the distal tibial marrow, with central inhomogeneous T_2 hypointensity (asterisk). Proton density axial view (b) shows the same lesion with hypointense rim (black arrow) and hyperintense centre. Features consistent with marrow infarction. Swelling and hyperintensity in the distal peroneus brevis muscle belly is suggestive of diabetic (ischaemic) myopathy or sterile myositis (b, long white arrow).

mimic osteomyelitis in its acute presentation, the diagnosis of which is frequently missed or delayed in up to 25% of patients with diabetes.^{80–82} Identifying acute CN as an acutely swollen, erythematous and warm foot is of paramount importance, as its treatment (immediate off-loading) differs from that for infection. Delayed detection and continued ambulation and weight bearing contribute to significant irreversible deformity and subsequent disability.⁷⁸ Anatomically, Charcot foot most commonly affects the mid-foot joints, *i.e.* tarsometatarsal (Lisfranc's), naviculocuneiform, talonavicular and calcaneocuboid joints (Chopart's).^{83–85}

The radiographic appearance of CN can be classified into three stages.⁸⁶ Stage 1 (development) demonstrates bony fragmentation

with resultant debris at the articular margins, joint capsular distension and joint dislocation. Stage 2 (coalescence) shows organization of previously formed debris and fragments with osteosclerosis at bony ends. Stage 3 (reconstruction) is characterized by new bone formation, reduced osteosclerosis, rounding of bony ends and permanent deformity.⁸⁶ In particular, subluxation or dislocation of Chopart's joint causes mid-foot collapse, leading to a "rocker-bottom" deformity (Figure 8). Angle analysis on lateral plain film demonstrates reduced calcaneal inclination and talar-first metatarsal misalignment. The cuboid bone becomes the weight-bearing tarsal bone increasing the susceptibility for ulceration of the overlying skin.⁴¹ Other radiographic findings include osteopenia—exaggerated by disuse from pain or deformity—osteophytosis, periosteal reaction and

Figure 12. MRI of the foot. Axial short tau inversion recovery (STIR) sequence (a) and sagittal STIR sequence (b) show a non-displaced vertically orientated cuboid fracture (white arrow), with surrounding marrow oedema (asterisk). A subcortical fracture is seen at the talar dome (arrow head).

Figure 13. X-ray of the foot. A heel ulcer with dressing is seen. Wedge shaped avulsion fracture (arrow) at the posterior calcaneum is consistent with the likely weakened bone owing to osteomyelitis and excessive traction from the Achilles tendon during ambulation.

subchondral geode cyst formation. Monckeberg's sclerosis is also present radiographically in 78–90% of patients with diabetes with neuropathy, manifesting as radio-opaque parallel lines (when viewed in profile), representing calcified vessel walls.^{87,88} The cause of this phenomenon is postulated to arise from a common proinflammatory cytokine system, receptor activator of nuclear factor-kappa B ligand and osteoprotegerin (RANKL/OPG) shared in the pathogenesis of Charcot foot.⁸⁹

In early Charcot (where there is a typical clinical picture, *i.e.* Stage 0),⁹⁰ plain radiography may be normal, whilst triple phase bone scan may demonstrate increased uptake, indicating abnormal bone turn over.⁷⁸ CT can show minor intra-articular fractures in addition to the typical radiographic findings.^{86,91} MRI is more sensitive in demonstrating early articular and soft-tissue changes,⁹² such as joint effusion, subluxation, articular surface erosion, periarticular soft-tissue oedema and marrow signal changes (Figure 15).⁹³

Charcot foot vs osteomyelitis

Differentiating acute early stage CN from osteomyelitis presents a difficult and important challenge. Clinically, acute CN and acute osteomyelitis may present with acutely inflamed extremities with warmth and swelling. There is frequently a “culprit”

underlying penetrating ulcer, which the astute clinician (in our High Risk Diabetic Foot unit, the subspecialty podiatrist) will gently attempt to “probe to bone”—a clinical technique consisting of exploring the wound for palpable bone with a sterile blunt metal probe.⁹⁴ In the context of an infected ulcer, a positive “probe to bone” result is highly specific for osteomyelitis.⁹⁵

Important radiological clues for osteomyelitis include the anatomical location, presence of deep adjacent ulcers and sinus tracts, and the pattern of marrow abnormality on MRI. Marrow signal abnormality in multiple mid-foot joints, confined to the subchondral bone but affecting both articular ends within a joint, with no evidence of adjacent skin ulcers or connecting sinus tracts, is more likely to represent an acute Charcot foot. True osteomyelitis commonly involves a single bone of the forefoot or the posterior calcaneus, directly deep to an ulcer, with more diffuse marrow signal abnormality.³⁷ As CN progresses into the coalescent or reconstruction stage, more permanent deformities and less marrow signal abnormality is observed, usually allowing easier differentiation between the two entities.^{34,37} This may, however, be confounded by new or persisting marrow signal abnormalities, particularly in the ambulating patient—the result of an abnormal stress response owing to altered biomechanics.

Charcot foot complicated by infection

Osteomyelitis superimposed on a pre-existing Charcot foot adds further diagnostic difficulty. MRI signs more closely correlated with infection include large soft-tissue fluid collection, diffuse and profound marrow abnormality, soft-tissue fat signal change and direct relationship with a sinus tract or skin ulcer. Subchondral cysts and intra-articular loose bodies, if present, favour a diagnosis of established CN.⁹³ The “ghost sign” has been proposed as a useful and reasonably specific sign to detect true superimposed infection in the neuropathic foot (Figure 16). In the case of established infection, increased water content within

Figure 14. X-ray of the foot. “Hammer-toe” deformity—fixed extension deformity of proximal interphalangeal joints.

Figure 15. MRI of the foot. Fat-suppressed T_2 axial sequence demonstrates subtle mid-foot periarticular marrow signal changes (arrows), soft-tissue oedema (right-pointing arrow head), multiple small volume joint effusions (left-pointing arrow head) and reactive tenosynovitis consistent with early Charcot neuropathic osteoarthropathy.

the marrow (infection related oedema) results in the affected bone(s) being rendered dark and thus poorly seen against a background of T_1 -dark skeletal muscle and T_1 -dark oedematous fat on T_1 weighted sequences.⁹⁶ These infected bones are well seen as having abnormally bright, and enhancing marrow on fat-suppressed T_2 , and post-gadolinium contrast-enhanced fat-suppressed T_1 imaging. This phenomenon of ghosting is not seen on MRI in the aseptic neuropathic foot.⁹⁶

Septic arthritis

Similar to cellulitis and osteomyelitis in the diabetic foot, septic arthritis commonly results from direct inoculation from adjacent skin ulceration. Frequently involved joints in the foot and ankle closely correlate with sites of ulceration, with the interphalangeal and metatarsophalangeal joints being the most common locations (Figure 17).^{27,97,98} Mid-foot involvement is seen in patients with Charcot foot, particularly when “rocker-bottom” deformity is present. Posterior calcaneal ulcers tend to spread to the ankle or subtalar joints.⁴¹ No single MR sign is pathognomonic for this diagnosis, but large joint effusions, intense synovial enhancement and perisynovial oedema are considered suggestive of a septic joint.⁹⁷ Septic arthritis can mimic mid-foot CN on MRI. Subchondral marrow oedema associated with septic arthritis demonstrates hyperintensity on T_2 weighted images, but the same may be seen in both Charcot foot and osteomyelitis. Generally in septic arthritis marrow signal abnormality is localized to subarticular bone, but superimposed osteomyelitis may result in more diffuse abnormal marrow signal beyond subchondral bone.³⁴

MUSCLES

Muscle atrophy

Motor neuropathy in diabetes causes striated muscle atrophy, typically affecting the distal pedal muscles first.^{99,100} The degree of atrophy can be assessed on CT or MRI by analysing the muscle volume and morphology, with significant fat replacement of atrophic muscle seen in advanced cases.^{32,101}

Diabetic myopathy

First described and termed in 1965 by Angervall and Stener¹⁰² as “tumoriform focal muscular degeneration”, this uncommon entity has been reported in the literature as diabetic muscle infarction or myonecrosis. Its occurrence reflects poor diabetic control with extensive atherosclerosis, microangiopathy and possibly underlying coagulopathy.¹⁰³ Diabetic myopathy was traditionally described in patients with Type 1 diabetes only but is increasingly seen in patients with Type 2 diabetes especially those requiring insulin.¹⁰⁴ The typical presentation is that of acute onset of pain and swelling in affected muscles, often bilateral, occasionally with a palpable mass. Importantly, systemic symptoms are unusual. The thigh muscles are the most commonly affected, followed by calf and short rotators of the hip.¹⁰⁵ Imaging, especially MRI (Figure 18), is useful in the diagnosis of this condition and thus helps to avoid unnecessary biopsies and surgical intervention. In most patients, diabetic myopathy will resolve spontaneously following conservative management.

In cases of acute diabetic myopathy/myonecrosis, MRI demonstrates muscle oedema, with T_1 hypointensity or isointensity. T_1 hyperintensity is observed in patients with intramuscular haemorrhage.¹⁰⁶ On T_2 weighted images, affected muscles show corresponding hyperintensity owing to oedema and inflammation. On post-contrast T_1 images, peripherally enhancing, centrally hypointense areas of muscle represent areas of necrosis, indistinguishable from intramuscular abscess.¹⁰⁷ Additional MRI findings include subcutaneous oedema, subfascial fluid and obliteration of fatty intermuscular septa. On MRI, the differential diagnoses of

Figure 16. MRI of the foot. Mid-foot structures in sagittal views were poorly defined on T_1 images (a), but regained their structural clarity on T_2 images (b and c) after intravenous gadolinium injection. This “ghost sign” suggests Charcot foot with superimposed osteomyelitis.

diabetic myopathy are pyomyositis/abscess, necrotizing fasciitis, acute denervation atrophy of muscle and other non-infective/incidental causes of myositis.¹⁰⁴

Figure 17. MRI of the foot. Abnormal T2 marrow hyperintensity (arrows) is seen in the periarticular region of the medial part of first metatarsophalangeal joint. The profound joint space loss and presence of adjacent infected skin ulcer (asterisk) further suggests septic arthritis.

MRI features of diabetic myonecrosis, tumour with necrotic centre and abscess may overlap. Ultrasound may help further differentiate diabetic myonecrosis from the other entities by demonstrating (1) the absence of a typical abscess such as anechoic centre, (2) hyperechoic lines within the lesion representing muscle fibres and (3) lack of fluid-like motion when applying probe pressure.¹⁰⁸

Pyomyositis

Bacterial infection of skeletal muscle is rare owing to its rich vascular supply. Being mostly a tropical disease, its occurrences in temperate regions are usually associated with trauma or immunocompromise, diabetes being a major risk factor.^{109,110} Oedematous muscle appears on ultrasound as poorly defined hypoechogenicity, whilst on CT as regions of slight hypo-attenuation. MRI is much more sensitive and demonstrates muscle enlargement, initial iso-hypointensity on T_1 weighted and hyperintensity on fluid sensitive sequences (Figure 19). As the disease progresses to necrosis and liquefaction, typical features of abscess common to other body regions can be seen, as discussed previously. Contrast-enhanced imaging shows variable enhancement of the affected muscle with non-enhancement of devitalized muscle or pus at the centre of the abscess if present.^{38,50,111}

TENDONS

Tendinopathy

Studies suggest a link between diabetes and tendon disorders.¹¹² Achilles and plantar fascia thickening have been demonstrated using CT, MRI and ultrasound^{113–115} and are associated with increased pedal tensile force and altered gait biomechanics.¹¹⁶ Tibialis posterior and flexor hallucis longus dysfunction contribute to flatfoot deformity. The spectrum of tendon abnormalities range from peritenonitis/paratenonitis to tendinosis, tendon tears and rupture. On ultrasound, paratenonitis/peritenonitis displays loss of normal paratenon hyperechogenicity with synovial fluid accumulation. Tendinosis demonstrates intratendinous ill-defined hyperechogenicity, disorganized fibres, increased thickness and calcifications. Partial or complete tendon tear shows well-defined hypo-echoic cleft that extends to tendon surface.¹¹⁷ MRI findings

Figure 18. Lower limb MRI. (a) Marked T_2 hyperintensity is seen in muscles of the adductor compartment (black asterisks). On T_1 images (b), rim enhancement (white arrows) with central hypointensity (white asterisks) in the same areas is seen, consistent with diabetes myonecrosis. (c) A pocket of sterile fluid (found at surgical drainage) is also seen (black arrow). 6-month follow-up MRI (d) showing marked muscle atrophy in the affected muscle groups.

include paratendinous T_2 hyperintensity, intratendinous hyperintensity on both T_1 and T_2 weighted images and loss of fibre continuity with hyperintense gaps in ruptured or fully torn tendons.^{67,118,119}

Septic tenosynovitis

Tenosynovitis can occur in the presence of skin ulceration, cellulitis or osteomyelitis. The most commonly involved are the peroneal, Achilles and plantar flexor tendons (Figure 20) owing to their close proximity to the lateral malleolus, calcaneus and

weight-bearing bones on plantar surface of the foot.^{41,120} MRI features include presence of peritendinous fluid as hyperintense signals on T_2 weighted sequence, thickened tendon and post-contrast synovial enhancement, suggesting increased vascularity and inflammation.^{41,120} If MRI signs are seen in conjunction with directly adjacent skin ulceration and soft-tissue infection, septic tenosynovitis is very likely.³⁴ Where MRI is not readily available, high-resolution ultrasound and power Doppler can demonstrate synovial thickening $\pm$ peritendinous fluid, with synovial hyperaemia seen on colour Doppler.⁵⁰

Figure 19. MRI of the pelvis. T_1 weighted fat-suppressed sequence with intravenous gadolinium in coronal (a) and axial (b) views demonstrate a lobulated fluid collection (asterisk) within a diffusely abnormal right iliacus muscle consistent with pyomyositis and abscess formation. Fluid is also seen in the right sacroiliac joint (arrow), indicating septic arthritis.

Figure 20. MRI of the foot. Contrast-enhanced T_1 weighted fat-suppressed coronal image demonstrates marked swelling and contrast enhancement of the flexor hallucis longus tendon at the level of the metatarsals (arrow), indicating infective tendonitis and tenosynovitis.

CONCLUSION

A multidisciplinary approach to the “high-risk diabetic foot”, in our experience, has proven to be very effective in managing complications in this ever increasing cohort of patients

specifically in reducing morbidity, including limb loss, as well as length of stay in hospital. As discussed, diabetes has broad spectrum of manifestations in the lower limb. Timely, combined expert input from dedicated podiatrists, endocrinologists, vascular surgeons and radiologists in this forum has proven to be a very successful model, resulting in early diagnosis of complications and the subsequent ability to expedite aggressive treatment.

Multiple imaging modalities are employed as appropriate, with increased reliance on high-resolution MRI, specifically to confirm or exclude the presence of early neuropathic osteoarthropathy, devitalized soft tissue or bone, septic arthritis, osteomyelitis and soft-tissue abscesses. The role of the radiologist is central in terms of providing accurate and early diagnosis of complications, as well as monitoring the progress of complications and treatment. Radiologists are also uniquely placed to advise on, and perform specific image-guided interventions such as lower limb arterial revascularization procedures for ischaemia, joint aspiration for suspected septic arthritis, bone biopsy for suspected osteomyelitis, as well as percutaneous drainage of soft-tissue abscesses.

In the experience of the authors, general radiologists perform interpretation of imaging of complications of the diabetic foot very variably. It is our hope that this review, incorporating perspectives from radiologists who work closely as part of a large multidisciplinary “high-risk diabetic foot team”, will substantially contribute to the body of knowledge on this topic and assist radiologists to provide a higher quality of service to this important and growing cohort of patients.

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