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Orthopaedic Tips: Nonunion

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Abstract

The term "nonunion" refers to a condition whereby bone fails to heal after fracture. The period that passes between the time of fracture and the determination that a nonunion has developed is highly variable, and may depend on several factors, including which bone is involved, any associated conditions (e.g., open fracture), and the type of treatment. This article provides a concise discussion of the basic science of fracture-healing and nonunion and of the workup and evaluation of nonunion, and a brief overview of the treatment of nonunion.

Welcome to Orthopaedic Tips, a recurring column that will discuss orthopaedic topics relevant to the practice of orthopaedic PAs. This section of JOPA will include technical tips, diagnostic dilemmas, or administrative issues faced by orthopaedic PAs. The senior author, John Riehl, MD, resides in Pensacola, Florida, and practices general orthopaedic surgery with an emphasis in orthopaedic trauma surgery. Dr. Riehl accepts applications from PA students who wish to perform visiting rotations with him.

Basic Science of Fracture-Healing and Nonunion

Normal bone-healing occurs by 1 of 2 mechanisms: primary bone-healing and secondary bone-healing. In primary bone-healing (also called direct bone-healing), the fracture site is healed by a process known as Haversian remodeling. In Haversian remodeling, osteoblasts bridge across a fracture gap behind osteoclasts ("cutting cones") that clear the way. Lamellar bone (organized bone) is formed in this process. This type of healing occurs when there is direct contact between the fractured bone ends. Rigid fixation and absolute stability are required for primary bone-healing. In this type of bone-healing, no callus is formed because of lack of micromotion. Primary bone-healing occurs with compression plating (e.g., when there is fracture of both bones in the forearm) and lag screw fixation (e.g., used in articular fixation of tibial plateau fractures).

In contrast, secondary bone-healing (also called indirect or endochondral bone-healing) occurs when small amounts of motion are present at the fracture site (relative stability). In secondary bone-healing, 4 stages that lead to healing transpire: hematoma, inflammation, repair, and remodeling. In the first stage, hematoma formation, the fracture gap fills with hematoma, which brings with it copious growth factors, osteoprogenitor cells, macrophages, platelets, etc. This process results in the release of inflammatory cytokines, which leads to the inflammatory stage and occurs within the first 1 to 2 weeks after fracture. During the inflammatory stage, swelling, warmth, and erythema at the fracture site are common and normal. The hematoma is gradually replaced by granulation tissue, and osteoclasts remove the necrotic bone ends. The reparative stage initially includes formation of a "soft callus," followed by formation of a "hard callus." Stem cells at the site of the fracture will be signaled to differentiate into osteoblasts,

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fibroblasts, and chondroblasts. Vascularity at the site is increased, and new blood vessels are formed through a process called neoangiogenesis. The thick cellular mass present at the fracture site begins to form a connection between the fractured bone ends. Bone growth begins at the periphery, and continues toward the center of the bone. Strain is lowest at the periphery. While strain is necessary to stimulate callus formation, too much strain will not allow bone formation to occur. As the callus forms at the periphery, it decreases the strain centrally, and additional mineralization occurs centrally. Mineralization leads to the formation of woven (immature) bone. This process takes place over the next 2 to 4 months in most instances. With the hard callus formed, the progression of healing continues with the remodeling stage. In the remodeling stage, lamellar bone replaces the woven bone over a period of months to years. Ultimately, the medullary canal is reconstituted through the remodeling process.

When the above processes fail to result in fracture-healing, a nonunion is said to have developed. A nonunion is present when a fracture lacks the potential to heal without additional intervention. Nonunion is often categorized into 1 of 3 types: atrophic, hypertrophic, and oligotrophic.

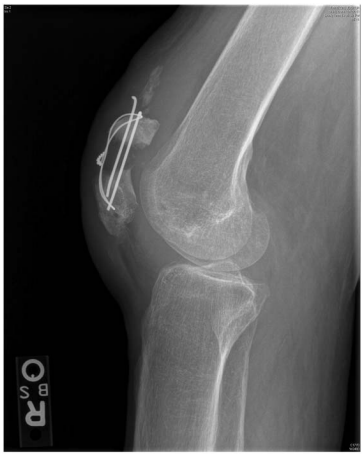

Fig. 1
Radiograph of a patellar fracture 6 months after open reduction and internal fixation showing hardware failure and atrophic nonunion.

The term atrophic nonunion refers to a failure of bone-healing where little or no callus has formed at the fracture site (Fig. 1). Atrophic nonunion is often a problem of biology, meaning that the necessary blood flow, cellular elements, or growth factors are not present to heal the fracture site. Soft-tissue damage from the injury coupled with excessive soft-tissue dissection and periosteal stripping around a fracture site can be cause for a decrease in vascularity. Certain medical conditions (peripheral vascular disease, endocrine disorders, etc.) and lifestyle choices (e.g., nicotine use) can lead to the development of atrophic nonunion. In cases where secondary healing through relative stability has been the goal, atrophic nonunion can be the result of providing too much stability (too stiff of a construct) without good osseous contact, thereby creating an environment with too little motion at the fracture site to stimulate callus formation.

Hypertrophic nonunion results from too much motion at a fracture site (Fig. 2). In hypertrophic nonunion, there is sufficient vascular supply to form bone, but the stability required to unite the fractured ends is lacking. Abundant callus is laid down, but due to excessively high levels of strain, the soft callus cannot be fully converted into hard callus. Despite large amounts of mineralization at the fracture site, gaps remain between the bone ends. These gaps are filled in with fibrous tissue. Hypertrophic nonunion is, therefore, primarily a problem of mechanical stability.

With oligotrophic nonunion, there is some callus present (unlike atrophic nonunion), but there is not an excessive amount of callus (unlike hypertrophic nonunion). Blood supply typically is not the causative factor in the development

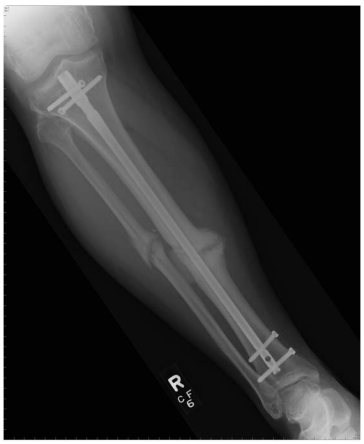

Fig. 2
Radiograph of a tibial shaft fracture 9 months after nailing showing hypertrophic nonunion.

of oligotrophic nonunion; it occurs from a fracture gap that is too large for bone to bridge across.

Nonunion can also occur as the result of infection, and when this is the case, it presents a complex clinical problem. Infection at the fracture site can disrupt the bone-healing process and lead to nonunion. Because of the formation of biofilm on inert orthopaedic implants, infection can be difficult to eradicate with hardware in place. The situation is further complicated by the condition that results from hardware removal as part of the treatment of infection. Bacteria survive better in an unstable environment, so eradication of infection is not as simple as just removing the hardware. Culture-directed treatment with intravenous antibiotics (or antifungals) often will be part of the plan of care. In many instances, antibiotic suppression and hardware retention until bone-healing has occurred will be an effective treatment strategy. Other options may exist in these complex cases, such as hardware removal and external fixation in combination with antibiotic treatment.

Evaluation

Nonunion is both a clinical and radiographic diagnosis. Many definitions of nonunion are present in

the literature and, as stated above, depending on the fracture location, any associated conditions, and the treatment type, the time after injury when the term "nonunion" is applied to an unhealed fracture can be highly variable. Throughout the orthopaedic literature, radiographic nonunion is often described for research purposes as failure to obtain osseous union at 3 of 4 cortices of the fracture site on anteroposterior and lateral radiographs. When primary bone-healing is the goal and absolute stability has been employed, the presence of a visible fracture line will indicate that union has not occurred. Failure of any progressive bone formation on radiographs taken at least 1 month apart may be an indication that a nonunion is developing. Additionally, broken hardware and sclerotic fracture edges can be radiographic signs of nonunion. Clinically, nonunion can be signaled by continued pain and motion at the fracture site after a period in which healing is expected for that particular fracture pattern and location.

When a fracture has been diagnosed as a nonunion, certain clinical, laboratory, and radiographic evaluations may be helpful (Table I). To begin with, a thorough history should be obtained if not already known. The history should include the age of the patient, when the injury occurred, what the injury mechanism was, whether it was an open or closed injury, and any history of infection. Any previous surgeries at the nonunion site should be documented, including the approximate date of surgery, the type of surgery performed, and what implants were used (including manufacturer names). The patient's ambulatory status should be known, as well as the patient's goals for ambulation and activity. The presence or absence of pain and any medications used because of the nonunion also should be documented.

Additionally, the medical and social history can play a role in the development of nonunion. The clinician should inquire about any comorbid medical conditions, especially diabetes, peripheral vascular disease, and chronic kidney disease, among others. Medication use, excessive alcohol or nicotine use, malnutrition, and previous radiation

TABLE I Evaluation of Nonunion*

History	Medical/social history
Previous surgeries (date, type, implants, etc.)	Diabetes
Injury characteristics (open injury, initial mechanism, history of infection)	Peripheral vascular disease
Ambulatory status (how far can patient walk, limp, ambulatory aid)	Metabolic disease
Painful/nonpainful, aggravating/alleviating factors, associated symptoms	Other medical problems
Pain medications for nonunion	Previous radiation
	Medications
	Alcohol use
	Nicotine use
	Drug use
Physical examination	Radiographic evaluation
Open wounds, drainage, prior surgical scars (location, size), appearance otherwise (erythema, swelling, etc.), range of motion of adjacent joints, pain location, motion at fracture site, sensory examination, motor examination, vascular examination, leg-length discrepancy	Anteroposterior and lateral views
	Oblique views and/or CT scan
	Look for any technical error in treatment; if a technical error is found, then correct the error; if no technical error can be found, consider endocrine referral
Laboratory tests for endocrine abnormality	Laboratory tests for infection
Vitamin D 25(OH)$_2$	ESRCRP
Vitamin D 1,25(OH)$_2$	WBC with differential
24-hour urine calcium	Aspiration/biopsy
TSH	Other laboratory tests
Free T3	Nicotine
Free T4	Albumin and prealbumin
Testosterone/estrogen	
FSH	
LH	
Alkaline phosphatase	
Parathyroid hormone	
Growth hormone	
Hgb A1C	

*CT = computed tomography, TSH = thyroid-stimulating hormone, FSH = follicle-stimulating hormone, LH = luteinizing hormone, Hgb = hemoglobin, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein, and WBC = white blood cell.

treatment all can contribute to nonunion.

The physical examination should include descriptive features of the nonunion site and any existent open wounds, drainage, prior surgical scars (location and size), or any other changes to the appearance of the area. Range of motion of adjacent joints, motion or pain at the fracture site, and a complete neurovascular examination also can be obtained.

The radiographic examination will consist of anteroposterior and lateral views of the area. Oblique views also may be of benefit. If the question of osseous union remains unclear on radiographs, computed tomography (CT) may offer more detail of the osseous structure at the fracture site. When evaluating the radiographs, it is important to determine whether the implant is meant to provide absolute stability (primary bone-healing) or relative stability (secondary bone-healing). Has a technical error been performed in the stabilization method that has been chosen? Is broken hardware present? The type of implant that is present and what instruments are needed for removal of any remaining implants are imperative pieces of information for preoperative planning.

Finally, laboratory tests may be indicated as part of the assessment of nonunion. See Table I for a list of laboratory tests that can be ordered to evaluate for possible contributing factors to nonunion.

Treatment

Treatment of nonunion depends largely on the causative factors that have been identified in the evaluation. Correcting problems that may have led to the nonunion should be a central part of the treatment strategy. Any known endocrine abnormalities should be corrected. In some instances, correction of endocrine pathology alone can lead to fracture union. The patient should strongly be urged to discontinue any nicotine use immediately. Proper nutrition, including adequate protein intake, will aid in fracture-healing. If an infection is present, debridement, with or without exchanging the hardware, and antibiotic bead placement may be necessary. In general, providing a stable fracture site is an important part of eradicating the infection.

When an atrophic nonunion has developed, as stated above, there is often a deficiency in the biologic environment surrounding the fracture. Therefore, treatment will often consist of bringing the biologic factors that are needed for healing to the area. Bone-grafting is 1 way in which to improve the local healing environment. The ideal graft material for healing a nonunion has both osteoconductive (providing a scaffold for new bone growth) and osteoinductive (stimulating bone growth) capacity. Autograft is an ideal material for use in atrophic nonunion because it contains both elements. Autograft can be taken from several sources. The location from which autograft is obtained often is dependent on the volume of graft that is needed and the location of the nonunion. The iliac crest is a common site for autograft harvest. The proximal tibial metaphysis and the medullary canal of long bones are other common sites for obtaining autograft. The major downside of using autograft is possible donor-site morbidity, including pain and fracture. Other materials (allograft, bone morphogenetic protein [BMP], stem cells, etc.) may play a role in the treatment of atrophic nonunion. In addition to adding to the biologic environment, debridement of fibrous tissue and avascular bone at the nonunion site often is necessary to stimulate healing.

In the case of hypertrophic nonunion, the underlying problem is too much motion at the fracture site. This can be remedied by adding more stability. Depending on the fracture type and location, this may be solved by exchange nailing, compression plating, or external fixation with compression. For example, 1 treatment option for a hypertrophic femoral shaft nonunion where an intramedullary nail has been placed would be to remove the nail, ream the canal, and increase the size of the nail. When compression plating is chosen as treatment, a tensioning device can be helpful to obtain the desired amount of compression. Mechanical stability also can be improved by increasing the size of the plate used or the number and position of the screws. External fixation can create a tremendous amount of compression at the fracture site, which can be recompressed, even after surgery, if necessary.

Additional techniques that have not yet been discussed can be employed in some cases to achieve osseous union. In some instances, injection of concentrated bone marrow aspirate at the nonunion site can lead to bone-healing. External devices aimed at stimulating bone growth also can be used and have shown clinical success. These devices can work by a variety of different mechanisms; they need to be worn by the patient for varying amounts of time in order to provide the desired effect.

When the evaluation of nonunion does not produce a probable reason for the nonunion to have developed, we recommend referral to an endocrinologist for workup and correction of any endocrine abnormalities that may have contributed to the formation of the nonunion. Additionally, when there is failure to heal at a fracture site where nonunion is particularly rare (e.g., the pubic ramus, the sacral ala, the proximal aspect of the humerus) and the treatment has been nonoperative, endocrine referral may be appropriate.

Summary

A fracture nonunion presents a complicated clinical problem that requires complex treatments to achieve union. An essential component for successful treatment occurs during the evaluation and

planning stage, where every effort is made to determine any underlying causes of the nonunion.

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Suggested Reading List

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