Infective Leg Ulcers

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16.1 Introduction

In the UK alone which has a population of 50 million, there are about 400,000 patients with leg ulcer disease of which at any given time 100,000 have open leg ulcers requiring treatment [1]. By simple extrapolation, India with a population of 1200 million should have a leg ulcer burden of approximately 10,000,000. It is a leading cause of morbidity especially in the elderly population. Treatment of the underlying cause is the mainstay of therapy, but the role of good nursing care especially at the community level is of paramount importance.

Leg ulcers are almost always secondary to a preexisting medical disease (Table 16.1). Although the list of causes is long, the most common etiological factors for leg ulcers in the West and now in urban India are venous ulcers (70 %), arterial (5 %), and mixed venous and arterial (20 %). However, this is not representative of the entire Indian subcontinent, and infective ulcers constitute a major share in tropical Asia and Africa.

Several studies have implicated infectious causes for lower-limb ulceration. However, there is no large cumulative experience, and the literature on infectious ulcers is composed of mostly of small series or case reports. Most infectious ulcers are bacterial although viruses, parasites, and fungi have been reported as causative agents mainly in the immunocompromised patients. A list of likely pathogens is included in Table 16.2.

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A.K. Khanna, S.K. Tiwary (eds.), *Ulcers of the Lower Extremity*,
DOI 10.1007/978-81-322-2635-2_16

Table 16.1 Causes of leg ulcers

1. Vascular
(a) Venous
(b) Arterial
(c) Mixed
2. Neuropathic
(a) Diabetes
(b) Tabes
(c) Syringomyelia
(d) Spinal injury
(e) Leprosy
3. Metabolic
(a) Diabetes
(b) Gout
4. Hematological
(a) Sickle cell disease
(b) Cryoglobulinemia
5. Trauma
(a) Injury
(b) Pressure
(c) Burns
6. Tumors
(a) Basal cell carcinoma
(b) Squamous cell carcinoma
(c) Sarcoma
7. Infection
(a) Bacterial
(b) Fungal
(c) Protozoal
8. Panniculitis
(a) Necrobiosis lipoidica
(b) Fat necrosis
9. Pyoderma gangrenosum
10. Autoimmune ulcers
11. Hypertensive ulcers

16.1.1 Mixed Etiology

Most ulcers have more than one etiology. Ulcers of any primary origin such as ischemic, venous, or neurotropic ultimately get infected as well. Though the dominant disease process must be treated first, the superimposed infections require treatment also.

Table 16.2 Infectious causes of limb ulcers

Disease	Pathogen
Erysipelas (bullosa)	*Streptococcus pyogenes*
Fasciitis necroticans	*Streptococcus hemolyticus*
Ulcerating pyoderma	*Staphylococcus aureus*
Gas gangrene	Clostridium
Ecthyma gangrenosum	Pseudomonas
Septic embolism	Meningococcus and others
Anthrax	Bacillus anthracis
Diphtheria	Corynebacterium diphtheria
Osteomyelitis	Several microorganisms
Herpes, CMV, Lues maligna	HSV, CMV, *Treponema pallidum*
Tularemia	*Francisella tularensis*
Tropical ulcer	Bacteroides, *Borrelia vincenti*
Maduramycosis (eumycetoma/mycetoma), *Exophiala jeanselmei*	*Nocardia brasiliensis*
Chondroblastomycosis, coccidioidomycosis	Several bacteria
Histoplasmosis	*Histoplasma capsulatum*
Bacillary angiomatosis	*Bartonella henselae*
Ulcerating cutaneous tuberculosis	Mycobacterium tuberculosis
Amebiasis	*Entamoeba histolytica*
Leishmaniasis	*Leishmania donovani* complex
Leprosy	*Mycobacterium leprae*

Taken from Spentzouris and Labropoulos [2]

16.1.2 Pyoderma Gangrenosum

This is a misnomer because these ulcers are noninfected and are an important cause of non-healing ulcers of the leg. Ulcers of pyoderma gangrenosum may be associated with inflammatory bowel disease, inflammatory arthropathy, or myeloproliferative disorders [3]. Half of these ulcers are associated with chronic disease and the remainder are idiopathic. Lesions of the lower limb start as painful pustules which progress to necrosis and ulceration. These ulcers may be single or multiple with raised purple serpiginous undermined borders. Besides antibiotics, immunosuppressive therapy forms the mainstay of treatment.

16.1.3 Mycobacteria-Associated Leg Ulcers

Chronic ulceration due to atypical mycobacteria is a rare but important cause of non-healing leg ulcers. The organisms implicated are *Mycobacterium ulcerans*, *Mycobacterium marinum*, and *Mycobacterium chelonae*. The ulcers may start as a subcutaneous nodule and later transform into an undermined ulcer with an areola. The diagnosis is established by polymerase chain reaction-based identification of

the organism. Treatment is with oral clarithromycin and topical silver sulfadiazine with hyperthermia [4]. The therapy needs to be continued for several months, and additional antibiotics may be required for secondary bacterial infection.

Tubercular vasculitis secondary to mycobacterium tuberculosis infection has been reported as a cause of leg ulcers with distal ischemia and occasionally peripheral gangrene [5]. The patients typically present with fever, lymphadenitis, and foot or leg ulceration. Diagnosis is confirmed by lymph node biopsy and CT angiography will demonstrate vasculitis. Conventional antitubercular therapy for 6–9 months is curative.

16.2 Leprosy Ulcer

In an epidemiological study of ulcers in India, leprosy was the most common cause of leg ulceration [6]. The predisposing cause of plantar ulcers in leprosy is nerve damage. This nerve damage results in loss of sensation, motor paralysis, and loss of autonomic nerve function which could lead to the loss of the ability to sweat. The weight-bearing points on the plantar aspect of the foot chiefly over the metatarsal heads and the heel tend to be subjected to excessive pressure because of the body weight. This in turn leads to the plantar skin and subcutaneous fat to be squeezed and temporarily deprived of blood supply. The tissues can stand this ischemia for about half an hour. If this continues for longer, reversible metabolic changes leading to blister formation or hematoma can occur, and if this continues for even longer, after 2 h, irreversible metabolic changes occur in this tissue, leading to infarction and gangrene of these compressed tissues. Blisters and hematoma can break down to form ulcers or lead to abscess formation and then ulcers and raw areas or spreading cellulitis. Patchy areas of infarcted and necrotic tissue separate out leaving behind ulcers. Corns and calluses act to increase pressure in a concentrated area and thus can cause hematoma and abscesses under them in anesthetic feet. These break down to form ulcers. They act like a stone within a shoe in a person with normal sensation, except that the person with normal sensation will remove the shoe, remove the stone, and move on. A corn, in such a person, will cause the person to either have the corn removed or limp, to avoid pressure and pain over the area. A person with loss of sensation continues to walk on the corn or callous and develops a blister or hematoma and maybe an abscess. Blisters and hematoma could also occur because of shearing stresses and later lead to abscess formation. Fissures or cracks occur because of dry skin, which in turn is because of loss of sweating. This leads to open wounds and infections. Prevention of plantar ulcers in leprosy therefore involves minimizing pressure, reducing force, reducing shearing stresses, looking for and taking care of direct trauma as soon as it occurs, looking for and treating pre-ulcerative conditions, and compensating the skin for loss of moisture. To heal such an ulcer requires rest. Absence of irritating pressure and shearing stresses will permit healing to take place. To rest a plantar ulcer requires that a person should not bear weight on the affected limb. Needless to say that in the Indian context, where most of our patients are from the unorganized labor sector, they cannot afford rest

as it interferes with their livelihood. They need to be provided with a method of "healing, while walking."

The patient has to be kept on medical treatment of leprosy. Various types of flap procedures may be required to heal the ulcer [7, 8].

16.2.1 Buruli Ulcer

This is a necrotizing cutaneous infection caused by mycobacterium ulcerans. It is the second most frequent mycobacterial disease in humans after tuberculosis [9]. It has been reported in parts of Africa, Australia, South East Asia, China, Central America, and South America. There are large lesions which progress to scarring, contractual deformity, disabilities, and sometimes amputation. The environmental mycobacterium is found in rivers, swamps, wetlands, areas of deforestation, dam construction, and agriculture. Buruli ulcer is also referred to as mysterious disease because the mode of transmission remains uncertain.

16.3 Leg Ulcer Infection

When the virulence factors of the microorganisms outweigh the natural host immune defense, infection with invasion of microorganisms into surrounding tissues will occur. The progression of an ulcer to an infected state involves multiple factors such as type, site, size, and depth of ulcer; presence of nonviable contaminants; level of blood perfusion; the immune status of the host; the microbial load; and the combined level of virulence of various microorganisms. Most leg ulcers harbor mixed population of aerobic and anaerobic organisms. The frequency of anaerobic bacteria in noninfected and infected leg ulcers is 36 % and 49 %, respectively [10].

16.4 Acute Soft Tissue Infections of the Leg

These include cutaneous abscesses, traumatic wounds, and necrotizing infections. The single most common organism found is *Staphylococcus aureus* which is present in 30 % of cutaneous abscesses and traumatic injuries and 47 % of necrotizing soft tissue infection of the leg have polymicrobial aerobic-anaerobic microflora [11].

Necrotizing soft tissue infections involve skin, subcutaneous tissue, and sometimes muscle tissue. It can vary in degree of severity and speed of progression. Although *S. aureus* remains the single most common pathogen, other organisms isolated include *Clostridium perfringens* and *Streptococcus pyogenes* predominantly. Associated organisms present could be *Peptostreptococcus* sp., *B. fragilis*, *E. coli*, and *Prevotella* sp. Potentiation of infection by microbial synergistic partnership between aerobes such as *S. aureus* and *S. pyogenes* and nonsporing anaerobes

has been reported in various types of non-clostridial cellulitis and necrotizing fascitis [12].

The treatment of necrotizing soft tissue infections requires early diagnosis, aggressive and repeated debridement, and appropriate antibiotic therapy. From a therapeutic view point, it is necessary to differentiate between pure clostridial myonecrosis which involves muscle invasion and is associated with a higher mortality rate from other non-muscle-associated soft tissue infections. The use of hyperbaric oxygen is controversial although it is believed to facilitate wound healing [13].

16.5 Diabetic Foot Infections

Mixed microflora infects plantar ulcers which are common in diabetic patients. The common organisms isolated are *S. aureus*, *S. epidermidis*, *Streptococcus* spp., *P. aeruginosa*, *Enterococcus* spp., and coliform bacteria. Anaerobes such as peptostreptococcus, Bacteroides, and Prevotella spp. can be isolated in 95 % of diabetic wounds [14]. Because of the polymicrobial infection, repetitive culture is not required, and treatment of infection should be based on an understanding of the general microbiology of these wounds.

16.6 Venous and Pressure Ulcer Infections

Both venous and pressure ulcers of the leg harbor polymicrobial microflora and anaerobes in 30 % as well. Aerobic-anaerobic synergistic interactions are more crucial than specific microorganisms in such infections. About 25 % of decubitus ulcers have underlying osteomyelitis, and bacteremia is common in such patients [15]. Management of infections in both these ulcers requires aggressive debridement and broad-spectrum antimicrobial agents.

16.7 Targeted Antibiotic Therapy

Accurate identification of pathogens rather than colonizing bacteria is a prerequisite for targeted antibiotic therapy for infective leg ulcers [16]. Although wound swab is the easiest and most commonly used sampling technique, a better technique is procurement of a tissue biopsy specimen from the wound bed. Mere presence of bacteria within a wound is not sufficient to diagnose infection because normal skin flora and sometimes opportunistic colonizing bacteria are present in all chronic wounds and skin surface. Infection is a clinical diagnosis made on the presence of fever, pus, pain or tenderness, erythema, warmth, and induration. These findings represent a significant shift in balance in favor of the bacteria over the host's defense with consequent destruction of host tissue.

Antibiotic therapy for infected ulcers is usually started empirically leading to overuse of broad-spectrum antimicrobials and increasing antibiotic resistance.

Culture and sensitivity results may take several days during which the patients usually receive broad-spectrum antibiotics. This may result in significant changes in the wound flora between the time of procurement of the sample and availability of the culture report. Quicker techniques for microbiological analyses such as DNA fingerprinting and PCR assay have been shown to be effective in rapid detection of causative organism and reduce the delay in institution of appropriate antimicrobial therapy.

The accuracy of culture information depends on an appropriate specimen. It should not be contaminated by the adjacent normal flora. Delay in transportation of the specimen and inoculation on culture plates can lead to loss of the pathogen as proliferation of contaminating organisms occur. Poor sensitivity (failure to identify a pathogen) and poor specificity (identifying a colonizer as a pathogen) can result in wrong antibiotic selection. As compared to a tissue specimen, the sensitivity of a superficial swab has been reported to be 79 % for detection of infection. Thus, swab is likely to miss one in five wound infections diagnosed by punch biopsy.

16.8 Factors Promoting Microbial Proliferation in Leg Ulcers

Wounds with good blood perfusion, oxygen, and nutrient delivery and good immune status are resistant to microbiological colonization. If the tissue oxygen tension is greater than 40 mmHg, ulcer infection is unlikely, while in tissues with an oxygen tension less than 20 mmHg, ulcers are invariably going to be infected [17]. The redox (oxidation-reduction) potential of tissues around ulcers is also important. A low redox potential (Eh) favors the proliferation of anaerobic bacteria. Ulcers with low oxygen tension and a low redox potential promote development of polymicrobial aerobic-anaerobic organisms.

Conclusion

Infective ulcers are relatively rare. Usually infection occurs secondary to some primary pathology, but sometimes primary cause may be the infection and in such cases specific treatment has to be offered like antitubercular treatment in tuberculous ulcers.

References

1. Sarkar PK, Ballaatyne S. Management of leg ulcers. Postgrad Med J. 2000;76:674–82.
2. Spentzouris G, Labropoulos N. The evaluation of lower extremity ulcers. Semin Intervent Radiol. 2009;26:286–95.
3. Khachemoune A, Kauffman CL. Diagnosis of leg ulcers. Internet J Dermatol. 2001;1(2):1–8 www.ispulo.com.
4. Mm K, Kurokawa I, Ito Y, Yamanaka K, Yamazaki T, Mizutani H. Leg ulcer caused by mycobacterium ulcerans ssp. Shinshuense infections. Int J Dermatol. 2009;48(12):1330–3.
5. Yao Y, Liu B, Wang JB, Li H, Liang HD. Tuberculosis should not be ignored in patients with peripheral gangrene. J Vasc Surg. 2010;52(6):1662–4.

6. Gupta N, Gupta SK, Shukla VK, Singh SP. An Indian community based epidemiological study of wounds. J Wound Care. 2004;13:323–5.
7. Joshua J, Chakraborthy V. Wound coverage of plantar metatarsal ulcers in leprosy using a Toe web flap. Indian J Plast Surg. 2005;38(2):123–7.
8. World Health Organisation; Weekly Epidemiological Record WER, 88, No.35 30 August 2013: Global leprosy: update on the 2013 situation. http://www.who.int/wer/2013/wer8835.pdf?ua=1.
9. Merritt RW, Walker ED Small PLC, Wallace JR, Johnson PDR, BenbowME, Boakye DA. Ecology and transmission of Buruli Ulcer disease: a systematic review. PLoS Negl Trop Dis. 2010;4(12):e911. www.plosntds.org.
10. Bowler PG, Davies BJ. The microbiology of infected and noninfected leg ulcers. Int J Dermatol. 1999;38:101–6.
11. Elliot DC, Kufera JA, Myers RAM. Necrotising soft tissue infections. Risk factors for mortality and strategies for management. Ann Surg. 1996;224:672–83.
12. Brook I. Aerobic and anaerobic microbiology of infections after trauma in children. J Acccid Emerg Med. 1998;15:162–7.
13. Pizzorno R, Borini F, Donelli A, Stubinski R, Medica M, Carmigani G. Hyperbaric oxygen therapy in the treatment of Fournier's disease in 11 male patients. J Urol. 1997;158:837–40.
14. Karchmer AW, Gibbons GW. Foot infections in diabetics: evaluation and management. Curr Clin Top Infect Dis. 1994;14:1–22.
15. Brown DL, Smith DJ. Bacterial colonization/infection and the surgical management of pressure ulcers. Ostomy Wound Manage. 1999;45:1195–205.
16. Nelson EA, Backhouse MR, Bhogal MS, Wright-Hughes A, Lipsky BA, Nixon J, Brown S, Gray J. Concordance in diabetic foot ulcer infection. BMJ Open. 2013;3:e2370.
17. Bowler PG, Duerden BI, Armstrong DG. Wound microbiology and associated approaches to wound management. Clin Microbiol Rev. 2001;14:244–69.