CHRONIC OSTEOMYELITIS OF LONG BONES

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REZUMAT

Osteomielita oselor lungi rămâne o afecțiune incitantă și costisitoare, în pofida progreselor recente ale antibioticoterapiei și ale tehnicilor chirurgicale. Radiografii simple sunt în continuare cea mai bună metodă de screening în osteomielita acută și cronică, înșă și alte metode imagistice pot fi utilizate în stabilirea diagnosticului, ajutând în procesul de decizie terapeutică. Decizia de a administra antibiotic pe cale orală sau intravenoz trebuie să se bazeze pe sensibilitatea bacteriană, complicația pacienților, consultația medicului specialist de boli infecțioase și nu în ultimul rând pe experiența chirurgului. O terapie antibiotică în scop bactericid trebuie condusă doar după rezultatele antibiogramei. Nu există un tratament chirurgical standardizat pentru toți pacienții, din cauza impotenței functionale induse de boală, a operațiilor reconstructive și a consecințelor metabolice ale unei terapii agresive. Tratamentul chirurgical include debridarea, oblierea spațiilor moarte, refacerea vascularizării, acoperirea adecvată cu teșuturi, stabilizarea și reconstrucția defectelor. Pentru a realiza acest obiectiv, sunt propuse căteva strategii terapeutice, bazându-ne pe experiența noastră.

Cuvinte cheie: osteomielita oselor lungi, tratament chirurgical, strategii de tratament

ABSTRACT

Osteomyelitis in long bones remains challenging and expensive to treat, despite advances in antibiotics and new operative techniques. Plain radiographs still provide the best screening for acute and chronic osteomyelitis. Other imaging techniques may be used to determine diagnosis and aid in treatment decisions. The decision to use oral or intravenous antibiotics should be based on results regarding microorganism sensitivity, patient compliance, infectious disease consultation, and the surgeon’s experience. The appropriate antibiotic therapy is indicated by the results of cultures. Standard operative treatment is not feasible for all patients because of the functional impairment caused by the disease, the reconstructive operations, and the metabolic consequences of an aggressive therapy regimen. Operative treatment includes debridement, obliteration of dead space, restoration of blood supply, adequate soft-tissue coverage, stabilization, and reconstruction of the defects. To achieve this goal, based on our experience, a few treatment strategies are proposed.

Key Words: osteomyelitis of the long bones, surgical treatment, treatment strategies

Learning Objectives: After studying this article, the participant should be able to: 1. Understand the epidemiology and different classifications of the osteomyelitis in long bones. 2. Have knowledge about the principles of diagnosis including relevant clinical examination and imaging studies. 3. Understand the principles of conservative and surgical treatment.

INTRODUCTION

Osteomyelitis is an acute or chronic inflammatory process of the bone and its structures secondary to infection with pyogenic organisms.¹

Osteomyelitis in long bones includes infections that differ from one another with regard to duration, etiology, pathogenesis, extent of bone involvement, and type of patient (infant, child, adult, or compromised/uncompromised host).

In the past thirty years, the pathogenesis of this disease has been almost clarified, and many factors that account for the persistence of infection have been identified.² A number of antimicrobial agents, with different spectrums of activity against pathogens and different pharmacokinetics and pharmacodynamics, have been used to treat osteomyelitis.³ New operative methods, including the use of muscle flaps, the Ilizarov technique, and antibiotic-loaded beads, have been applied to the field of bone infection. Despite many advances, osteomyelitis remains difficult to treat, and the cure rates are still unsatisfactory.

Osteomyelitis is an infection of bone and bone marrow and can be subdivided into acute, subacute, and chronic stages. Chronic osteomyelitis may appear as such at the initial presentation, as not all patients show progression through the 3 phases.
The epidemiology of osteomyelitis has several broad trends. The incidence of hematogenous osteomyelitis seems to be decreasing.

In one study from 275 cases of acute hematogenous osteomyelitis in children under thirteen years of age, the authors reported a decrease in incidence from eighty-seven to forty-two per 10,000 per year over the twenty-year period of the investigation. The number of cases of osteomyelitis involving long bones decreased, while the rate of osteomyelitis at all other sites remained the same. The prevalence of Staphylococcus aureus infections also decreased, from 55% to 31%, over the twenty-year time period.

In contrast to hematogenous osteomyelitis, the incidence of osteomyelitis due to direct inoculation or contiguous focus infection is increasing. This is probably due to motor-vehicle accidents and the increasing use of orthopaedic fixation devices and total joint implants.

Males have a higher rate of contiguous focus osteomyelitis than females the ratio being approximately 2:1.

Finally, osteomyelitis occurs with a higher frequency in immunocompromised patients.

Acute osteomyelitis develops within two weeks after disease onset, subacute osteomyelitis within one to several months and chronic osteomyelitis after a few months.

Based on the patient age, the following organisms were commonly isolated in osteomyelitis. (Table 1)

This infection occurs predominantly in children and is often seeded hematogenously. In adults, osteomyelitis is usually a subacute or chronic infection that develops secondary to an open bone and surrounding soft tissue injury, in most cases after traumatic accidents.

Because osteomyelitis is a complex disease state, various classification systems have emerged beyond the general categories of acute, subacute and chronic.

1. The Waldvogel classification is the first long bone osteomyelitis staging system and was described in 1970 by Waldvogel. It includes 3 categories of osteomyelitis: hematogenous; contiguous focus; and osteomyelitis associated with vascular insufficiency. (Table 2)

Hematogenous osteomyelitis
Osteomyelitis secondary to contiguous focus of infection
No generalized vascular disease
Generalized vascular disease
Chronic osteomyelitis (necrotic bone)

Osteomyelitis secondary to a contiguous focus of infection can derive from a direct infection of bone, from a source outside the body (i.e. soft tissue trauma, open fracture, or surgery), or from the spread of infection from an adjacent focus (i.e. soft tissue infection, dental abscess, or decubitus ulcer). Contiguous focus osteomyelitis has a biphasic age distribution: the infection occurs in younger individuals secondary to trauma and related surgery; and in older adults secondary to decubitus ulcers and infected total joint arthroplasties.

Osteomyelitis associated with vascular insufficiency is usually seen in individuals with diabetes mellitus. Of the 31 patients in Waldvogel’s study with this form of osteomyelitis, 25 were diabetic, five had severe atherosclerosis not related to diabetes, and one had vasculitis secondary to rheumatoid arthritis. All of the infections affected the toes, metatarsals, tarsals or hindfoot. The patients in this group were mainly between the ages of 40 and 70 years.

2. Cierny-Mader Staging System for Osteomyelitis is based upon the anatomy of the bone infection and the physiology of the host. (Table 3)

The systemic or local factors that affect immune surveillance, metabolism and local vascularity and which differentiate the B host into the two subtypes (Bs and Bl) are as following: (Table 4)
The stages are dynamic and may be altered by therapy outcome, or change in host status.

Stage 1 or medullary osteomyelitis indicates infection confined to the intramedullary surfaces of the bone. Hematogenous osteomyelitis and infected intramedullary rods are examples of this anatomic type.

Stage 2 or superficial osteomyelitis, is a true contiguous focus infection of bone; it occurs when an exposed infected necrotic surface of bone lies at the base of a soft tissue wound.

Stage 3 or localized osteomyelitis is usually characterized by a full thickness, cortical sequestration which can be removed surgically without compromising bony stability.

Stage 4 or diffuse osteomyelitis is a through-and-through process that usually requires an intercalary resection of the bone to arrest the disease process. Diffuse osteomyelitis includes those infections with a loss of bony stability either before or after debridement surgery.

The patient is classified as an A, B, or C host:12

- The A host represents a patient with normal physiologic, metabolic, and immunologic capabilities
- The B host is either systemically and/or locally compromised
- The patient is given a C host classification when the morbidity of treatment is worse than that imposed by the disease itself.

## DIAGNOSIS

The diagnosis of osteomyelitis is based primarily on the clinical findings, with data from the initial history, physical examination and laboratory tests serving primarily as benchmarks against which treatment response is measured.

### History

General symptoms of chronic osteomyelitis include: nonhealing ulcer, sinus tract drainage, chronic fatigue and malaise.

### Physical examination

Signs may include:12 fluctuance of tissue, tenderness to palpation, reduction in the use of the extremity (eg, reluctance to ambulate, if the lower extremity is involved or pseudoparalysis of limb in neonates) and sinus tract drainage (usually a late finding or one that occurs with chronic infection).

### Laboratory Studies

Complete Blood Count (CBC),13,15-17

- a. the leukocyte (White Blood Cells – WBC) count may be elevated in cases of acute osteomyelitis, but it is often normal in chronic cases;
- b. the erythrocyte sedimentation rate is usually elevated in both acute and chronic osteomyelitis, and it decreases after successful treatment;
- c. the C-reactive protein level is another inflammatory index that rises in acute and chronic osteomyelitis;

The erythrocyte sedimentation rate usually (ESR) rises immediately after operative debridement, returns to normal during the course of therapy is a favorable prognostic sign and decreases after successful treatment. However, the interpretation of a persistently elevated erythrocyte sedimentation rate as an isolated finding after treatment should be carefully scrutinized, especially when it is found in a compromised host, in whom the ESR may be altered for reasons other than osteomyelitis. Finally, the erythrocyte sedimentation rate is not sensitive enough to rule out acute or chronic osteomyelitis. The C-reactive protein level decreases faster than the ESR in successfully treated patients.

### Microbiology

The diagnosis and determination of the etiology of osteomyelitis in the long bones depend on the isolation of the pathogen or pathogens in cultures of specimens from the bone lesion, blood, or joint fluid.14 In patients with Cierny-Mader Stage-1 osteomyelitis,
positive cultures of blood or joint fluid can often obviate the need for a bone biopsy, if there is radiographic evidence of osteomyelitis. With the exception of hematogenous osteomyelitis, for which positive blood or joint fluid cultures may suffice, antibiotic treatment of osteomyelitis should be based on sensitivity studies in meticulously performed cultures of bone taken at the time of debridement or deep bone biopsies.\textsuperscript{15,16}

**Imaging studies**

In osteomyelitis of the extremities, plain-film radiography and bone scintigraphy remain the primary investigative tools.\textsuperscript{17,18}

a. X-Rays: Radiographic evidence of bone destruction by osteomyelitis may not appear until approximately two weeks after the onset of infection. (Fig. 1) The radiographs may reveal osteolysis, periosteal reaction and sequestra (segments of necrotic bone separated from living bone by granulation tissue).\textsuperscript{19}

b. For nuclear imaging, technetium Tc-99m methylene diphosphonate is the radiopharmaceutical agent of choice.\textsuperscript{20} The specificity of bone scintigraphy will not be high enough to confirm the diagnosis of osteomyelitis in many clinical situations.\textsuperscript{21} On a bone scan, osteomyelitis often cannot be distinguished from a soft tissue infection, a neurotrophic lesion, gout, degenerative joint disease, postsurgical changes, a healing fracture, a noninfectious inflammatory reaction or a stress fracture. In many instances, a bone scan will be positive despite the absence of bone or joint abnormality.

c. Magnetic resonance imaging (MRI) can be extremely helpful in unclear situations. This imaging modality is particularly useful when a patient is suspected of having osteomyelitis, discitis or septic arthritis involving the axial skeleton and pelvis. Compared with bone scintigraphy, MRI has equivalent or greater sensitivity, specificity and accuracy for the detection of osteomyelitis. MRI also provides greater spatial resolution in delineating the anatomic extension of infection.\textsuperscript{22}

d. CT scanning. CT scans can depict abnormal calcification, ossification, and intracortical abnormalities. It probably is most useful in the evaluation of spinal vertebral lesions. It may also be superior in areas with complex anatomy: pelvis, sternum, and calcaneus.

e. Ultrasonography. This simple and inexpensive technique has shown promise, particularly in children with acute osteomyelitis. Ultrasonography may demonstrate changes as early as 1-2 days after onset of symptoms. Abnormalities include soft tissue abscess or fluid collection and periosteal elevation. Ultrasonography allows for ultrasound-guided aspiration. It does not allow for evaluation of bone cortex.\textsuperscript{23}

Diagnosis requires 2 of the 4 following criteria:\textsuperscript{24}

1. Purulent material on aspiration of affected bone
2. Positive findings of bone tissue or blood culture
3. Localized classic physical findings of bony tenderness, with overlying soft-tissue erythema or edema
4. Positive radiological imaging study

**TREATMENT**

Acute hematogenous osteomyelitis is best managed with a four- to six-week course of appropriate antimicrobial therapy.

Chronic osteomyelitis is generally treated with antibiotics and surgical debridement.

**Acute hematogenous osteomyelitis**

Children with acute osteomyelitis should receive two weeks of initial parenteral antibiotic therapy before they are given an oral agent.\textsuperscript{25,26}

Adult osteomyelitis almost always requires a combined medical and surgical approach. Surgical debridement is not necessary when the diagnosis of hematogenous osteomyelitis is made early. Current treatment recommendations rarely require surgical debridement. However, if antibiotic therapy fails, debridement (or repeated debridement) and another four- to six-week course of parenteral antibiotic therapy is essential.\textsuperscript{27,28}

After cultures have been obtained, an empiric parenteral antibiotic regimen (nafcillin plus either cefotaxime or ceftriaxone) is initiated to cover clinically
suspected organisms. When the culture results are known, the antibiotic regimen is revised.

**Chronic osteomyelitis**

Chronic osteomyelitis in adults is more refractory to therapy and is generally treated with antibiotics and surgical debridement. Empiric antibiotic therapy is not usually recommended. Depending on the type of chronic osteomyelitis, patients may be treated with parenteral antibiotics for 2-6 weeks. However, without adequate debridement, chronic osteomyelitis does not respond to most antibiotic regimens, no matter what the duration of therapy. Outpatient intravenous therapy using long-term intravenous access catheters (i.e., Hickman catheters) decreases the length of hospital stays.26,29,30

**Pharmacologic treatment by stages**

Stage 1 (hematogenous) osteomyelitis in children can usually be treated with antibiotics alone. Antibiotic therapy alone is possible as children have extremely well vascularized bones and an effective immune and metabolic response to infection.

Stage 1 osteomyelitis in adults is more refractory to therapy and is usually treated with antibiotics and surgery. The adult patient is treated for 4 weeks with appropriate parenteral antimicrobial therapy, dated from the initiation of therapy or after the last major debridement surgery. If the initial medical management fails and the patient is clinically compromised by a recurrent infection, medullary or soft tissue debridement is necessary in conjunction with another 4-week course of antibiotics.

In stage 2 osteomyelitis, the patient may be treated with a 2-week course of antibiotics after superficial debridement and soft tissue coverage. The arrest rate is approximately 80%.31

In stages 3 and 4 osteomyelitis, the patient is traditionally treated with 4 to 6 weeks of intravenous antimicrobial therapy dated from the last major debridement surgery.32 Without adequate debridement, most antibiotic regimens fail no matter what the duration of therapy. Even when all necrotic tissue has been adequately debrided, the remaining bed of

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<th>Table 5. Specific antibiotic treatment</th>
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<td><strong>Organism</strong></td>
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<td>Staphylococcus aureus or coagulase-negative (methicillin-sensitive) staphylococci</td>
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<td>S. aureus or coagulase-negative (methicillin-resistant) staphylococci</td>
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<td>Various streptococci (groups A and B b-hemolytic organisms or penicillin-sensitive Streptococcus pneumoniae)</td>
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<td>Enteric gram-negative rods</td>
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<td>Serratia species or Pseudomonas aeruginosa</td>
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<td>Anaerobes</td>
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<td>Mixed aerobic and anaerobic organisms</td>
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tissue must be considered contaminated with the responsible pathogens. Therefore, it is important to treat the patient with antibiotics for at least 4 weeks. With a thorough debridement surgery, the arrest rate is approximately 90%. Outpatient intravenous therapy using long-term intravenous access catheters decreases hospitalization time.

Initial antibiotic regimens for patients with osteomyelitis are described in Table 5.3

Surgical treatment

Surgical management of osteomyelitis can be very challenging. The principles of treating any infection are equally applicable to the treatment of infection in bone.

The optimal goal of surgical management of osteomyelitis includes the following:

a. adequate drainage of intramedullary or subperiosteal pus;

b. extensive debridement of all necrotic bone and soft tissue;

c. obliteration of dead spaces;

d. adequate soft tissue coverage;

e. restoration of vascular anatomy for an effective blood supply;

f. maintenance of healthy viable tissue;

g. restoration of stability.

The Cierney-Mader classification of osteomyelitis serves as a useful guide in stratifying surgical management of osteomyelitis.27

In stage 1 osteomyelitis, the nidus of infection is entirely within the medullary canal of the bone. It is predominately secondary to hematogenous seeding of the bacteria or it is due to the introduction of surgical hardware such as an intramedullary (contaminated) nail.

In adults with primary or secondary stage 1 osteomyelitis, a thorough intramedullary reaming and unroofing is usually done with or without bone grafting. Soft tissues are reapproximated and the limb is protected by external means (brace or cast) until the structural integrity of the bone is reestablished by normal bone remodeling.

In stage 2, or superficial osteomyelitis, the surface of the bone is exposed to an overlying soft tissue defect. The superficial cortex is infected and eventually becomes sequestered (stage 3 progression) if treatment is delayed. Treatment consists of bony debridement until visible bleeding is seen on the cortex. The most important aspect of treatment is soft tissue coverage after adequate debridement to bleeding cortex. This may be a simple problem involving local tissue, or it may require free tissue transfer.

Stage 3 or localized osteomyelitis combines the problems of stages 1 and 2. The treatment involves the modalities used for both of these categories of disease. Bone is sequestered, medullary extension of the infection is common, and major soft tissue defects may be present. These patients may require external fixation for structural support while the bone graft is incorporated. Complex reconstruction of the bone and soft tissue is frequently necessary.

Stage 4 or diffuse osteomyelitis combines the problems of stages 1, 2, and 3. Instability is a problem before or after surgery; therefore, treatment must often be directed toward establishing structural stability and obliterating debridement gaps by means of cancellous bone grafts or the Ilizarov technique. Free flaps and vascularized bone grafts are other possible treatment options.

All of the modalities previously discussed may have a place in the treatment of diffuse osteomyelitis.

Debridement

Debridement of necrotic osteomyelitic bone is the standard approach in treating osteomyelitis. The goal of debridement is to leave healthy, viable tissue. Usually, the tissues surrounding the osteomyelitic lesions have a fibrous appearance due to the intense scarring process. Debridement of bone is done until punctate bleeding is obtained, giving rise to the term “paprika sign.”33 This procedure always results in the formation of a large bony defect termed dead space. However, even when all necrotic tissue has been adequately debrided, the remaining bed of tissue must still be considered contaminated. Recently, the importance of the extent of operative debridement has been reinvestigated in both normal and compromised hosts.34 B hosts treated with marginal resection (i.e., with a clearance margin of <5 mm) had a higher rate of recurrence than did normal hosts. According to the authors of that study, the extent of resection therefore appears to be much more important in B hosts, whereas a marginal resection may be acceptable in normal hosts.31

Antibiotic beads

Antibiotic-impregnated acrylic beads may be used to sterilize and temporarily fill the dead space.35 After 2 to 4 weeks in place, the beads are removed and the space is filled with a cancellous bone graft.34 These beads deliver a high local concentration of antibiotics. Because these antibiotics are not absorbed systemically, local concentrations of antibiotics may be increased up to 5 to 10-fold, more than concentrations...
that result after systemic administration. As a result, bacteria resistant to lower serum concentrations may be sensitive at the higher concentrations established in the wound environment by the antibiotic-impregnated beads. The release of antibiotics from the beads is bimodal. There is an initial rapid release of 5% of the total antibiotic administered within the first 24 hours, followed in weeks to months by a slow sustained release with a progressively decreasing antibiotic elution from the beads; Vancomycin, Tobramycin, and Gentamicin are commonly impregnated in the antibiotic beads. The rate of arrest of osteomyelitis has ranged from 55% in a study of 54 patients to 96% in a study of 46 patients using above described combined antibiotic treatments. Since most beads act as a biomaterial surface to which bacteria preferentially adhere, infection associated with beads use has been described. To avoid such a problem, biodegradable antibiotic-impregnated beads have been employed recently and have shown favorable antibiotic release kinetics. Antibiotic-impregnated cancellous bone grafts were recently used in a clinical trial of forty-six patients, and the osteomyelitis was arrested in 95% of them. Local delivery of antibiotics may also be delivered into the dead space by an implantable pump.

Reconstruction of bone defects and management of dead space

Adequate debridement of the osteomyelitic lesions will constantly leave an important bone defect, termed a dead space. This space represents a problem by being poorly vascularized, thus predisposing to persistence of infection. Appropriate management of any dead space created by debridement is mandatory to arrest the disease and to maintain the integrity of the skeletal part.

The goal of dead-space management is to replace dead bone and scar tissue with durable vascularized tissue. A free vascularized bone graft has been used successfully to fill dead space. These grafts are usually obtained from the fibula or iliac crest. Local tissue flaps or free flaps can also be used to fill dead space because dead space cannot be allowed to heal by secondary intention. This is due to the fact that the scar tissue filling the defect may later become avascular. The advantages of using these grafts include an increasing blood supply to the affected area. An alternative technique is to place cancellous bone grafts beneath local or transferred tissues where structural augmentation is necessary. Careful preoperative planning is critical to the conservation of the patient's limited cancellous bone reserves. Open cancellous grafts without soft-tissue coverage are useful when a free tissue transfer is not an option and local tissue flaps are inadequate.

Vascularized fibula graft to reconstruct osseous defects

Free vascularized fibula grafts have been used to reconstruct long tibial bone defects since Taylor's report in 1975. A pedicled vascularized fibula graft (Figure 2b) is also useful for small bone defects or pseudoarthrosis because of its excellent vascularity. The pedicled vascularized fibula transfer does not need the microvascular anastomosis and can be performed in much less time. The pedicle may be disal or proximal, depending on the site of the bone defect.

In the free vascularized fibula grafts, the controlateral fibula is taken. Depending on the position of the tibial problem and the arteriographic findings in the lower leg, including the peroneal vessels, it can be decided whether a proximally pedicled or a distally pedicled fibula should be used.

| Figure 2 a, b | Operative diagram of the pedicled vascularized fibula graft. a. Proximally pedicled fibula graft. b. Distally pedicled fibula graft. Pop, popliteal artery; A, anterior tibial artery; F, fibular vessel; P, posterior tibial artery; F, monitoring flap. From Satoh K, Effectiveness of the pedicled vascularized fibula graft to reconstruct tibial defects. J Plast Surg. |

Vascularized fibula with a vascular peristomal flap for the reconstruction of the osseous defects

The immediate reconstruction of a missing bone segment may be reconstruct with a primary osteoperiostial tube that will secondarily be
The osteoperiosteal tube is formed by the combination of two techniques: the vascularized fibular transfer, which is modified by splitting the bone graft longitudinally, and transfer of vascularized periosteum. (Fig. 3)

The arrangement of both vascularized grafts as an osteoperiosteal tube exemplifies the concept of given space. Inside the osteoperiosteal tube a consolidation chamber is created in which all the factors required for bone formation can be concentrated.

If skeletal instability is present at the site of an infection, measures must be taken to achieve stability with plates, screws, rods, and/or an external fixator.

External fixation is preferred over internal fixation because of the tendency of the sites of medullary rods to become secondarily infected and to spread the extent of the infection. Ilizarov external fixation allows reconstruction of segmental defects and difficult infected nonunions. This method is based on the technique of distraction osteogenesis whereby an osteotomy created in the metaphyseal region of the bone is gradually distracted to fill in the defect. The Ilizarov technique is used for difficult cases of osteomyelitis when stabilization and bone-lengthening are necessary. The method may also be used to compress non-unions and to correct malunions. The technique is labor-intensive and requires an extended period of treatment with the device, averaging 8.5 months. In addition, the sites of the wires or pins usually become infected and the device is painful. In studies in which this technique was used, osteomyelitis arrest rates have ranged between 75% and 100%.

Adequate soft-tissue coverage of the bone is necessary to arrest osteomyelitis. Small soft-tissue defects may be covered with a split-thickness skin graft. In the presence of a large soft-tissue defect or an inadequate soft-tissue envelope, local muscle flaps and free vascularized muscle flaps may be placed in one or two stages. Local muscle flaps and free vascularized muscle transfers improve the local biological environment by bringing in a blood supply important for host defense mechanisms, antibiotic delivery, and osseous and soft-tissue healing. Local and microvascular muscle flaps as well as microvascular flaps alone have been used in combination with antibiotics and operative debridement. The rate of arrest of the osteomyelitis ranged from 90% to 100%.

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Donor muscle selection depends on the size of the defect and pedicle length requirements.

Types of muscle- or musculocutaneous flaps:

- latissimus dorsi
- gracilis
- scapular
- rectus abdominis
- pectoralis major
- gastrocnemius
- soleus
- groin / groin with iliac bone

Use of vein loops in reconstructive procedures.

The application of the arteriovenous fistula concept is an important adjunctive procedure in microsurgical tissue transfer, when appropriate recipient vessels are not available, or when better arterial or venous flow characteristics are desired.

The use of a temporary arterio-venous (A-V) fistula prior to flap harvesting was suggested by Threlfall in 1982.

Osteomyelitic lesions are also affecting perivascular sheaths and induce a constrictive inflammatory syndrome which significantly impairs the integrity of the vascular wall. Thus, it may be necessary to locate vessels remote from the area of reconstruction and to construct long venous grafts.

The use of A-V loops have two main indications in this selected patient group:

1. creation of “neovessels” to provide recipient vessels for a free flap if all local option have already been used or are destroyed by various underlying causes

2. improvement of quality of arterial inflow in situations with compromised perfusion.

There are two different strategies:

One is the creation of the A-V fistula and free
flap transfer in the same operation.\textsuperscript{36,37}

The other option is a two step procedure where the fistula is created in the first sitting and the free tissue transfer is performed after an interval of several days, usually waiting 3-7 days before dividing the interpositional vein loop, providing one artery and one vein, and before defect closure.

The other advantages of the technique are: the procedure can be carried out under local anesthesia, ease of positioning of the patient on the operating table, and a reduction in the time taken to perform the tissue transfer.\textsuperscript{1}

The A-V loop increases the blood flow in the arterial system and free flap transfer provides improvement of peripheral tissue perfusion. Another advantage of the A-V loops is that anastomosis can be performed to a large-caliber “healthy” vessel, usually in end-to-side manner.

Vacuum assisted device

An additional option that may aid healing of soft-tissue wounds is the vacuum-assisted closure system, a device that applies localized negative pressure over the surface of wounds and aids in the removal of fluids.\textsuperscript{38} In one case study involving children, this system helped to increase the rate of granulation tissue formation and healing of extensive soft-tissue injury.\textsuperscript{39}

Herscovici et al also demonstrated its usefulness as an adjunct therapy for high-energy soft-tissue injuries, in a nonrandomized study of twenty-one patients who had sustained trauma; the authors reported that 57\% of the patients did not require additional treatment or a split-thickness skin graft after approximately twenty days of negative-pressure treatment.\textsuperscript{40} The potential applications of vacuum-assisted closure systems are promising; however, to our knowledge, no large, controlled clinical trials have been completed to determine their efficacy and risks in patients with established osteomyelitis. The authors of one case study reported the development of an anaerobic wound infection, apparently potentiated by topical negative pressure.\textsuperscript{61}

Hyperbaric oxygen therapy

The Cierny-Mader classification of osteomyelitis can be used as a guide to determine which types of osteomyelitis may be benefited by adjunctive hyperbaric oxygen (HBO\textsubscript{2}).

Adjunctive HBO\textsubscript{2} is used to treat stage 3B and 4B of osteomyelitis when the above definition for refractory osteomyelitis is met. HBO\textsubscript{2} is adjunctive and must be used with appropriate antibiotics (determined by bone culture and sensitivity testing), surgical debridement, nutritional support, and reconstructive surgery.

It has been demonstrated that:

- Decreased oxygen tensions found in infected bone can be elevated to normal or above-normal bone oxygen tensions when animals breathe 100 \% oxygen in a hyperbaric chamber.\textsuperscript{62,63} Hyperbaric oxygen provides periodic elevation of bone and tissue oxygen tension from hypoxic levels to normal or supranormal levels.
- The increased oxygen tension in hypoxic tissue promotes collagen production by fibroblasts,\textsuperscript{64} and capillary angiogenesis since structural collagen provides support for the new budding capillaries.\textsuperscript{65} Intermittent oxygen tensions of 30 to 40 mmHg are necessary for neovascularization in an ischemic environment.\textsuperscript{66}
- Neutrophils require tissue oxygen tensions of 30 to 40 mmHg to kill bacteria by oxidative killing mechanisms at the focus of infection.
- Leukocyte killing of aerobic Gram-positive organisms including \textit{Staphylococcus aureus} and aerobic Gram-negative organisms is returned to normal or above-normal levels when the osteomyelitic bone’s low oxygen tension is increased to physiologic or supraphysiologic levels. Elevating the oxygen tension above 30 to 40 mmHg further improves leukocyte killing. HBO\textsubscript{2} has proved effective as adjunctive therapy in animal models of chronic \textit{S. aureus} and \textit{Pseudomonas aeruginosa} osteomyelitis.
- HBO\textsubscript{2} has a direct and indirect killing effect on anaerobic organisms. The indirect effect is mediated through the oxygen dependent killing mechanisms of the polymorphonuclear leukocyte. In chronic nonhematogenous osteomyelitis, anaerobes make up approximately 15 \% of the isolate.\textsuperscript{67}
- HBO\textsubscript{2} therapy enhances transport and augments the antibiotic efficacy.
- HBO\textsubscript{2} may enhance osteogenesis.

Composite bone and muscle grafts and distraction histogenesis (Ilizarov technique) add additional dimensions to the management of osteomyelitis. Adjunctive HBO\textsubscript{2} should be used, in cases where these measures have failed, the patient is not a candidate for these techniques, and/or the host is locally compromised.

The initial treatment depends on the severity of the patient’s clinical disease. The HBO\textsubscript{2} treatments are at a pressure of 2.0 to 2.5 atm abs and last for 90 to 120 minutes. Following major debridement surgery the patients should be treated daily, if possible.
COMPLICATIONS

Possible complications may include: bacteremia, bone abscess, fracture, local spread of infection, loosening of the prosthetic implant, reduced limb or joint function and the most severe one, amputation.

PROGNOSIS

Without proper treatment the prognosis is unfavourable and the evolution of the disease relies heavily on a timely diagnosis and aggressive therapy.

With the appropriate treatment most cases have a good prognosis and the patient usually regains the full function of the affected limb.

STRATEGIES IN SURGICAL TREATMENT

The standard therapeutic approach today consists in aggressive bone and soft tissue debridement, followed by an immediate reconstruction and coverage of the defect, usually by free flaps.

The optimal results involve minimal intra- and post-operative complications including flap necrosis, no recurrences, short hospitalization period and maximal recovery of the limb function.

However several factors play an important role in the operative decision making:

- local conditions (extension of the injury and of the scarring, fibrosis of the surrounding soft tissues and bone, availability of viable receptor vessels with presence of distal pulses)
- particularities of the history e.g. etiology, disease period (assessed by proper history taking)
- the general state of the patient, e.g. smoking, diabetes, atherosclerosis

These particular preoperative conditions require a differentiation of the microsurgical techniques used in the defect reconstruction. Based on our clinical experience and on the literature data we suggest 4 strategies for the management of the osteomyelitis patients.

Strategy 1: Soft tissue reconstruction 3-7 days later.
Strategy 2: Soft tissue reconstruction 3-7 days later, using a vein graft.
Strategy 3: Soft tissue reconstruction 3-7 days later using a vein loop.
Strategy 4: Soft tissue reconstruction and callus distraction.

The patients treated according to the first strategy have limited bone and soft tissue injuries, while the vessels are capable to sustain a free flap. Presence of a distal pulse, local inflammatory signs and partial fibrosis of the injury site is characteristic for these patients with a short evolution of the disease. See case reports 1 and 2.

The second strategy applies to patients who have developed osteomyelitis since a long period and display extended bone and soft tissue injuries. The local signs include: tegument retraction, fistulae sinus drainage, extended fibrosis with presence of distal pulses. This situation usually allows preparation of the receptor artery, but contraindicates the dissection of the receptor veins. The venous drainage will be provided by a vein graft, anastomosed in the deep (femoral or popliteal) venous system far away from the zone of injury. This strategy may be applied as a primary solution or as a salvage procedure in venous thrombosis, as shown in case reports 3 and 4.

When extensive bone and soft tissue injuries are present and the local conditions after chronic infection do not allow finding the recipient vessels for the free flap, the third strategy is recommended. These patients are usually either smokers, diabetics or with occlusive arterial disease and with a long disease history. Absent or weak distal pulse, important local bone and soft tissue defects with scarring and severe fibrosis sites are typical for these patients. In these cases vessels dissection is not possible even at the distance of the lesion. New receptor vessels are created using a long saphenous A-V loop for vascularization of the free flaps covering the defect. In the A-V loop technique we performed end-to-side anastomoses to avoid a vessel caliber mismatch. See case report 5.

The fourth strategy involves patients with large soft tissue defects and bone infection, comprising the entire circumference and length of the infected site, with local areas of osteolysis. Segmentary bone resection is thus performed with a Hoffman external fixator. Extensive debridement of the soft tissues needs to be performed followed by coverage with free flaps and filling the bone defect with cement containing antibiotics. Reconstruction of the bone defect is performed six weeks post-operatory using callus distraction.

CASE REPORTS

Case 1

This 47-years-old man sustained a bilateral tibial and fibular bone fracture of the right lower leg fixed with plate and screws. Subsequently, the patient developed chronic osteomyelitis with bone sequestra and skin defect. (Fig. 4) The bone and the soft tissue was thoroughly debrided (Fig. 5) and the defect covered using combined latissimus dorsi and serratus muscle free flaps. (Fig. 6) The fracture was stabilized using...
Figure 4. Distal antero-medial side of the right leg with extensive soft tissue necrosis.

Figure 5. Radical debridement of the soft tissue and bone.

Figure 6. Serratus and latissimus dorsi musculo-cutaneous flap harvested.

Figure 7. Defect coverage using the free flap and bone stabilization using external Hoffman fixator.
Case 1

A 18-years-old male sustained a fracture of the tibial diaphysis during a traffic accident 3 months ago. A plate was used to stabilize the fracture. By the time the patient arrived in our department he developed chronic osteomyelitis and a sinus tract fistula. Bone and soft tissue debridment was performed and the defect was covered using gracilis muscle free flap. Three years after the operation the patient shows no sign of osteomyelitis and a good consolidation of the tibial bone.

Case 2

A 18-years-old male sustained a fracture of the tibial diaphysis during a traffic accident 3 months ago. A plate was used to stabilize the fracture. By the time the patient arrived in our department he developed chronic osteomyelitis and a sinus tract fistula. Bone and soft tissue debridment was performed and the defect was covered using gracilis muscle free flap. Three years after the operation the patient shows no sign of osteomyelitis and a good consolidation of the tibial bone.

Case 3

A 18-years-old male sustained a fracture of the tibial diaphysis during a traffic accident 3 months ago. A plate was used to stabilize the fracture. By the time the patient arrived in our department he developed chronic osteomyelitis and a sinus tract fistula. Bone and soft tissue debridment was performed and the defect was covered using gracilis muscle free flap. Three years after the operation the patient shows no sign of osteomyelitis and a good consolidation of the tibial bone.

Figure 8. Postoperative plain X-Ray showing a thin tibial bone. a. and b. spontaneous hypertrophic callus formation after muscle flap coverage.

Figure 9. Aspect of the reconstructed leg 7 years post-operative.

Figure 10. Chronic osteomyelitis of the right leg with significant soft tissue involvement and a sinus drainage.
A 42-years-old male sustained 19 years ago a type III B fracture in the distal third of the right leg following a work accident, for which reduction of the fracture site has been performed. Excision of the callus was performed after one year. The patient developed chronic osteomyelitis of the right leg before coming to our institution. We practiced soft tissue and bone sequestra debridment followed by a latissimus dorsi musculo-cutaneous free flap using a safenous vein graft. (Fig. 13) His hospitalization progressed without complications and he regained full function of the leg.

Figure 11. Failed flap due to thrombosis of the vein microanastomosis. Salvage by interpositional saphenous vein graft.

Figure 12. Postoperative view of the reconstructed right leg showing optimal flap integration and acceptable cosmetic aspect after 3 years.

Case 4

A 42-years-old male sustained 19 years ago a type III B fracture in the distal third of the right leg following a work accident, for which reduction of the fracture site has been performed. Excision of the callus was performed after one year. The patient developed chronic osteomyelitis of the right leg before coming to our institution. We practiced soft tissue and bone sequestra debridment followed by a latissimus dorsi musculo-cutaneous free flap using a safenous vein graft. (Fig. 13) His hospitalization progressed without complications and he regained full function of the leg.

Case 5

A 52-years-old male developed chronic post traumatic osteomyelitis of the left thigh after a comminuted patella fracture, sustained 35 years ago. (Fig. 14) Initially, the fracture site was stabilized using an external fixator and an saphenous vein graft was placed. (Fig. 15)

Bone and soft tissue debridement was performed, followed by a rectus abdominis muscular free flap, (Fig. 16) using the arterio-venous vascular loop technique with controlateral vena saphena magna anastomozed in an end-to-side fashion between the superficial femoral artery and vein. (Fig. 17) The postoperative period was uneventful and the patient was discharged free of disease. (Fig. 18)
A 33-years-old male sustained a comminuted open fracture of the tibia during a traffic accident 3 years ago, for which surgical reduction of the fracture and centromedular nail osteosynthesis has been performed. Due to fracture site infection, repeated bone and soft tissue debridment were performed after 3 months from the primary surgery. Because of defective healing complicated with chronic osteomyelitis in the medial third of the left tibia and anterior cutaneous leg fistula drainage, (Figs. 19, 20) bone and soft tissue debridment was performed (Fig. 21) and stabilization of the fracture with external Hoffman II fixator. The bone defect was filled with cement, after this, callus distraction was performed, and covered the defect with a latissimus dorsi musculocutaneous free flap and full thickness skin graft 5 months after intervention. (Figs. 22, 23) Postoperative healing progressed without complications during the follow-up examination.
Figure 22. The bone defect was filled with antibiotic coated cement and soft tissues reconstructed using a latissimus dorsi muscular free flap.

Figure 23. Postoperative plain X-Ray showing the level of bone resection and cement filling.

CONCLUSIONS

Diagnosing osteomyelitis may be an easy step in the initial stage of the disease. In spite recent advances, it remains most difficult to treat both medically and surgically and requires commitment and patience from the patient as well as from the physician. The golden rule in osteomyelitis involves a surgical act, comprising various, complex and aggressive methods of debridement as well as bone and soft tissue reconstruction. Favorable outcomes can be insured through timely diagnosis and correct surgical strategies.

REFERENCES

CHRONIC OSTEOMYELITIS OF LONG BONES

Bogdan Maciuceanu, Mihai Ionac

1) The stage I lesions in osteomyelitis according to Cierny-Mader Staging System can be described as:
   a) medullary osteomyelitis
   b) superficial osteomyelitis
   c) infected intramedullary rods
   d) diffuse osteomyelitis
   e) localized osteomyelitis

2) The diagnosis of osteomyelitis is primarily based on:
   a) clinical examination
   b) laboratory studies
   c) MRI
   d) biopsy and histopathology
   e) X-rays

3) Physical examination findings in chronic osteomyelitis may include:
   a) intense local pain
   b) tenderness on palpation
   c) sinus tract drainage
   d) crepitation
   e) nonhealing sinus tract

4) Absolute criteria for positive diagnosis of osteomyelitis are:
   a) spontaneous discharge of purulent material from the affected area
   b) aspiration of purulent material from the affected bone
   c) positive radiological findings suggesting focal osteolysis and periosteal fragmentation
   d) positive hemocultures
   e) localized classic physical findings of bony tenderness

5) Surgical debridement of osteomyelitic lesions is performed:
   a) using aggressive initial excision of all devitalized tissues excluding bone
   b) using aggressive initial excision including both devitalized tissues and visibly affected bone
   c) multiple staged, daily debridements until healthy, well vascularized tissues remain
   d) multiple staged every three days debridement until healthy, well vascularized tissues remain
   e) multiple staged debridement followed by early soft tissue coverage

6) The optimal goal of surgical treatment is osteomyelitis comprises:
   a) eradication of infection
   b) reconstruction of complex bony and soft tissue defects remained after extensive excision
   c) restoration of the vascular anatomy of the affected region
   d) restoration of bone stability
   e) maintenance of healthy viable tissue

7) Bone defects may be reconstructed with:
   a) fibula osseous flap
   b) cancellous bone graft
   c) groin osteocutaneous flap with iliac crest
   d) serratus anterior osteocutaneous flap with rib
   e) cement

8) Non-surgery procedures used in treatment are:
   a) antibiotic beads
   b) vacuum assisted device
   c) hyperbaric oxygen
   d) local gauze
   e) debridement and soft tissue coverage

9) Complication of osteomyelitis are:
   a) enlarge limb or joint function
   b) chronic osteomyelitis
   c) bone consolidation
   d) amputation
   e) reduced limb or joint function

10) Strategy 3 consists in:
    a) soft tissue reconstruction 3-7 days later
    b) soft tissue reconstruction 7-14 days later
    c) soft tissue reconstruction 3-7 days later using a vein loop
    d) soft tissue reconstruction and callus destruction
    e) soft tissue reconstruction using a safenous vein grafts

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1 - cd; 2 - acd; 3 - d; 4 - a; 5 - ad; 6 - cd; 7 - abcde; 8 - ab; 9 - abe; 10 - de.