INSTRUCTIONAL ARTICLE

Management of septic non-unions

P Pelser MBChB (Pret)
Registrar, National Hospital, Department of Orthopaedic Surgery, University of Orange Free State, Bloemfontein, South Africa

Presented at the Johnson&Johnson Registrar Congress, Durban, February 2009

Reprint requests:
Dr PC Pelser
Department of Orthopaedic Surgery
Univaersity of the Free State
Bloemfontein
Tel: (051) 405-2242
Fax: (051) 430-7101
Email: legraner@fshealth.gov.za

The treatment of septic non-unions is a complex problem with high morbidity and prolonged and costly treatment with significant psycho-social implications. Good communication with the patient and individualised treatment objectives are therefore essential. With appropriate treatment and complete elimination of infection a good to excellent outcome can be expected.

This article outlines the current thoughts and recommendations for the management of septic non-union.

Definitions

A delayed union has occurred when healing of a fracture takes longer than expected for any specific fracture. A non-union is said to have occurred once there is clinical and/or radiological evidence of cessation of fracture healing, usually after 6-8 months.[1]

A septic non-union is defined as a non-union complicated by local infection at the fracture site and in the surrounding tissues.

Classifications

Jain and Sinha have proposed a classification system for septic non-unions.[2] Septic non-unions are divided into two groups based on the absence or presence of a draining sinus. A fracture is considered to be non-draining if there has been no drainage from the site of infection for at least three months. The two groups are further subdivided according to the size of the fracture gap after debridement.

- **Group A Non-draining infection (for > 3 months)**
  1. Fracture gap < 4 cm (after debridement)
  2. Fracture gap > 4 cm (after debridement)
- **Group B Draining sinus**
  1. Fracture gap < 4 cm
  2. Fracture gap > 4 cm

The general classification of non-unions is also useful, and in it non-unions are divided into being either hypervascular (hypertrophic) or avascular (atrophic). Hypervascular non-unions can be subdivided according to the shape of the fracture ends into elephant foot, horse hoof and oligotrophic. Avascular non-unions are subdivided into torsion wedge, comminuted, with a defect or atrophic types.[1]

Hypervascular type non-unions will heal with adequate reduction and immobilisation, whereas avascular type non-unions will need intervention to re-simulate and enhance the bone-healing process.[3]

Another useful classification for non-unions has been described by Paley. Type A has bone loss of less than 1 cm, and can be either mobile with deformity, stiff with deformity or stiff without deformity. Type B has bone loss of more than 1 cm with either a bony defect, loss of length or both.[4]

May has proposed a prognostic classification predictive of the rehabilitation period for lower leg non-unions.

Where the tibia and fibula are intact, rehabilitation will take 6-12 weeks. If the tibia is intact but needs bone graft for support, rehabilitation will take 3-6 months. If the tibial defect is less than 6 cm with an intact fibula, rehabilitation will take 6-12 months. If the tibia defect is more than 6 cm with the fibula intact, rehabilitation will take 12-18 months. Lastly, if the tibia defect is more than 6 cm and the fibula is not intact, rehabilitation can be expected to take more than 18 months.[2]

When dealing with chronic infection, the classification of osteomyelitis by Cierny and Mader has proven to be useful. The infection is classified according to its anatomical description as well as patient (host) factors. Anatomically,

type I is medullary, with endosteal disease. Type II is superficial where the cortical surface is infected and a coverage defect exists. Type III is a localised cortical sequestrum without instability after debridement, and type IV is a diffuse type with mechanical instability associated with type I, II or III *(Figure 1).*

The host can be classified according to physiological class as A (normal immunocompetency with good local vascularity), B (local or systemic factors that compromise immunity or healing) or C (prohibitive morbidity anticipated and/or poor prognosis for cure).[5]

Location of non-unions

The incidence of non-union is determined by the extent of soft tissue injury as well as the fracture pattern and consequent treatment. Accordingly, certain fracture locations are more prone to development of non-unions and justify a high index of suspicion. In order of prevalence, firstly the tibia, then the femur, humerus, radius, ulna, radius-ulna and lastly the clavicle are affected.

Diagnosis of septic non-union

Clinically, the diagnosis of a septic non-union is made by the observation of local signs and symptoms such as redness, swelling, a sinus or draining wound and pain and tenderness, as well as systemic symptoms such as fever, malaise and nausea[6] *(Figure 2).*

Raised inflammatory markers such as the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and a raised white cell count usually confirm the presence of infection, but have poor specificity.

Confirmation of the diagnosis is obtained by culture and sensitivity on a biopsy from the non-union site. Specimens for biopsy must be comprehensive and taken from tissue that is representative of the diseased area. A minimum of five biopsies need to be taken and samples can consist of pus, tissue and bone. The diagnosis of infection is confirmed if two or more specimens yield a positive culture. It is imperative that a sample is also sent for histological examination, which will show changes in keeping with chronic osteitis.[6]

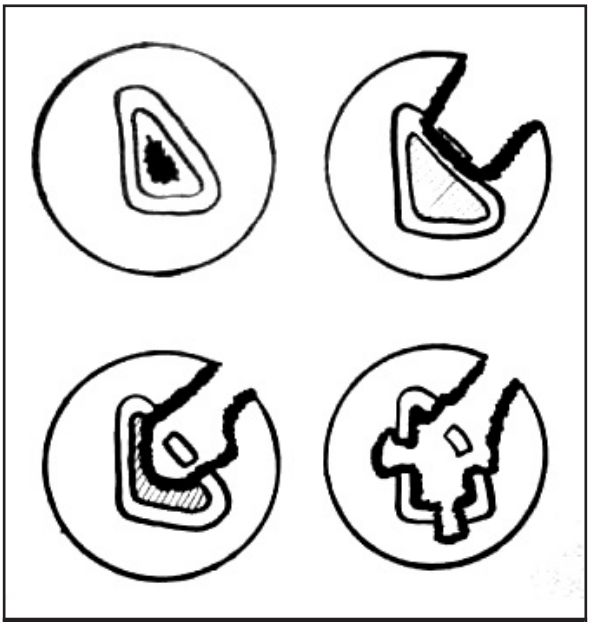

Figure 1:
Anatomical classification of osteomyelitis according to Cierny and Mader

Figure 2:
Clinical picture of a septic non-union

The X-ray picture of septic non-unions can be varied, and includes osteopaenia, scalloping and cortical thinning; loss of trabecular and cancellous architecture; radiodense appearance of sequestrum and periosteal changes and soft tissue swelling. X-ray imaging often underestimates the extent of bony involvement *(Figure 3).*

CT is of value to evaluate the extent of bony infection and intramedullary osteitis, but is not routinely used.

MRI is of value to differentiate soft tissue infection from infected bone and to assess the extent of involvement.

Skeletal scintigraphy with Technetium has 100% sensitivity for infection but low specificity. 111-Indium-IgG has 93% specificity and therefore a high negative predictive value. 111-Indium-oxime is useful to detect both infection and bone necrosis.[7]

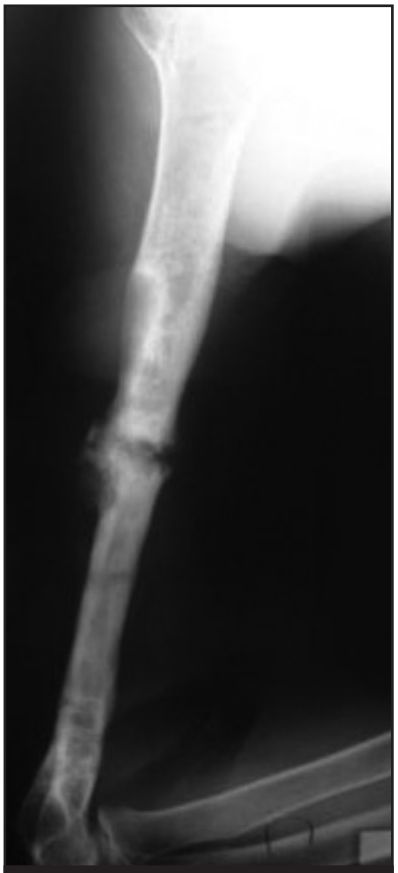

Figure 3:
X-ray picture of a humeral non-union

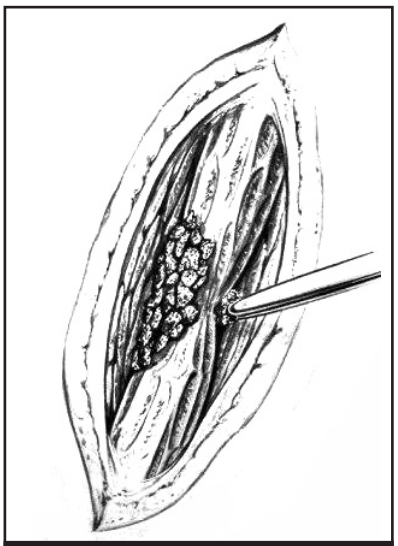

Figure 4:
Technique for subperiosteal decortication and osteoperiosteal bone graft

Considerations in the treatment of septic non-unions

Certain systemic factors influence the occurrence and healing of septic non-unions. Among these are the patient's metabolic condition, nutritional status and general health. Some medications, such as steroids, anticoagulants and non-steroidal anti-inflammatory drugs (NSAIDs), as well as radiation and chemotherapy are also known to compromise healing of fractures. Both alcohol usage and smoking have been shown to delay healing of non-unions. Systemic diseases that affect the healing of infection and fractures, such as HIV and diabetes, must be treated optimally.[1]

There are many local factors that need to be taken into account when planning the surgical approach and technique, as well as the form of fixation to be used in treating the non-union and soft tissue reconstruction.

The bone can be hypervascular or avascular. Irradiation of the bone will influence healing negatively.

The soft tissue needs to be evaluated for previous scars and scar tissue, as well as loss of coverage. Arterial injury or impaired circulation can delay union. Lymph drainage of the extremity and possible venous stasis must be evaluated.

The fracture must be evaluated with regards to comminution and bone loss, as well as the fracture gap and previous fixation and instrumentation.

When evaluating the infection, the virulence, sensitivity and resistance of the organism must be determined. The extent of involvement and spread of the infection must also be determined.

The socio-economic status, as well as the expectations and needs of the patient must be taken into account when formulating an individualised treatment protocol. It must be remembered that early amputation with an orthosis might be a suitable option for the patient to regain independence.

The specific problems that need to be addressed during treatment should be identified and a treatment strategy worked out that will not compromise future function of the limb. The aim is healing of the fracture with eradication of infection with the fullest functionality possible. This relies on maintaining range of movement of joints and correction of deformities.[8]

Surgical methods of treating infected non-unions

There are two slightly opposing strategies for treating non-unions. Either one or a combination of the two methods can be used in any given non-union, and the surgeon must be ready to change the approach if needed.

The first school of thought is the **conventional or classic treatment** method. The goal is firstly to achieve control of the infection and restoration of skin coverage, followed by bone graft and fracture fixation as a later procedure. The drawbacks are the long duration of treatment (often more than a year), the multiple operations that are needed to normalise the overlaying skin and stiffness of the adjacent joints.

The steps in the treatment are an extensive debridement of the infected bone and soft tissue, local and systemic antibiotic treatment and temporary stabilisation of the fracture with an external fixator or plate and screws. This is followed by a split-thickness skin graft after four days over the newly formed granulation tissue. Soft tissue cover or reconstruction with a full-thickness vascularised graft is performed 4-6 weeks after the split skin graft has healed.

Bone grafting is only done after the soft tissue has healed completely and the infection has been dormant for at least 6 months, if the non-union still persists.

The second method which was born out of the difficulty in gaining control of the infection due to instability at the fracture site, is the more **active or modern treatment**. Here the restoration of bony continuity takes precedence over infection control, and the focus is on attaining bone and soft tissue stability, and preserving function and motion in the adjacent joints.

The treatment consists of exposure of the non-union through the old scar and sinuses followed by a thorough debridement of all infected tissue and bone. Subperiosteal decortication of the fracture ends with a resultant osteoperiosteal graft is performed *(Figure 4),* after which external fixation is applied to align, compress and stabilise the fracture. If the existing plate or intramedullary nail fixation is adequate it can be left in place, provided there is no active drainage from the wound pre-operatively. Autogenous cancellous bone graft can be added, after which soft tissue closure is obtained and biological dressings applied to any remaining open areas. Suction drainage is inserted and systemic antibiotic treatment is commenced. After healing of the non-union a final sequestrectomy is performed with split-thickness skin grafts to any remaining skin defects.

Alternatively, if fixation is deemed inadequate the medullary canal can be reamed to accommodate a larger nail or an antibiotic coated nail as described by Thonse and Conway[9] especially in those patients not suited to application of an external fixator.

Whichever method is used, the mainstay of surgical treatment remains an adequate debridement with stable fixation, soft tissue coverage and filling of defects and dead space management. This needs to be combined with correction of deformity and restoration of limb length.

Surgical treatment techniques

Treating a non-union with the conventional and/or active methods will entail using a combination of the following surgical techniques:

Sequestrectomy and curettage/ debridement

A tourniquet is applied with passive exsanguination of the limb. Gentle soft tissue handling and incisions following previous scars are used to excise sinus tracts, all infected soft tissues and all unhealthy granulation tissue. Debridement of sequestrum, purulent material and necrotic tissue is done and a cortical window can be made to expose the medullary cavity if necessary. Dead bone must be removed until punctate bleeding is encountered. This is best achieved by using a high speed burr. Any potential dead space needs to be filled with the surrounding soft tissue or a muscle flap. Suction drains are inserted after which skin cover and closure is obtained without tension. Radical debridement entails surgical margins through healthy tissue.[10]

Figure 5:
Septic non-union treated with the Ilizarov technique

Figure 6:
X-ray picture of the non-union in *Figure 5*

The mainstay of surgical treatment remains an adequate debridement with stable fixation

Figure 7:
X-ray picture showing antibiotic PMMA beads in the treatment of a femoral septic non-union

Fracture reduction and fixation

All infected instrumentation needs to be removed unless it is an IM nail without any active drainage, especially in the femur. An external fixation device is applied according to the fracture configuration and local anatomy. Insertion of an IM nail is permissible if it is a non-draining infection. Plate and screw fixation can only be used as a temporary measure.[11]

Ilizarov method (spatial frame)

This technique is indicated for metaphyseal non-unions complicated by leg length discrepancies, deformities and/or malrotation. It is contraindicated in patients with poor compliance or at the extremes of age. The technique is chosen according to the type of non-union: hypertrophic non-unions are treated with compression, atrophic non-unions are treated by osteotomy or corticotomy with shortening; and segmental bone loss is treated with bone transport or acute shortening followed by distraction histogenesis. Very good bone results are usually achieved with good functional results *(Figures 5 and 6).* It remains, however, a high risk procedure for both major and minor complications.[12,13]

Polymethylmethacrylate (PMMA) antibiotic beads

Beads are made by adding antibiotic preparations to 40 g of PMMA cement. By placing these beads into the infected tissues *(Figure 7)*, local concentrations of antibiotics are achieved of up to 200 times higher than with systemic administration, making the antibiotics lethal to otherwise resistant organisms. At the same time, the systemic and route-of-administration complications are prevented. The beads can be of short- or long-term use, but are removed on average 10 days after insertion. Soft tissue defects can be covered with a double layer Opsite™ dressing with frequent changes, enabling effective dead space management. Current thought is that these beads should only be used to control potential infection in the short term as they, with the passage of time, will be populated with organisms in the biofilm that develops around them and may act to perpetuate the infection.

When choosing the type of antibiotic to be used, there are a few points to take into consideration. Antibiotics which are heat-resistant are gentamycin and tobramycin. A high level of release from the cement is possible with penicillin, the cephalosporins and clindamycin. Vancomycin is less effective after combining it with bone cement but is active against resistant organisms.

The dosages of the commonly used drugs are: vancomycin 4 g, tobramycin 3.6 g and cephalosporins 4 g.[2]

Bone graft and bone graft substitutes

Bone graft is used for augmentation of bone healing and to fill voids that may otherwise act as sumps that will promote infection.

Autogenous bone grafts can be cortical grafts, which supply immediate structural support but show slower incorporation; or cancellous grafts, which offer no structural support but induce osteogenesis and incorporate, mature and remodel faster.

Allografts, demineralised bone matrix, collagen, hydroxyapatite or tricalciumphosphate need to be used with discretion in the vicinity of sepsis due to the risks involved when introducing foreign bodies to an infected wound.[14]

A number of bone-grafting techniques are available.[2]

A block of cancellous bone can be used for fracture gaps larger than 2.5 cm. Full thickness iliac crest is routinely used and then fixed with a plate and screws or threaded over a nail.

A vascularised graft consists of a segment of bone harvested along with its nutrient vessel which is transplanted to the non-union site and then re-anastomosed. A 70-90% union rate can be expected. Fibula, iliac crest or rib grafts are commonly used, and best results are achieved when the procedure is performed after the infection is quiescent.

Postero-lateral grafting of the tibia has been described for midshaft tibia defects with an intact fibula. The graft is applied through the deep posterior compartment to the tibia and fibula shafts in order to create a synostosis between the bones.

A fibula pro-tibia transfer is performed by raising the ipsilateral fibula and transferring it to the tibia on a vascular pedicle.

Open bone grafting by means of the Papineau technique is indicated for small defects of 3-4 cm with stable fixation. Extensive debridement is performed with segmental resection of the diaphysis if necessary. Daily dressings are started five days after the debridement and continued until healthy granulation tissue covers the whole area. An autogenous cancellous bone graft with 5×5 mm slivers is then performed. Antibiotic-soaked dressings are commenced five days after the bone graft and changed daily. The wound is covered with a skin graft or flap once there are no signs of infection.

Antibiotic treatment

Antibiotics are administered enterally, parenterally or through a biodegradable delivery system, the local administration is discussed under PMMA antibiotic beads. The choice of drug is made according to the sensitivity of the organisms from the wound culture and biopsy. Initial treatment with an anti-Staphylococcus drug such as cloxacillin is commenced empirically until specific sensitivities are known. The duration of the antibiotic treatment is dependent on the duration of the infection; the organism's virulence, sensitivity and resistance; the adequacy of the preceding surgical debridement; the host resistance and response to treatment (as monitored clinically and with inflammatory markers) and the type of antibiotic used. A minimum of 6 weeks of antibiotic treatment is advised.[15]

Non-surgical treatment modalities

These treatment modalities have all been shown to advance the healing of septic non-unions, but have limited clinical application.

Low intensity ultrasound

Ultrasound treatment is applied daily for 20 minutes. It works by stimulating the genes involved in inflammation and bone healing, as well as dilating the capillaries and enhancing angiogenesis, which increases local blood flow.[1]

Electrical and electromagnetic stimulation

This modality is indicated for hypertrophic non-unions with acceptable alignment. Contraindications include synovial pseudoarthrosis, fractures with malalignment and fracture gaps of more than half the shaft diameter. Different techniques are available such as a direct current through implanted electrodes, inductive coupling or pulsed electromagnetic fields through external coils and capacitive coupling through capacitive plates on either side of the non-union.[16]

The mainstay of treatment is mechanical combined with soft tissue repair and optimisation of functionality

Hyperbaric oxygen

One to two sessions of 1 to 2 hours a day with 100% oxygen at 2 to 3 atmospheres of pressure are advised. The beneficial effects are ascribed to the direct inhibition of anaerobic organisms, the increase in phagocytic killing by polymorphonuclear leukocytes, the augmentation of the effects of aminoglycosides, quinolones and sulfonamides, promotion of bone repair and the sustaining of soft tissue flaps.[1]

High energy extracorporeal shock waves

This is a non-invasive technique indicated for hypertrophic non-unions with a fracture gap of less than 5 mm. The mechanisms of advancing bone healing are through the creation of microfractures which stimulate neovascularisation and osteoblast formation, the increase in the inflammatory medium and growth factors and the increase in osteogenic differentiation of the mesenchymal cells.[1]

Summary

The mainstay of treatment is mechanical: an adequate debridement of bone and soft tissue together with stable fracture fixation; augmentation of bone healing with autogenous bone grafting, and further assistance with eradication of infection by appropriate antibiotic treatment. This must be combined with repair of the soft tissue and the optimisation of functionality.

No benefits of any form have been received from a commercial party related directly or indirectly to the subject of this article.
The content of this article is the sole work of the author.

References

1. Rodriques-Merchan EC, Forriol F. Nonunion: general principles and experimental data. *Clin Orthop* 2004;**419**:4-12.
2. Jain AK, Sinha S. Infected nonunions of the long bones. *Clin Orthop* 2005;**431**:57-65.
3. Babhulkar S, Pande K, Babhulkar S. Nonunions of the diaphysis of long bones. *Clin Orthop* 2005;**431**:50-6.
4. LaVelle DG. Delayed union and nonunion of fractures. In: S. Terry Canale (ed). *Campbell's Operative Orthopaedics vol 1. 11th Ed.* Mosby;2003:3125-3166.
5.. Dabov GB. Osteomyelitis. In: S. Terry Canale (ed). *Campbell's Operative Orthopaedics vol 1. 11th Ed.* Mosby;2003:662-85.
6. Motsitsi NS. Management of infected nonunions of long bones: The last decade (1996-2006). *Injury* 2008;**39(2)**:155-60.
7. Cleveland KB. General principals of infection. In: S. Terry Canale (ed). *Campbell's Operative Orthopaedics vol 1. 11th Ed.* Mosby;2003:643-60.
8. Cierny G. Infected tibial nonunions (1981-1995) The evolution of change. *Clin Orthop* 1999;**360**:97-105.
9. Thonse R, Conway J. Antibiotic cement-coated interlocking nail for the treatment of infected nonunions and segmental bone defects. *J Orthop Trauma.* 2007 Apr;**21(4)**:258-68.
10. Tetsworth K, Cierny G. Osteomyelitis debridement techniques. *Clin Orthop* 1999;**360**:87-96.
11. Rodriques-Merchan EC, Gomez-Castresana F. Internal fixation in nonunions. *Clin Orthop* 2004;**419**:13-20.
12. Patil S, Montgomery R. Management of complex tibial and femoral nonunion using the Ilizarov technique, and its cost implications. *J Bone Joint Surg (Br)* 2006;**88-B**:928-32.
13. Garcia-Cimbrelo E, Marti-Gonzales JC. Circular external fixation in tibial nonunions. *Clin Orthop* 2004;**419**:65-70.
14. Perry CR. Bone repair techniques, bone graft and bone graft substitutes. *Clin Orthop* 1999;**360**:71-86.
15. Mader JT, Shirtliff ME, *et al.* Antimicrobial treatment of Chronic Osteomyelitis. *Clin Orthop* 1999;**360**:47-65.
16. Aaron RK, Ciombor DM, Simon BJ. Treatment of nonunions with electric and electromagnetic fields. *Clin Orthop* 2004;**419**:21-9.