Chapter 12

Diabetic Foot Ulcers — Treatment and Prevention

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Additional information is available at the end of the chapter

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1. Introduction

Diabetic foot ulcers are a growing problem in the diabetic community. Globally, diabetes mellitus has grown to pandemic proportions, affecting 194 million people worldwide and is expected to increase in prevalence to 344 million by the year 2030 [1]. Of these patients, between 2 and 6% will develop a diabetic foot ulcer (DFU) yearly [2]. The onset of a DFU often precipitates a complex chain of events that may lead to limb loss. The long-term outcome for a diabetic patient after a major limb amputation is grave, with 50% of these patients deceased at 5 years [3].

In the United States public discussion and much research money goes to the investigation and treatment of breast and prostate cancers. However, when the 5 year mortality percentages are analyzed, a diabetic neuropathic ulcer has a worse survival rate than each of these cancers. The same is true if a diabetic has had a prior amputation. Add peripheral arterial disease and the mortality statistics worsen. In fact having a neuropathic ulcer or prior amputation has the same poor survival rate as colon cancer [4]. It is unknown if the lower extremity complications themselves lead to greater mortality, but it may be assumed that complications such as a foot ulcer are indicators of more significant diabetic disease with its well-known increased risk of cardiovascular complications.

This chapter will focus on key concepts related to prevention and treatment of diabetic foot ulcers and their complications. A detailed discussion will cover pathogenesis and risk factors of diabetic foot ulcers; clinical presentation; initial evaluation; treatment methods, both nonsurgical and surgical care; and complication management, including infection of soft tissue and bone, Charcot neuroarthropathy, and limb preservation amputation. A rational approach to the evaluation and treatment of diabetic foot ulcers will be discussed, utilizing the most current research.

2. Pathogenesis of the diabetic foot ulcer

The diabetic foot ulcer is a complex multifactorial entity with a well-known etiologic pathway. The most common pathway is considered to be due to reduced peripheral sensation [5] coupled with increased shear and/or compressive pressure [6]. Brand discussed the concept of "tenderizing" the foot [7] in which peripheral neuropathy leads to a loss of function of two types of mechanoreceptors in the skin, responsible for delivering nociceptive signals. High threshold mechano-receptors, carried via A-delta fibers, normally become sensitized to increased repetitive pressures on healthy tissues. This sensitization lowers the pain threshold in the patient with normal sensation, carried by polymodal nociceptors, leading to altered behaviors which reduce pain and subsequent damage. In the neuropathic patient this sensitization system is absent, allowing tissue damage to occur without any pain response with the subsequent diabetic foot ulcer.

Diabetic peripheral neuropathy also causes motor and autonomic dysfunction. Motor dysfunction is seen in the form of weakness and atrophy [8]. As the intrinsic pedal musculature becomes poorly functional muscular imbalances occur causing deformity. This deformity allows for focal areas of increased pressure, becoming risk areas for ulceration. Autonomic neuropathy contributes via sudomotor dysfunction causing loss of sweat glands as well as loss of nutritive supply with subsequent dry skin that breaks down easily [5]. An ill-fitting pair of shoes may be all that was required for the shear forces to lead to an ulceration of a patient's foot who has diminished sensation.

If skin breakdown and wound formation occurs by a combination of high pressures in the insensate foot then wound chronicity is upheld by altered and inappropriately functioning biochemical pathways and chemical mediators. Various cytokines and matrix proteins have been implicated in the process of delayed wound healing. One of these mediators that has received much emphasis over the recent past is matrix metalloproteinase 8 (MMP-8), which is the primary collagenase in normal wounds [9]. In chronic wounds MMP-8 is upregulated due to reduction of its regulating enzyme TIMP-1 (tissue inhibitor of metalloproteinase 1). This overexpression of MMP-8 causes enzymatic destruction of the wound extracellular matrix, thus retarding wound healing. The diabetic foot ulcer may also be lacking growth factors such as platelet-derived growth factor (PDGF) and tumor growth factor beta (TGF-β) which stimulate fibroblast proliferation and synthesis and act as chemoattractants for neutrophils, smooth muscle cells, and macrophages [10] in the healthy wound. In diabetic wounds these factors may be diminished or absent.

3. Risk factors

Several clinical causal pathways have been researched, allowing the clinician to grade the primary risk factors associated with the onset of DFUs. Lavery et al, described an update to the clinical staging method previously proposed by the International Working Group for the Diabetic Foot [11, 12]. Table 1 demonstrates increasing trend of ulceration, infection,

and amputation, with an extremely high risk of hospitalization with increasing stage. The presence of peripheral arterial disease and a history of prior ulceration or amputation greatly increases the risk of complications beyond the introducing factors of peripheral neuropathy or deformity.

The presence of peripheral neuropathy with loss of protective sensation is the sine qua non of diabetic foot ulceration, diagnosed using the 5.07 Semmes Weinstein monofilament. This simple, rapid test is easily performed in the primary or specialty clinic. The monofilament is constructed to produce a standard 10 grams of force when bent and has been found to accurately predict the presence of ulceration [13]. Ten sites are tested (plantar toes and metatarsal heads 1, 3, and 5; two points on the medial arch; one point on the heel; and one on the dorsum of the foot). If the patient is unable to feel 4 of 10 sites, he is diagnosed with peripheral neuropathy.

Stage	Description	Risk of Complications (by Odds Ratio)			
		Ulcer	Infection	Amputation	Hospitalization
0	No PN*, No PAD	N/A	N/A	N/A	N/A
1	PN, No PAD, no deformity	2.4	1.9	0	10
2a	PN and deformity, No PAD	1.2	2.3	10.9	13.6
2b	PAD	9.3	13.5	60.9	124.8
3a	Ulcer history	50.5	19.2	36.3	60.7
3b	Amputation	52.7	62.3	567.9	650.3

Table 1. IWGDF staging system for diabetic patients at risk for lower extremity complications. Adapted from Lavery, et al [11]. *PN = Peripheral Neuropathy; PAD = Peripheral Arterial Disease

4. Clinical presentation and initial evaluation

As in all medical conditions the initial evaluation of a patient with a diabetic foot ulcer begins with a detailed history. Important components of the history include length of time the ulcer has been present; etiology of the wound (if known); any self or professional treatment; prior ulcer, infection, or amputation history; personal medical history; allergies; medications; surgical history; family history; tobacco use; alcohol abuse; recreational drug use; and a detailed review of systems to elicit the presence of macrovascular or microvascular disease [14].

On physical examination one may appreciate the classic appearance of the diabetic plantar foot ulcer (Figure 1). This is most commonly a partial or full thickness wound underlying a bony prominence or area of deformity. When chronic low grade elevated plantar pressures are present the skin forms reactive hypertrophic tissue, indicated by hyperkeratotic callus, the tell-tale sign of the neuropathic ulcer. The wound should be examined for size, undermining

(in which the edges of the wound overlap the base), general appearance, and the probe to bone test should be performed.

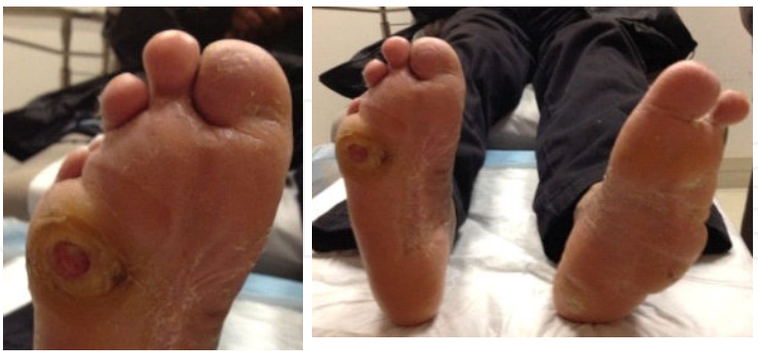

Figure 1. Classic appearance of the diabetic foot ulcer. Note the characteristic red, granular base and hyperkeratotic rim under an area of increased pressure as well as the contralateral foot with prior amputation of the 3rd, 4th, and 5th rays.

During this test the examiner uses a sterile metal probe (often the blunt end of a cotton swab is used) to gently but firmly push into the base of the wound. The examiner then determines the depth to which the probe may go, whether to subcutaneous, capsular, or bone layers. If the probe is able to touch bone this is considered a positive probe to bone test and is highly predictive of osteomyelitis. The predictive ability of this test differs based on the population studied. In patients with severe infection and a higher likelihood of osteomyelitis, this test has a positive predictive value of 89% [15]. However, in a patient population less likely to be infected, i.e. the outpatient wound clinic population, the positive predictive value is 57% but with a negative predictive value of 98% [16]. In this situation the inability to palpate bone with the probe indicates a low likelihood of osteomyelitis.

A thorough physical examination should also include an evaluation of arterial outflow and the presence of peripheral arterial disease (PAD). This includes palpation of all pulses in the lower extremity, including the dorsalis pedis/tibialis anterior, posterior tibial, popliteal, femoral, and abdominal aortic pulses. The absence or diminution of a peripheral pulse (specifically the dorsalis pedis or posterior tibial) has a sensitivity between 63% and 95% and a specificity between 73% and 99% for peripheral arterial disease [17-19]. Capillary refill time, in which the limb is elevated to heart level and pressure placed on multiple digits, counting the time for refill of the blanched skin, has a sensitivity of 28.3% and specificity or 85.3% [17]. Auscultation for femoral bruits may also be performed. However, this test has a low sensitivity (2-29%) but high specificity (95-96%) [19, 20]. Trophic changes of the skin may include atrophic, shiny appearance with loss of hair, coolness to touch, cyanosis, and thickened nails. Trophic changes generally have a lower sensitivity and specificity for PAD [17].

In the diabetic patient with a neuropathic foot ulcer and concomitant PAD the wound appearance may be slightly different. In some situations the wound will look similar to the well vascularized ulcer with the exception of a more pale or light pink appearance to the wound base instead of a red, granular appearance. In more advanced neuroischemic wounds the

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appearance will be markedly different with a fibrous yellow appearance and an often irregular, sometimes punched out-appearing, shape (Figure 2).

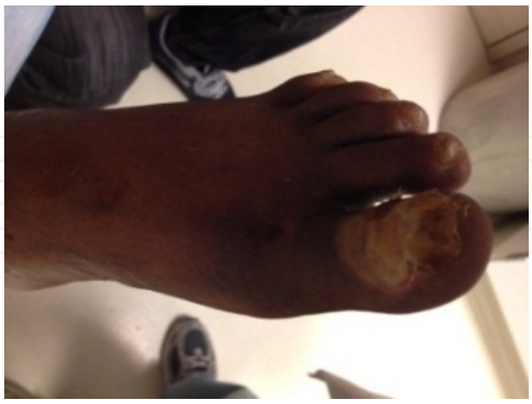

Figure 2. DFU with ischemic appearance demonstrating a yellow, fibrotic base and lack of healthy red granulation tissue.

The musculoskeletal examination is also fundamentally important to evaluate the patient with a diabetic foot ulcer. In the majority of patients an examination of the biomechanical contribution will reveal the cause of the ulcer. The common factor is a focal increased shear or vertical pressure. As such, a thorough examination for pedal deformity is of paramount importance. Overall appearance of the foot should be appreciated, followed by a detailed examination of specific deformities, including joint position, range of motion, and rigidity versus flexibility (Figure 3).

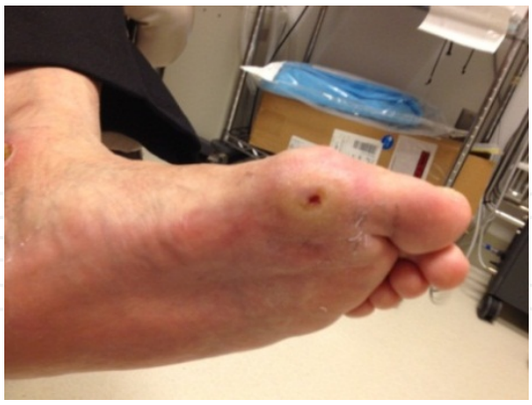

Figure 3. Diabetic neuropathic plantar foot ulceration underlying tibial sesamoid bone with involved hallux valgus deformity.

Functional compensation at one joint for lack of motion of another is also commonly seen. For example, lack of motion of the great toe joint (hallux limitus) often leads to a compensatory increased motion at the hallux interphalangeal joint. This compensation increases plantar pressures at the joint with a subsequent DFU (Figure 4).

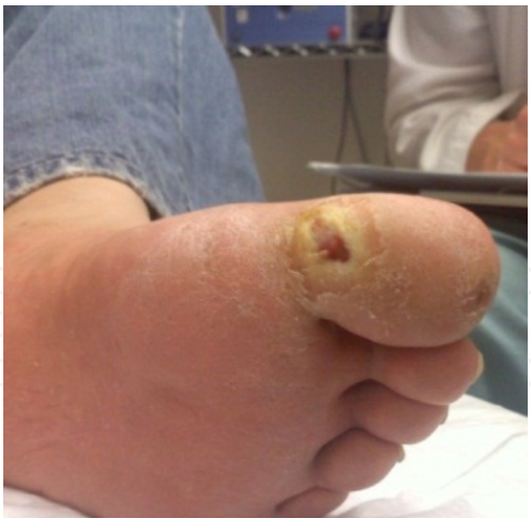

Figure 4. Diabetic foot ulcer located plantar to the hallux interphalangeal joint resulting from increased pressure after compensation at this joint for lack of motion at the first metatarsophalangeal joint.

Another highly important mechanical contributor to the creation of diabetic foot ulcers, especially those on the plantar forefoot area, is ankle joint equinus, or lack of dorsiflexion of the foot on the ankle during active walking. Plantar pressures have been shown to be increased three fold in diabetic patients with ankle equinus when compared with those without [21]. The relationship between callus and ulceration was confirmed by Murray and colleagues who found a relative risk of 11.0 for an ulcer developing under an area of callus [22]. As such, the relationship between ankle equinus, increased plantar pressures, and DFU is well established.

Upon completion of the physical examination, laboratory and imaging methods may be employed in certain circumstances to better appreciate the underlying anatomy and will be discussed below.

A simple, rapid examination of the foot takes no more than one to two minutes. From a clinical standpoint a significant sign of impending ulceration is the preulcerative callus. This is seen as hyperkeratotic tissue with visible hemorrhage within the epidermal or dermal skin layers.

Treatment of diabetic foot ulcerations can be intimidating and complex without a basic understanding of the treatment options available and a thorough evaluation of the ulcer's characteristics. Current literature suggests that, if the initial treatment plan does not reduce the size of the ulcer by 50% in four weeks that the course of treatment should be re-assessed [23-26]. Essential components of any initial or re-evaluated treatment plan should consist of debridement, moist wound healing environment, offloading and infection control [27]. Conservative options are typically employed initially [28] but if progress stalls, surgical components to the treatment plan may help to decrease time to healing or even promote healing. Characteristics of the diabetic foot ulcer are important to consider because they directly influence what treatment modalities are used. Evaluation of the diabetic foot ulcer's location, size and depth, tissue type, presence or absence of drainage, length of time the ulcer has been present, vascular supply, and any pathomechanics present are all important variables when formulating the treatment plan.

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4.1. Debridement

The type of tissue found within the diabetic foot ulceration is an important treatment consideration. When yellow fibrotic tissue or dusky necrosis is noted, steps must be taken to covert the diabetic ulcer base to a beefy, red, healthy granular tissue. Surgical debridement of avascular tissue may improve rates of ulcer closure by removing the tissue that had served as a foreign body. Several types of debridement are commonly employed today but there is no scientific evidence suggesting that one type is superior to another [29, 30] only that diabetic foot ulcers receiving a regular debridement are found to heal faster [30]. Debridement is a necessary step that prepares the wound bed to promote healing [30] and is helpful when converting a chronic wound to an acute ulcer [25]. Sharp debridement is considered the gold standard [30, 31] and can be performed at the bedside or in the operating room [32]. Enzymatic debridement, such as collagenase for fibrotic tissue is a good option when the risk of debriding small quantities of healthy tissue is not acceptable or if the patient experiences pain with sharp debridement. Hydrosurgical debridement, as with Versajet® (Smith and Nephew corporation), demonstrates no statistically significant reduction in bacterial contamination [33] and was found only to decrease the duration of time spent debriding the ulcer [31]. Biologic debridement, using medically sterilized *Lucilia sericata* larvae, aims to rid the ulcer of necrotic tissue and pathogens [30, 34]. However, maggot therapy has not demonstrated improvement of healing rate or reduction of bacterial load as compared with hydrogel [29, 30]. Applying hydrogel or hydrocolloid dressings introduces moisture, and if placed under occlusion, serves as a form of autolytic debridement that allows the body's own enzymes to liquefy necrotic tissue. Hydrogel, additionally, has been found to increase the rate of healing as compared with plain gauze [29]. Mechanical debridement, also known as "non-selective debridement" is performed by applying saline moistened gauze to the ulcer and allowing it to dry before the dressing is periodically changed. The removal of the gauze mechanically removes both healthy and unhealthy tissue and is no longer considered the best dressing for diabetic foot ulcers [26].

The size and depth of the diabetic foot ulcer are important factors to evaluate because a deep ulcer may have avascular tissue such as tendon exposed. Instead of allowing the avascular tissues to desiccate and require debridement, potentially losing long-term function in the foot, immediate use of a negative pressure wound therapy (NPWT) system has been shown to increase volume of granulation tissue within the ulcer [29, 35, 36] which may possibly preserve that structure. NPWT has also been shown to significantly improve the rate of wound closure as compared to simple saline gauze dressings [26, 29, 37] and NPWT has demonstrated a reduced amputation incidence [26] and decreased hospital stay [38].

Ultrasound, lasers, electrical and electromagnetic therapies have been evaluated in laboratory research but there is insufficient evidence to suggest these have any effect on diabetic foot ulceration healing times [29].

4.2. Moist wound healing environment

The presence or absence of drainage helps to determine what type of adjunct dressing the diabetic foot ulcer may require. By converting a chronic diabetic foot ulcer to an acute wound and maintaining a moist wound bed, the inflammation, infection and exudate are controlled

while increasing epithelial advancement [25, 34]. This prevents retardation of cellular proliferation and angiogenesis by eliminating the excessive levels of matrix metalloproteinase's, growth factors and cytokines [34] present in the chronic wound. Applying a hydrocolloid or hydrogel may help to introduce moisture. If excessive drainage is present an absorbent dressing should be used, such as a calcium alginate or another absorbent fiber. Other dressing components have been found to increase healing in small studies such as the use of topical and oral β-glucan [39]. In another study, comparison of various dressing options demonstrated no statistical difference in ulcer healing but did note that the basic wound contact dressing, was more cost-effective in healing diabetic foot ulcers than a fibrous hydrocolloid dressing [40].

If the diabetic foot ulcer has been present for 30-90 days [35] it is considered chronic. Chronicity may dictate whether or not to use bioengineered products that deliver fibroblasts superficially, such as Dermagraft® (Advanced Tissue Sciences), Apligraf (Organogenesis) or healthy doses of growth factors, such as platelet rich protein gel delivered superficially. Both, Dermagraft® and Apligraf®, used with effective offloading, have demonstrated decreased healing time [41, 42] and several studies suggest that utilization of near-physiological concentration of platelet rich protein gel on recalcitrant or chronic wounds demonstrate a rapid and consistent healing [32, 34, 35, 43] and is cost-effective [42]. A smaller study suggests that injected, rather than topical, epidermal growth factor at the lesion's base may result in improved healing [44] due to elimination of high levels of proteases that reduce levels of growth factors needed for healing [34].

4.3. Offloading

The location of the diabetic foot ulcer is commonly found overlying a bony prominence [25, 34] or involving a deformity (Figure 5). Early treatment may consist of pressure reduction. Total contact casting (TCC) (Figure6A), is considered the best method of offloading as compared to a removable walking cast [27]. However, when a total contact cast is unavailable or contraindicated, placing the patient in a wedge-type shoe (Figure 6B) or a walking boot (Figure 6C, 6D), using flexible and rigid casting tape [45], complete bed rest [28] or by using felt aperture padding have also been noted to reduce healing times [25, 35].

When these conservative means for offloading are ineffective, surgical resection of the underlying bony prominence, termed internal off-weighting, is an option [25]. This surgical treatment may entail bony procedures such as an exostectomy, condylectomy, arthroplasty [25, 36], metatarsal osteotomy [28] or arthrodesis [28]. Additionally, tendon transfers to rebalance the foot and amputation may also be applied as indicated (Figure 7).Surgical procedures should be chosen and performed by those with expertise in surgical reconstruction of the diabetic foot and ankle.

Pathomechanics of the patient's foot, such as gastrocnemius-soleus equinus or a taut plantar fascial ligament both leading to plantar forefoot ulcerations, may necessitate conservative offloading measures as previously mentioned. However, if the offloading attempts are ineffective, a surgical release (plantar fascial ligament resection [28, 46, 47]) or surgical lengthening (tendo-achilles lengthening [25, 28, 46, 48]) of the contracture may allow the forefoot to be more flexible when met with ground reactive forces thus healing the diabetic

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plantar foot ulcer [49]. Mueller et al's randomized clinical trial found that patients treated with a tendo-achilles lengthening and a TCC were 12% more likely to heal a plantar foot ulcer than with a TCC alone. At two years post operatively, the group with both the TAL and TCC re-ulcerated at a rate of only 38% compared to 81% recurrence in the group with only a TCC [24, 49].

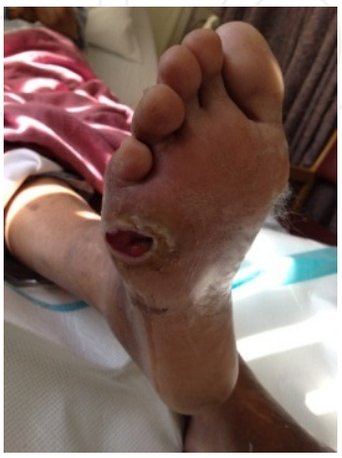

Figure 5. DFU overlying a prominent fifth metatarsal head deformity.

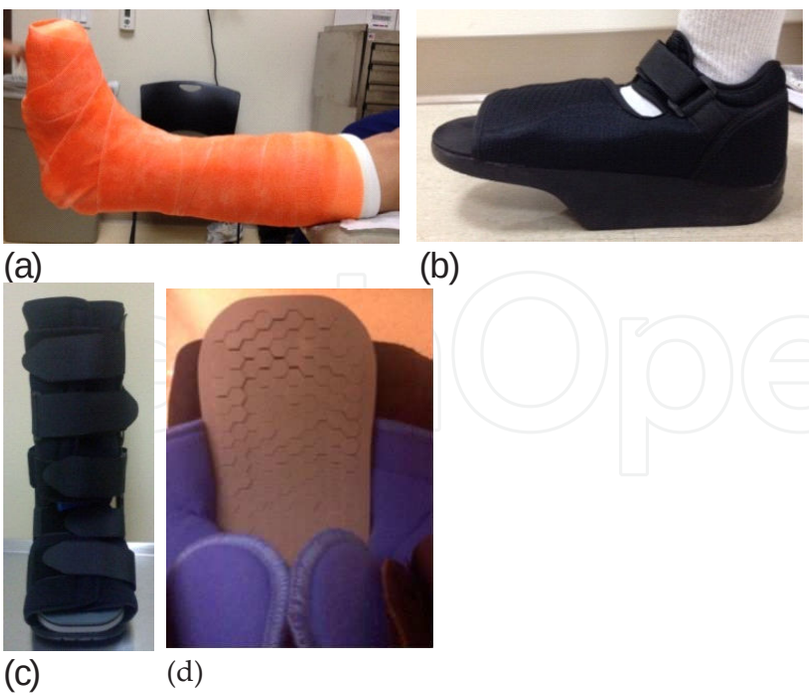

Figure 6. Off-loading devices; A – Total Contact Cast (TCC); B – Wedge type shoe to off-load the plantar forefoot; C – Darco® brand offweighting boot with removable hexagonal pegs for offweighting DFUs.

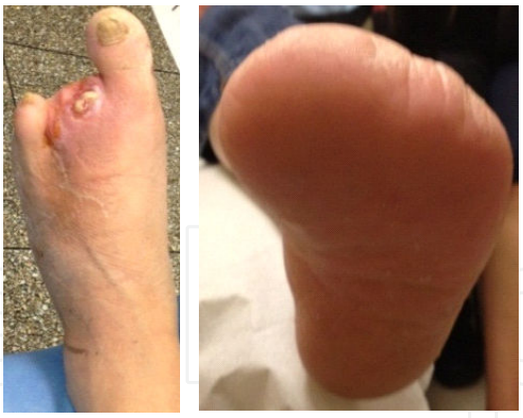

Figure 7. Nonfunctional foot with underlying osteomyelitis successfully treated with transmetatarsal amputation and percutaneous tendoachilles lengthening with 6 month follow-up (note lack of callus or recurrent ulceration).

4.4. Additional methods

Various types of skin grafts and flaps may assist with closure of the ulceration (Figure 8) as healing an ulcer by means of secondary intention represents a major burden to patients, health care professionals and the health care system [50]. Bioengineered skin grafts and split-thickness skin grafts do not show statistically significant success in healing diabetic foot ulcers [29] despite small studies suggesting grafts improve rates of healing and decreased evidence of amputations [51, 52]. Local muscle flaps have also been found to be successful in closing complicated diabetic foot wounds and are far superior as compared to the survival rates of amputees [53]. Despite an increased complication rate, pedicled flaps were found to have comparable limb salvage success as compared with free flaps [53]. A successful flap closure extends the life of an amputee [53].

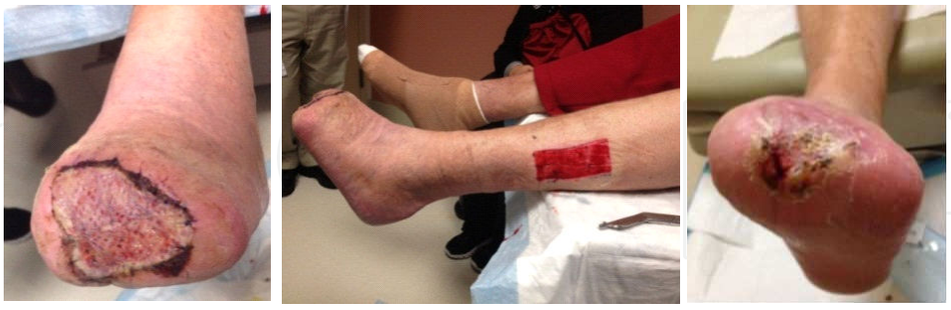

Figure 8. A. Complicated diabetic wound after guillotine-type trans-metatarsal amputation treated with split thickness skin graft. B. Donor site from lateral leg shown. C. Successful healing.

Hyperbaric oxygen (HBO) therapy systemically has been found to decrease the rate of major amputations [29] but not in the rate of minor amputations [54]. HBO therapy in diabetic foot ulcers has not yet demonstrated its cost effectiveness [29]. When a conservative treatment plan is found to improve the ulcer but does not heal it, utilizing HBO therapy may help to increase

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the partial pressure of oxygenation to tissues and help heal the wound [54, 55]. A study has demonstrated that the use of HBO facilitates wound closure when there is a change in transcutaneous oxygen measurements of ≥ 10 torr [56]. Topical hyperbaric oxygen therapy has not been found to decrease the rate of major amputations [29] and cannot be recommended for use in diabetic foot ulcers at this time.

When various treatment modalities are not successful, if possible, a limb salvage attempt is advised. External fixation is an additional option, boasting skeletal stability, easy access for soft tissue management, and assisting with plastic surgery wound closure techniques [36, 57]. If external fixation is not available or possible, there are many levels of amputations to consider [36]. While a trans-tibial amputation has the same long-term survivorship as some mid and rearfoot amputations (Symes, Lisfranc, calcanectomy or Chopart's) a partial foot amputation allows higher ambulatory levels and longer durability with less morbidity and mortality than trans-tibial amputations [51]. Allowing the patient to have a good quality of life, maintain as much function as possible and increase ease of prosthetic use following the amputation are important advantages to consider.

5. Complications

5.1. Infection

One of the earliest complications of diabetic foot ulcerations is infection [58] and if not treated adequately, may require amputation. This of particular concern because the 3 year survival rate following a lower limb amputation is 50%, decreasing to only 40% after 5 years [59].

All skin surfaces, and thus all wounds, have a certain level of bacteria on the surface at baseline, referred to as surface *contaminants*, defined as bacteria which are present but do not multiply. When those bacteria multiply, they are referred to as *colonizers*. Whether the bacteria are able to surmount a response from the host immune system will dictate whether there is an *infection*. Some believe that observing 10^5 bacteria per 1 gram of tissue is the threshold between a colonizer and an established infection. However, depending on the bacterial species or strain, an infection can result with far fewer than the 10^5 bacteria per 1 gram of tissue. Take for example β-hemolytic *streptococci*, which produce enzymes that promote tissue invasion and cause progressive infections without the same bacterial burden as other organisms [58, 60-62].

Risk factors for infection include a non-healing ulcer, advanced age, male sex, black race and a history of smoking in addition to sensory and autonomic neuropathy [63]. Diabetic foot infections are difficult to manage due to the associated comorbidities affecting the patient such as neuropathy, peripheral vascular disease, immunopathy and nephropathy [59]. Organisms such as methicillin resistant strains of *Staphylococcus aureus,* among others, pose a challenge to healthcare providers. Several factors such as prolonged hospital stays, exposure to surfaces and personnel who may have come into contact with resistant strains, and prolonged or prior antibiotic treatment can result in infections with these organisms. Many patients with chronic ulcerations have a history of recurrent ulcerations and infections that place them at high risk

for infection with resistant organisms [65]. Immunopathy increases a patient's susceptibility to infection. Poor glycemic control has been connected to impairment in leukocyte phagocytosis and chemotaxis, which increase the risk for infection. Infections lead to hyperglycemia which potentiates in a vicious feedback loop [59, 62, 66, 67].

5.2. Clinical findings

Patients with infections typically present with erythema, edema, purulent drainage, malodor, calor, induration, lymphangitis, soft tissue edema and occasionally gangrene or necrotic tissue (Figure 9). Complaints of pain in an insensate patient should raise suspicion for an infection. Patients also complain of recalcitrant hyperglycemia and other constitutional symptoms such as fevers, malaise and chills, sometimes referred to as the 'diabetic flu', which should raise suspicion for a deep infection [59, 61, 68].. Due to the immunopathy however, some patients may not present with any constitutional signs or symptoms [59, 66].

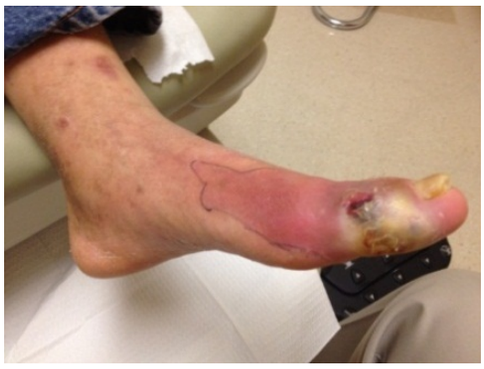

Figure 9. Diabetic patient with acute infection—notice the lymphangitis and local erythema.

Infections can be categorized by anatomical location and severity of illness. Superficial infections typically show no signs of systemic toxicity and glycemic levels remain unaffected. Deep foot infections, in contrast, result in contiguous spread of erythema and edema with accompanying constitutional symptoms such as fever, chills, malaise, and occasionally blood glucose elevations. When necrosis of tissue or skin is encountered, this signals impaired arterial supply, either from systemic arterial disease or from local vascular impairment [6] (Figure 10).

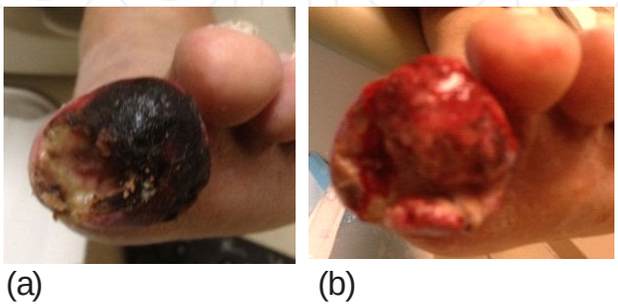

Figure 10. Diabetic patient with an infected hallux; A – at presentation, note necrotic and gangrenous tissue; B – after debridement.

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5.3. Diagnosis

Identification of infecting organisms for diabetic foot wounds is of great interest, particularly when considering antibiotic therapies. Depending on the chronicity of the wound there can be a slight difference in the organisms that can be isolated from a wound culture. Acute wounds typically grow gram positive cocci while chronic wounds are polymicrobial, with a mixture of gram positive cocci, gram negative bacilli and anaerobic organisms (Table 2) [58, 69, 70]. Those patients who have been previously hospitalized or have had prolonged antibiotic therapy can have an altered profile of organisms. Patients who have not been on any recent antibiotics typically grow gram positive organisms with a greater likelihood of gram negative organisms and organisms that are resistant to antibiotics [65].

Performing a surface swab evaluation has been deemed diagnostically unreliable. Instead, deep tissue specimens should be taken from the wound after a sharp debridement either with a scalpel or curette. Alternatively, in the presence of an abscess, aspiration of the abscess can provide more accurate information regarding the infecting organisms [58, 61, 63, 64].

Chronicity	Organisms	Examples
Acute	Gram + cocci	*S. aureus, β-hemolytic streptococcus* (A, B, C and G)
Chronic	Gram + cocci	Staphylococcus, Streptococcus, Enterococcus
	Gram - bacilli	Enterobacter, E. coli, Proteus, Klebsiella, P. aeruginosa
	Anaerobe	Peptococcus, Peptostretococcus, Clostridium, Fusobacterium, Bacterioides

Table 2. Typical organisms found in Diabetic foot infections, acute vs. chronic. [58]

Laboratory testing can also help to guide or evaluate the effectiveness of therapy. The difficulty with diabetic patients is their lack of systemic response due to immunopathy, where leukocytosis may be absent. However, in a subset of patients elevation of white blood cells (WBC) may be found at initial presentation. Recent studies have shown that C-reactive protein (CRP) is the most sensitive and specific lab test to distinguish between grade 2 and grade 1 ulcers [71].

Plain radiographs can provide useful information in the presence of a diabetic foot ulcer when there is suspected soft tissue emphysema. Advanced imaging techniques such as magnetic resonance imaging (MRI) can provide information regarding the extent of tissue and bone involvement [58, 61, 63, 69]. The imaging techniques will be discussed to a greater extent in the osteomyelitis section.

5.4. Treatment

The consensus from multiple studies and practice guidelines is to utilize a multi-disciplinary approach, including providers from primary care, endocrinology (diabetologist), podiatry, vascular surgery, plastic surgery, infectious disease, microbiology, wound specialty nursing, physical therapy, orthotist and prosthetists [43, 58, 59, 61, 63, 69, 72, 73]. However, there is no evidence-based consensus on specific treatment algorithms for soft tissue infections. Unfortu-

nately any attempt at making such a consensus based on existing data is challenged by inconsistent definitions of infection, improvement and cure, and patient to patient variability. Therapy is typically guided by knowledge of likely pathogens, based on history and clinical presentation and spectrum of available antibiotics that can reliably provide coverage [58].

Patients who have a Grade 2 non-limb threatening infection should be treated on an outpatient basis, covering for gram-positive cocci, and reassessed in 48-72 hours. If the infection has not improved the patient should be admitted for parenteral antibiotics and possible incision and drainage. Patients with grade 3-4 infections that are considered limb- or life- threatening should be admitted for parenteral antibiotics and incision and drainage. Caution should be exercised as approximately half of the patients in this category will not mount an immune response. Therapy should be broad spectrum, including coverage for gram negative rods and anaerobes [59] in addition to gram positive cocci.

A familiarity with antibiotics available in specific hospital formularies and profiles of microbial resistance patterns (via antibiogram) will improve targeted therapies. It was previously thought that parenteral antibiotics were necessary initially for all severe infections. However studying the high serum concentrations achieved with oral forms of some antibiotics such as Linezolid and trimethoprim-sulfamethoxazole, for example, suggest that intravenous administrations may not always be necessary [58]. Recommendations regarding the duration of therapy also vary. Mild infections warrant a short course of 1-2 weeks, while moderate to severe infections can require up to 2-4 weeks of targeted therapy. Inflammatory markers such as CRP and erythrocyte sedimentation rate (ESR) are used to define duration of therapy [58].

The SIDESTEP study published by Lipsky et al. in 2005 compared ertapenem to piperacillin/tazobactam in the treatment of diabetic foot infections in a prospective, randomized, controlled, double-blinded study, with a study population of 576 initial enrollees and 445 available for follow up. Although ertapenem did not provide specific coverage for *Pseudomonas* or *Enterococcus* species, at the end of the therapy period the success rate for both groups of patients was similar. This raises the question of whether certain bacteria such as *Pseudomonas* and *Enterococcus* require antibiotic coverage. These organisms are colonizers and become primary pathogens in very specific instances, acting as opportunistic pathogens. In order to prevent further propagation of multi-drug resistant organisms, practitioners should choose antibiotics with slightly narrower coverage [58, 60, 74].

Occasionally soft tissue infections accompanied by abscess, substantial necrosis or necrotizing fasciitis require surgical debridement in addition to broad spectrum, followed by targeted, antibiotic therapy. Vascular status must be evaluated and restored if possible. For moderate to severe diabetic foot infections, surgical intervention is often the key to limb salvage [69]. The incision should be centered on the abscess and extended proximally until there is no evidence of infection. Non-viable tissues can be debrided, and exposed tendons and bone can be removed in preparation for eventual closure [72].

There are three methods for wound closure: primary, delayed primary and closure by secondary intention. Primary closure can be achieved when the surgeon is confident the necrotic tissue and infection has been removed using a combination of sharp debridement and

lavage. However, in cases of severe infection or when there is suspicion for additional drainage to be encountered, a wound may be left open initially then closed several days later when it is free of any signs of infection –delayed primary closure. Finally, for those wounds with significant undermining or other potential complicating factors, closure by secondary intention may be undertaken in which a wound is left open and allowed to granulate or contract, often with the help of advanced modalities such as NPWT, split thickness skin grafting or other synthetic graft materials [59, 72].

Ultimately, the goal in treatment is tissue preservation and restoration of foot function. When superficial infections are encountered physicians should aggressively treat them to prevent progression and involvement of deeper or wider margins of tissue. Some infections warrant early surgical debridement, which can reduce morbidity and cost [63]. When amputations are considered, they should be performed as far distal as possible as there are higher energy expenditures and disturbance to quality of life with proximal amputations. In paraplegic and quadriplegic patients or other patients who are otherwise non-ambulatory, surgical planning should take into account the future risk of complications such as decubitus or neuropathic ulcerations, contractures or infection [59]. Caution should be taken in patients with peripheral arterial disease. Debridement and amputations should be conservative, with later definitive amputations after revascularization for optimal healing [59].

Following amputation, the patient will have altered biomechanics and plantar pressures that will require bracing, orthotics, custom shoegear or adjunctive surgical procedures to avoid future complications [59].

6. Osteomyelitis

Occasionally, soft tissue infections can be severe and deep, involving underlying bony structures. When there is a break in the soft tissue, and the infective organisms have entered the bone directly, this is referred to as contiguous or direct extension osteomyelitis [15, 61, 75]. Infections most commonly will involve soft tissue but about 20% will extend to bone [64]. Other types of osteomyelitis include hematogenous osteomyelitis which is seen in prepubescent children and in elderly patients in which spread occurs through the blood [75].

6.1. Pathogenesis

Infections in the bone are initiated by adhesion of bacteria in the acute osteitis phase followed by firm attachment, which is the chronic phase. The adhesions are formed through a polysaccharide capsule that links strongly to the bone matrix. The bacteria are then protected from antibiotics and macrophages. Bacteria such as *S. aureus* create surface proteins after about 1 week that are osteolytic, resulting in a decrease in bone matrix production. In reaction to the bacterial antigens, the body will also produce interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α) which result in an increase in osteoclast-mediated osteolysis [60, 62].

As mentioned above, emergence of drug resistant organisms is a large problem facing healthcare providers today. It has been shown that gradual exposure of antibiotics through

the biofilm layers can result in resistance as the organisms are able to tolerate 10-1000 times higher levels of antimicrobial agents in comparison to the minimum inhibitory concentration. *S. aureus*, the most common infecting organism, is able to survive within osteoblasts. When osteoblasts die, the bacteria are released and infect new osteoblasts. Small colonies of *S. aureus* with lower metabolic rates can exist latent for indefinite periods, resulting in chronic osteomyelitis [60, 75].

6.2. Diagnosis

6.2.1. Clinical evaluation

Thorough history of patients who present with suspected osteomyelitis should be performed in addition to a thorough physical exam as previously discussed.

6.2.2. Lab evaluation

Complete blood count is of limited usefulness in diagnosing osteomyelitis as leukocytosis is infrequent [62, 75]. ESR and CRP may be more sensitive, but is of questionable specificity [62, 75]. Unlike in metastatic or metabolic bone diseases, the serum calcium, phosphate and alkaline phosphatase all remain normal [75].

6.2.3. Microbiologic evaluation

Similar to the evaluation of infections, surface wound swabs are unreliable for identification of infecting organisms [58, 63, 75]. Specimens of deep tissue obtained from areas adjacent to bone in question can also grow different bacterial isolates [62, 63]. Therefore, bone biopsy is considered the gold standard for diagnosis [59, 60, 62]. Because osteomyelitis is a focal disease, multiple specimens of bone should be taken to provide a representative sample. The specimens can be obtained through core sample with CT guidance through uninvolved skin or tissue. Alternatively, surgical excision can also be performed [62]. Any systemic antibiotics should be discontinued for at least 3 drug half-lives, prior to biopsy [60]. Bone specimens should be sent for gram stain, culture and sensitivity and histology. In some instances, fungal and AFB may also be considered [60, 75].

Similar to infections above, osteomyelitis is also polymicrobial with an average of 2.25 pathogens per patient. The most commonly isolated organisms include *S. aureus*, *S. epidermidis*, *Streptococcus* and *Enterococcus* species. Wounds that are long standing with necrotic tissue and a foul odor should be tested specifically for anaerobic organisms [62].

6.3. Imaging

X-rays of the foot are the most readily available modality and is most cost effective, except they have a low sensitivity in early cases of osteomyelitis. Focal osteopenia and cortical erosions as well as periosteal reactions suggest osteomyelitis. Unfortunately, these changes can also be observed in patients with Charcot neuroarthropathy, which will be discussed in detail later. There can be a delay of 10-20 days before acute changes are detected on radiographs, when

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40-70% resorption has occurred. Therefore, x-rays have a higher utility when used serially, once the diagnosis has been established [59, 62, 63, 75].

Technetium 99 bone scintigraphy has also been cited as a useful tool in identifying osteomyelitis. Although the sensitivity is very high, nearly 100% in some studies, the specificity for osteomyelitis is quite low. Other examinations such as the Tc99 –HMPAO (Tc-Hexamethyl-propyleneamine oxime) leukocyte scan (also known as *Ceretec* ™scan) has been shown to have both high sensitivity and specificity for osteomyelitis. It is also considered to be more cost effective in comparison to the Indium scan.

CT can be utilized to reveal medullary destruction, periosteal reaction, cortical destruction and articular damage, even when plain radiographs appear normal [76]. Soft tissue structures can be better observed with MRI, which has been reported to have sensitivities as high as 90-100% with specificities between 80 and 100% [75]. Typically in the presence of osteomyelitis, there will be decreased signal intensity on T1 images in the bone marrow. There is also increased signal intensity on T2 weighted images due to edema (Figure 11). Unfortunately, these findings can also be observed in fractures, tumors, inflammatory arthritis, Charcot and post-operative changes. Therefore, clinical correlation is required [62].

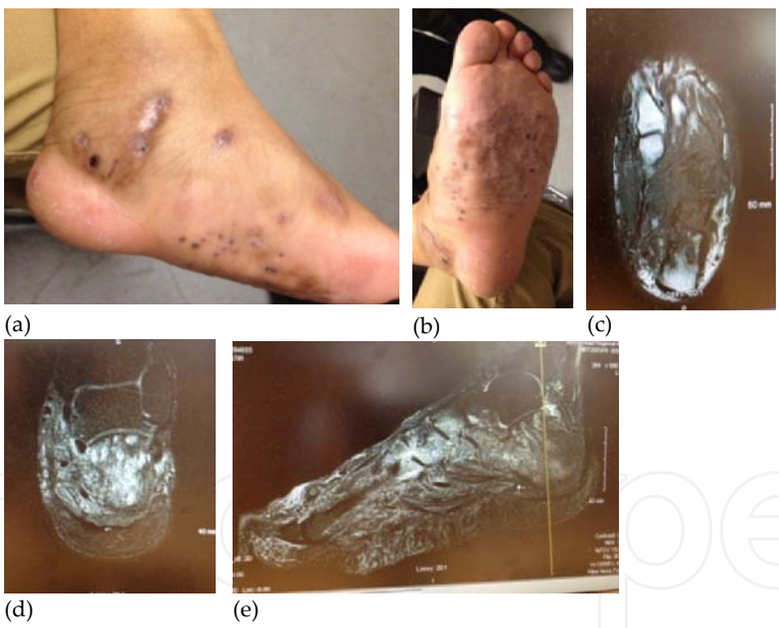

Figure 11. Patient with long-term chronic osteomyelitis; A-B – clinical images showing previous ulceration site; C – T1 transverse image, note low intensity signal throughout midfoot; D – T2 coronal image, note high intensity signal through calcaneus; E – T2 sagittal image, note high intensity signal throughout midfoot structures and calcaneus. Images courtesy of Jacqueline Truong, DPM.

Positron Emission Tomographic scans, particularly those with fluorine-18-fluoro-D-dehoxy-glucose (FDG), can provide information as uptake of the agent occurs specifically in inflammatory cells such as macrophages and leukocytes. Combining PET scans and CT scanning can help to distinguish between osteomyelitis and Charcot neuroarthropathy [75].

6.4. Treatment

As with soft tissue infections, a team approach should be employed to improve outcomes [58, 59, 61, 63, 69, 72, 73, 77]. Optimization of patient health status including glycemic control, vascular status, nutritional status, and smoking cessation should be managed [4]. Control of hyperglycemia has been shown to increase leukocyte function. Wound healing has also been shown to improve when nephropathy, nutrition and smoking status are addressed [62].

Medical treatment following any necessary surgical debridement of necrotic tissue must take into account the most likely infective organisms. The most effective treatment includes coverage for both aerobic and anaerobic organisms. Side effects to medications as well as renal dosing and measuring trough levels as appropriate must be taken into account when employing antibiotic therapies. As soon as culture and sensitivity results are available, transition to targeted therapy must take place [63].

There is wide debate between whether to treat medically with antibiotics or surgically with debridement and primary amputations. Some authors are proponents of timely surgical intervention to prevent spread of infection, further necrosis of tissue, and bone [58-60, 62]. There are, however, some who argue that surgical debridement is not necessary to treat osteomyelitis. In fact, with the advent of newer drugs with high serum to bone ratios, they are able to penetrate through biofilms and enter eukaryotic cells better than drugs of the past. In a retrospective study by Faglia and colleagues (2012), however, each day of delay of surgical debridement increased the risk for major amputation [69]. The decision between surgical and non-surgical treatment for chronic osteomyelitis will likely continue to be debated over time [60].

The goal of surgical intervention is to salvage the foot and retain the greatest amount of foot after surgery. The harsh reality is only about 60% of diabetic patients ambulate with a prosthesis following a trans-tibial amputation. And, 50% of those patients develop an infection in the remaining limb requiring additional amputation. Every effort must be made to salvage the greatest amount of the limb as possible [62]. Following surgery, adjunctive procedures and protective devices such as bracing, orthotics and specialty shoegear must be provided in order to prevent further complications [62].

7. Charcot neuroarthropathy

Charcot neuroarthropathy is defined as a progressive joint dislocation with pathologic fracture resulting in debilitating deformity causing disruption to the bony architecture [68]. This disorder can be caused by a multitude of disorders that involve neuropathy such as diabetes, leprosy, syphilis, spina bifida, cerebral palsy, meningomyelocele, syringomyelia and alcohol abuse. Of the list, the most common associated disorder with Charcot neuroarthropathy is diabetes [78-83].

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7.1. Pathogenesis

Early theories include the neurotraumatic and neurovascular theories. The *neurotraumatic theory* (also referred to as the German theory) is based on the notion that a neuropathic foot results in abnormal plantar pressures, in addition to intrinsic minus foot leading to pedal architectural changes due to overpowering by long extensor or flexor tendons during function. The repetitive trauma from activities of daily living causes extension of ligaments, joint distension and eventually microfractures and dislocations of the bones. The *neurovascular theory* (also referred to as the French theory) on the other hand focuses more on autonomic neuropathy resulting in a hyperemic state. Arteriorvenous shunts cause an increase in vascular flow leading to osteopenia and bone resorption. Microtrauma from activities of daily living cause microfractures and dislocations in the weakened bone. Although both of these theories are attractive, they do not account for why the problem commonly presents unilaterally [76, 78, 80-84].

The most recent accepted theory describes an increased expression of the receptor activator of nuclear factor KB/ostopotegerin (RANK-L/OPG), resulting in changes we see with Charcot neuroarthropathy. Some triggering event such as minor trauma that is unrecognized by the patient, vascular or orthopedic surgery results in localized inflammation which causes localized osteolysis. RANK-L is increased as it is potentiated by free radicals and hyperlipidemia, hyperglycemia and advanced glycation end-products, all of which exist in diabetics. Antagonists to RANK-L include nerve derived peptides and insulin which are low in diabetics [78, 85]. The breakdown in bone results in an up-regulation of TNF-α and IL-1β, which are both seen following fracture. TNF-α and IL-1β both increase RANK-L expression, causing maturation of osteoclasts, which are responsible for continuing to weaken the bone. A sensate patient would recognize a problem and seek treatment, such as immobilization at this point, which would help to decrease inflammation, and thus break the cycle. Unfortunately, these patients have profound insensitivity, peripheral sympathetic dysfunction and normal arterial outflow, resulting in bony destruction [68, 73, 78, 80, 85].

In 2011, La Fontaine and colleagues published a study comparing bone specimens from patients without diabetes, those with diabetes but without peripheral neuropathy and those with Charcot neuroarthropathy. Through histologic and histomorphometric evaluation, they concluded that bone in diabetic patients is more fragile and increases the risk for fracture. Whether a patient results in a fracture or dislocation appears to depend on the bone mineral density. Those with lower bone mineral density appear to have a greater propensity towards fracture, while those with normal bone mineral density result in a combined pattern of fracture and dislocation [79].

7.2. Clinical presentation

A thorough history and physical examination including dermal, vascular, neurological and musculoskeletal components should be performed for patients who present with a suspected Charcot foot. Affected feet typically exhibit warmth and swelling with occasional pain that is typically seen unilaterally, although bilateral cases have been reported [68, 73]. An infrared dermal thermometer can be used to show a difference in the temperature between the involved

foot and the contralateral limb, ranging between 3-6 °C [86]. Although this is sensitive, it is not specific and thus can only be used to evaluate the progression of disease after diagnosis has been established [86]. Most patients have bounding pulses in the acute phase, owing to vascular sympathetic denervation, although patients with chronic Charcot may have elements of vascular compromise. In cases with concurrent ulcerations or if considering surgical therapy, it may be beneficial to perform the ankle brachial index (ABI), arterial Doppler, and transcutaneous pulse oximetry (TcPO2) [73, 81, 87]. Special attention should be paid to the neurologic examination where extent of neuropathy can be assessed. If a previously neuropathic patient begins to complain of pain, clinical suspicion should be raised [81]. The patient should also be evaluated for ankle equinus, particularly in cases where midfoot breakdown is present. The signs and symptoms are not specific to Charcot, thus a thorough evaluation to rule out infection or other disease process must be undertaken [73, 78, 88].

Patients may present at any point in the disease process, with varying structural abnormalities that result. In chronic midfoot Charcot neuroarthropathy, the medial arch may collapse or prolapse resulting in a rocker bottom foot-type with a varus or valgus deviation of the forefoot. Hindfoot or ankle involvement can result in frontal plane alterations of the calcaneus [78]. With proper, timely intervention, limited deformity may be observed, with resolution of the acute phase, which will be discussed in more detail later [81].

7.3. Lab evaluation

Complete blood cell count with differential, ESR, CRP, blood cultures, albumin, pre-albumin, chemistry panel, and glycosylated hemoglobin concentration (HbA1c) should be collected to rule out infection and determine metabolic competence. As was mentioned above, these values may be normal even in the presence of infection due to immunopathy secondary to diabetes [87]. If planning for surgical intervention, these values can also help to predict outcomes [87].

7.4. Imaging

Diagnosis can be delayed on average 29 weeks in Charcot neuroarthropathy [86, 89]. Plain radiography is universally available and inexpensive. In the first stage, the findings include debris formation, fragmentation at subchondral bone and capsular distention (Figure 12). In subsequent stages, the debris becomes absorbed in stage 2 with fusion of large fragments and sclerosis of bone ends. Finally, in the reconstruction phase, the bone ends are rounded [68, 73, 82, 89]. The most common joint to see destruction is the tarsometatarsal joint, likely secondary to equinus at the ankle resulting in midfoot collapse. Medial calcific sclerosis (*Mönckeberg's medial calcific sclerosis*) may also be visible on plain film studies in these patients as RANK-L is suspected to increase calcifications to the vascular smooth muscle wall [89].

CT and MRI can also be utilized particularly for early detection of Charcot neuroarthropathy. On CT, pseudocysts can also be revealed. Although the CT studies can provide useful information, it is more applicable for surgical reconstruction planning [89]. MRI will demonstrate similar findings as described above for osteomyelitis. However, osteomyelitis typically occurs through contiguous spread. Therefore, absence of an ulcer can increase suspicion for

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Charcot. Osteomyelitis typically affects one bone while Charcot arthropathy is polyarticular. Deformity is common in Charcot, but the same is not observed in osteomyelitis. Location of effect also differs in that osteomyelitis typically affects the digits and forefoot while Charcot typically affects the midfoot [89]. MRI is superior to CT because it can provide earlier changes, even in stage 0, with edema of bone, soft tissue and joint effusion [89].

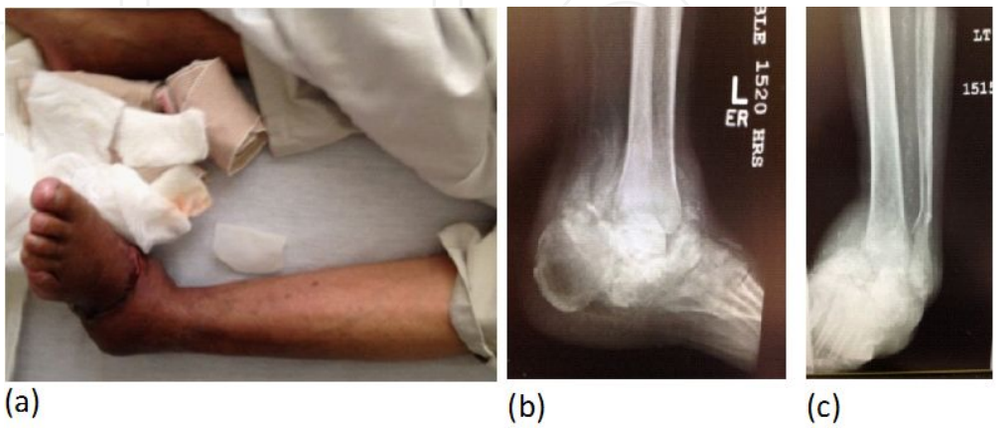

Figure 12. Acute Charcot ankle (6 weeks old) in a patient with peripheral arterial disease after sustaining a nondisplaced fibular fracture initially treated with cast immobilization. Patient eventually underwent transtibial amputation; A – Clinical images showing the collapse of normal architecture; B-C – plain radiography showing the debris formation, fragmentation and dislocation that is classic for stage 1 Charcot neuroarthropathy; also note the Monckeberg's medial calcinosis that is prominent throughout the images.

Bone scintigraphy including Tc99, Gallium, Indium, Ciprofloxacin-labeled scan, Leukocyte labeled Tc HMPAO (*Ceretec*™) scan and sulfur colloid bone scans have been described for use in diagnosing Charcot. The standard Tc99 scan has high sensitivity but low specificity. Indium scans are both sensitive and specific for osteomyelitis and can help to distinguish between Charcot and osteomyelitis. *Ceretec*™ scans provide high sensitivity and specificity for osteomyelitis but is very time consuming [89]. As for osteomyelitis, F-FDG-PET scan with glucose radiolabeling has also been described for use with Charcot. The primary disadvantage is poor anatomic resolution. CT and PET scans can be combined to provide better resolution [89].

7.5. Classification

There are several classification systems that have been introduced to define Charcot neuroarthropathy, including the Eichenholz system, Sanders and Frykberg classification, Schon et al and Brodsky's anatomical classification (Tables 6-8) [73, 80, 86, 88-90]. The Eichenholz system is based on radiographic findings, while the Sanders and Frykberg and Brodsky classifications are based on anatomical location [73, 78, 79, 81-84, 86].

7.6. Differential diagnoses

The clinical presentation for Charcot and osteomyelitis is often very similar with a red, hot, swollen foot [62]. Examples of differential diagnoses include cellulitis, DVT, acute gout and

pseudogout, osteonecrosis and osteomyelitis. Patients who are suspected to have Charcot neuroarthropathy may have ulcerations that can confuse the diagnosis [62, 79]. However, in the acute situation, a foot which is warm, erythematous, and edematous without ulceration or known site of pathogen entry must be considered Charcot neuropathic until proven otherwise.

7.7. Treatment

Extensive patient and family education is crucial to the successful treatment of Charcot neuroarthropathy [78, 86, 88]. As discussed above, a team approach is necessary to provide timely, appropriate care for these patients. In the active phase (stage 1), the affected limb should be immobilized in a cast, with the goal to minimize stress to the foot by reducing shear forces and peak plantar pressures and maintain a stable, plantigrade foot [68, 73, 81, 84, 92]. Choices often utilized include a TCC, instant total contact cast (iTCC), and removable CAM walker although the gold standard is considered the TCC. [84, 88, 90].

The duration of immobilization is on average 3-6 months but can vary based on the anatomical location that is involved [78, 81, 86]. When the skin temperature differential becomes less than 1-2 °C, the patient should be transitioned into a Charcot restraint orthotic walker (CROW) device or removable CAM walker and finally into a custom molded shoe with orthotics [68, 81, 83, 88, 93]. Patellar tendon bearing orthotics can also be considered [80]. Some researchers recommend partial weight bearing instead of strict non-weight bearing in a protective device to avoid disuse osteopenia [86, 93]. Skin temperatures should be evaluated regularly.

Medications as an adjunctive therapy to immobilization have been gaining popularity over the last several years, starting with bisphosphonates [41, 73, 80]. Some studies have shown that with even a single dose administration of bisphosphonates clinical and radiologic improvements may be seen with a decreased bony turnover, evaluated as an increase in bone mineral density on dual-energy X-ray absorptiometry (DEXA-scan), and reductions in alkaline phosphatase levels in acute phase Charcot [41, 80, 94]. Salmon calcitonin, which has been shown to decrease osteoclastic activity, is another antiresorptive agent that has been gaining attention recently. It also has been shown to be associated with reduction in bone specific alkaline phosphatase [78, 80, 86, 88]. With the new information regarding the pathophysiology, TNF-α specific antagonists and RANK-L antagonists have been suggested to decrease the duration of time to resolution [78, 80].

Surgical therapies can range and selection is based on the needs of the patient, stability of the joint and the anatomical location involved as well as patient specific characteristics. Acute dislocations or instability should be reduced and possibly primarily fused. Alternatively, in a stable foot, an exostectomy or osteotomy can be performed to aid in ulcer healing [82, 88, 91]. Indications to surgery include recurring ulceration, joint instability, pain with malalignment, prominent exostoses, potential skin complications from bracing and non-platigrade foot. An area of controversy with surgical intervention is timing. It was once believed that performing any surgery during the acute phase was not recommended as further destruction of bone and joints would occur, making fixation nearly impossible. However, increasing numbers of surgeons are advocating for earlier surgery, even in the acute phase to prevent deformity. As with any procedure, benefits should outweigh the risks involved [73, 81, 90-92, 95, 96].

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Considerations should be made to the patient's expectations with assessment of willingness to comply with post-operative recommendations before performing surgery [87, 92].

The procedures can be divided by anatomic location. The midfoot deformity reconstructions typically involve wedge shaped osteotomies or exostectomies [81, 82, 95]. Achilles tendon lengthening or tenotomy may be necessary to restore appropriate calcaneal sagittal position [73, 79, 82, 87, 95]. Hindfoot procedures are also approached with a mixture of fixation devices including screws, plates, intramedullary rodding and external fixators.

Arthrodesis in patients with poor bone stock can be challenging to fixate. Some surgeons advocate using an external fixator to provide constant compression during the post-operative period [82, 88]. Others use internal fixation alone with screws and plates or intramedullary rods [82, 90, 95]. Superconstructs, where fixation is extended to involve normal bone, are being described to improve the long term stability following surgical repair [79, 87, 90, 91]. Still others advocate for combinations of internal and external fixation or doubling the amount of internal fixation to decrease the likelihood for non-union [82, 87]. With the advent of locking plates, significant improvements in the strength of fixation have been demonstrated, even with osteopenic bone [79, 88].

Regardless of the location, the goals of surgery are the same, to prevent further deformity, increase stability in near anatomic alignment, while prevent subsequent ulcerations [73, 82, 95]. Occasionally, in severe deformities, the procedure can be staged for better anatomical correction without neurovascular compromise [95]. The proper alignment for surgical correction is to place the heel under the mechanical axis of the leg with the forefoot perpendicular to the rearfoot [95]. When concomitant midfoot deformity is seen with hindfoot pathology, an intramedullary nail in combination with external fixator has been shown to be beneficial for correction [96]. Surgical templates and use of 3-D reconstruction CT imaging should be utilized to plan the corrections [88, 91].

Bone growth stimulation is considered another adjunctive therapy that can be used with immobilization, medications or following surgery. Studies using electrical or ultrasound stimulators have shown statistically significant decreases of consolidation times [73, 87]. With severe deformities, bone deficits can result following osteotomies, particularly with angular corrections. In these instances, grafting may be necessary to fill the void. Several options exist including autogenous grafting from the fibula, iliac crest, proximal tibia, or decorticated osteotomized material [97]. Orthobiologic products can be used as an alternative to improve bone healing; e.g. demineralized bone matrix (DBM), osteoconductive and osteoinductive allografts, calcium phosphate, calcium sulfate and hydroxyapatite substitutes, bone marrow aspirates and platelet rich plasma [95, 97].

Post-operative complications are similar to any surgical intervention involving osseous work, including wound dehiscence, infection, osteomyelitis, delayed union, nonunion, malunion, fracture and failure of hardware. When external fixators are employed pin tract infections can also be observed. Meticulous surgical technique, pre-operative planning, patient education, wound care and pin care can all contribute to decreasing the rate of complications that may result in amputation [82, 88].

8. Conclusion / Prevention

As important as the treatment of immediate pedal complications are, prevention is the key to long term increases in survival rates and reduction of morbidity. In addition, an interprofessional patient-centered approach garners the greatest opportunity for success. For example, recent research shows a seven fold decreased risk of amputation in diabetic patients when treated using a vascular surgery-podiatry team approach with a 5 year rate of avoiding limb loss of 83% [62]. A multi-disciplinary approach [60, 62-64] is helpful to first confirm that the patient has adequate lower extremity blood flow for healing [60, 62], good glycemic control [60, 62, 65], adequate nutritional status [66] and that the ulcer is not infected [62]. A team of specialists may be better equipped to resolve any of these concerns prior to attempted treatment plans. A multi-disciplinary team may help avoid diabetic foot ulcerations with careful evaluation and preventative measures [63]. Without first addressing any above abnormalities, it may prove difficult to heal the diabetic foot ulcer.

Early recognition with timely treatment are emphasized to curb the development of permanent deformities [79]. Practitioners should maintain a high index of suspicion when treating neuropathic patients. No one diagnostic technique can provide both sensitive and specific conclusions. Incorporating history, clinical findings, and results of diagnostic imaging together will provide the most accurate diagnosis. There are many options to consider when treating patients with diabetic foot ulcers and their complications. Unfortunately, simple algorithms for treatment cannot be applied to all patients with these presentations. Post-intervention compliance plays a large role in the ultimate success of treatment, requiring buy in from the patient and care-givers [79]. Adherence to the evidence-based guidelines presented in this chapter will decrease patient morbidity and greatly improve clinical outcomes.

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