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ID TEACHING CASES

Infected Nonunion of the Tibia Due to *Paenibacillus turicensis* in a Healthy Young Adult After an All-Terrain Vehicle Accident

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We present the case of a 19-year-old man with an open fracture of the tibia and fibula secondary to an accident with an all-terrain vehicle. He underwent operative excisional irrigation, debridement, and fixation on the day of injury. His course was complicated by nonunion of the tibia fracture. Infection is a common factor in fracture nonunion, even in patients who receive appropriate surgical and antimicrobial management. *Paenibacillus turicensis*, an organism adapted to survive in the environment via spore formation, was responsible for nonunion in our patient. A brief discussion of this unusual organism, fracture nonunion, and the role of infection in etiology of nonunion follows.

Keywords. fracture nonunion; musculoskeletal infection; spore formation.

CASE REPORT

A healthy 19-year-old male, nonsmoker, sustained an open fracture of his left tibia and fibula while attempting a jump with an all-terrain vehicle. A 16-cm open wound over the anterior shin was noted with bone extruding through the soft tissue defect (Figure 1). There was no pulsatile bleeding and only minimal contamination was described. X-ray showed mildly comminuted distal tibial and fibular diaphyseal fractures with soft tissue air indicating an open fracture (Figure 2). The remainder of the trauma evaluation was negative. He received a tetanus immunization, followed by vancomycin and ceftriaxone for antimicrobial prophylaxis for open fracture.

Operative findings included extensive periosteal stripping of the tibia extending 8 cm proximal to the fracture site. Adjacent to the soft tissue stripping he had a large, devitalized bone fragment that was resected. All necrotic tissue and debris were removed and the wound underwent copious irrigation. Open reduction internal fixation with an intramedullary nail of the tibia and plate and screw fixation of the fibula was performed. He also underwent a lateral compartment fasciotomy. Postoperatively he received cefepime instead of ceftriaxone; vancomycin was continued. His 25-OH vitamin D was low at 19 ng/mL and was supplemented.

He had fever and mild leukocytosis in the postoperative period, which resolved quickly. Oral cephalexin 500 mg 3 times daily and trimethoprim-sulfamethoxazole double strength twice daily for 7 days were prescribed at discharge.

Follow up at 3 weeks' showed well healed incisions and stable hardware. At 2 months after injury, the patient had no pain in the left leg and no limitation in level of activity. Radiographs at the visit demonstrated healing of the fibula but no substantial healing of tibia fracture.

At approximately 6 months postinjury, the patient reported the onset of stabbing pain in the left lower extremity that radiated to the knee. Radiographs continued to demonstrate persistent radiolucency of the distal tibia fracture concerning for developing nonunion (Figure 3). He was otherwise clinically well without fever or signs of systemic illness. Laboratory tests including complete blood count, erythrocyte sedimentation rate (ESR), C-reactive (CRP) protein, and 25-OH vitamin D level were found to be within normal limits. With symptoms of pain and radiographic nonunion, the patient agreed to additional surgery.

At revision surgery, a dense fibrous atrophic nonunion was found as well as a necrotic piece of bone along the distal tibia. There were no obvious signs of infection. Previous hardware was removed. The nonunion was resected and deep tissue and fluid samples were obtained and sent for aerobic, anaerobic, fungal, and acid-fast bacillus culture. The distal medial aspect

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Figure 1. Original injury.

of the tibia had been stripped of periosteum, was described as dense, and did not bleed. Bone from the proximal tibia was harvested for autograft. The autograft and cancellous allograft chips were both mixed with vancomycin powder. A new tibial nail was placed and after irrigation, the previously obtained bone graft was impaction bone grafted into the nonunion site. He received 24 hours of perioperative cefazolin but was discharged on no additional antibiotics.

Multiple cultures of the nonunion site returned positive for Gram-positive bacilli on the third day of incubation. Matrix-assisted laser desorption time-of-flight mass spectrometry was used to make the identification of *Paenbacillus turicensis*.

In spite of aggressive initial operative debridement and appropriate antibiotics, eventual sporulation of *P turicensis*, in the presence of residual avascular bone, lead to an infected nonunion. Antimicrobial susceptibility testing demonstrated sensitivity to penicillin, ciprofloxacin, vancomycin, and tetracycline. With the revision surgery, the patient had resection of bone back to bleeding surfaces and bone autograft mixed with vancomycin powder at the site of nonunion. He has been treated with a 6-week course of oral ciprofloxacin. He has been observed regularly in our multidisciplinary orthopedic infectious disease clinic with follow-up radiographs that demonstrate callus formation consistent with early fracture healing (Figure 4).

Figure 2. Anterior-posterior radiograph of distal tibia shows comminuted and displaced distal tibia and fibular diaphysis fractures. Note the soft tissue air (arrow) indicating an open fracture.

Patient Consent Statement

The patient was informed that data concerning the case would be submitted for publication and he provided consent. The patient provided the photograph of his injury.

DISCUSSION

The genus *Paenibacillus* is a group of facultative anaerobic Gram-positive, rod-shaped bacteria widely distributed in nature. The majority of the members of the genus are found in soil, and they are associated with the roots of plants [1]. *Paenibacillus* can produce compounds that are beneficial in both agriculture and medicine [1]. Antimicrobial peptides manufactured by this species include the cyclic cationic lipopeptides or polymixins, including colistin. In humans, these bacteria may cause incidental infection after ingestion, injection, injury, inhalation, or other contact with material contaminated with vegetative cells

Figure 3. Anterior-posterior radiograph 7 months after open reduction and internal fixation shows intramedullary nail fixation of the tibial fracture that has not healed. Note the smooth, sclerotic margins of the tibial fracture without bridging callus.

or their spores [2]. *Paenibacillus* species are an unusual cause of orthopedic infection. *Paenibacillus turicensis* was first reported after isolation in the setting of a fracture nonunion of the tibia and fibula due to a motorbike accident [3]. Two other cases of musculoskeletal infection due to *Paenibacillus* species are reported: pyogenic tenosynovitis of the hand [4], and a cellulitis of the knee [5]. *Paenibacillus macerans* was found as the cause of a recurrent soft tissue infection of the thigh, from a large stick penetrating the limb many years prior [6]. The original injury had healed without operative intervention. The authors proposed recurrent infection resulted from transition of *Paenibacillus* spores to vegetative cells due to inoculation at time of remote injury.

In our case, *P turicensis* was isolated in the setting of nonunion of an open fracture that occurred due to high speed trauma. Infection as an etiology for nonunion is common. In a prospective cohort study performed in Canadian trauma centers, Westgeest et al [7] found deep infection to be significantly associated with the development of nonunion, with an odds ratio of 12.75.

Nonunion of the tibia is also common (estimated range from 2% to 10%) compared with other long bone fractures [8]. The term nonunion is applied to a fracture that will not unite without additional intervention. For the tibia, this time period is approximately 6 to 9 months. Nonunion risk is associated with the severity of injury, including open fractures with substantial soft tissue damage, those with comminution, or due to a high-energy mechanism (automobile or motorcycle accidents). Patient factors that may contribute to nonunion include cigarette smoking, diabetes mellitus, renal failure, and peripheral vascular disease.

Fracture union is dependent on the biologic environment and the mechanical properties of the fracture. Nonunion may first be suggested by radiographic findings, as in our patient who was initially asymptomatic. Radiographically, union can be suggested by the presence of bridging callus at 3 of 4 cortices on anterior-posterior and lateral views [10]. Nonunion can be classified into 2 major types: hypertrophic and atrophic. On imaging, hypertrophic nonunion typically presents as exuberant callus formation at the fracture margins without osseous bridging. This type of nonunion often results from inadequate immobilization of the fracture. Atrophic nonunion is caused by not only inadequate immobilization, but also poor blood supply to the fracture or a biologic inability for bone to form/remodel. On radiographs it presents with the absence of callus and remodeled bone ends with tapered, smooth, sclerotic margins. Active infection may be radiographically occult or present with concomitant periosteal reaction, regional osteopenia, and soft tissue swelling [11]. Chronic osteomyelitis typically appears as inhomogeneous osteosclerosis sometimes accompanied by sequestrum formation (necrotic bone acting as a nidus) with an associated draining sinus, or cloaca, and surrounding thick involucrum (reactive new bone formation) [12]. Computed tomography scan can be helpful to estimate the percentage of cross-sectional area of bone bridging and potentially guide surgical planning when radiographs are inconclusive [9]. Labeled leukocyte (tagged white blood cell [WBC]) studies can lead to false-positive diagnosis in uninfected fractures due to the presence of hematopoietically active marrow, which is part of the reparative process. The specificity can be increased when combine with labeled sulfur colloid bone marrow imaging [13].

Identifying infection as the cause of nonunion can be a diagnostic challenge. The patient, may have no systemic signs of illness and exam findings may be subtle. Patients with nonunion may report an inability to bear weight, have pain at the fracture site, and exhibit tenderness on palpation [9]. Recognizing these difficulties and a lack of uniformity in the diagnosis of fracture-related infection, a consensus definition has been published identifying confirmatory and suggestive criteria [14]. Confirmatory criteria include fistula, sinus, or wound breakdown; presence of purulence from the wound or at

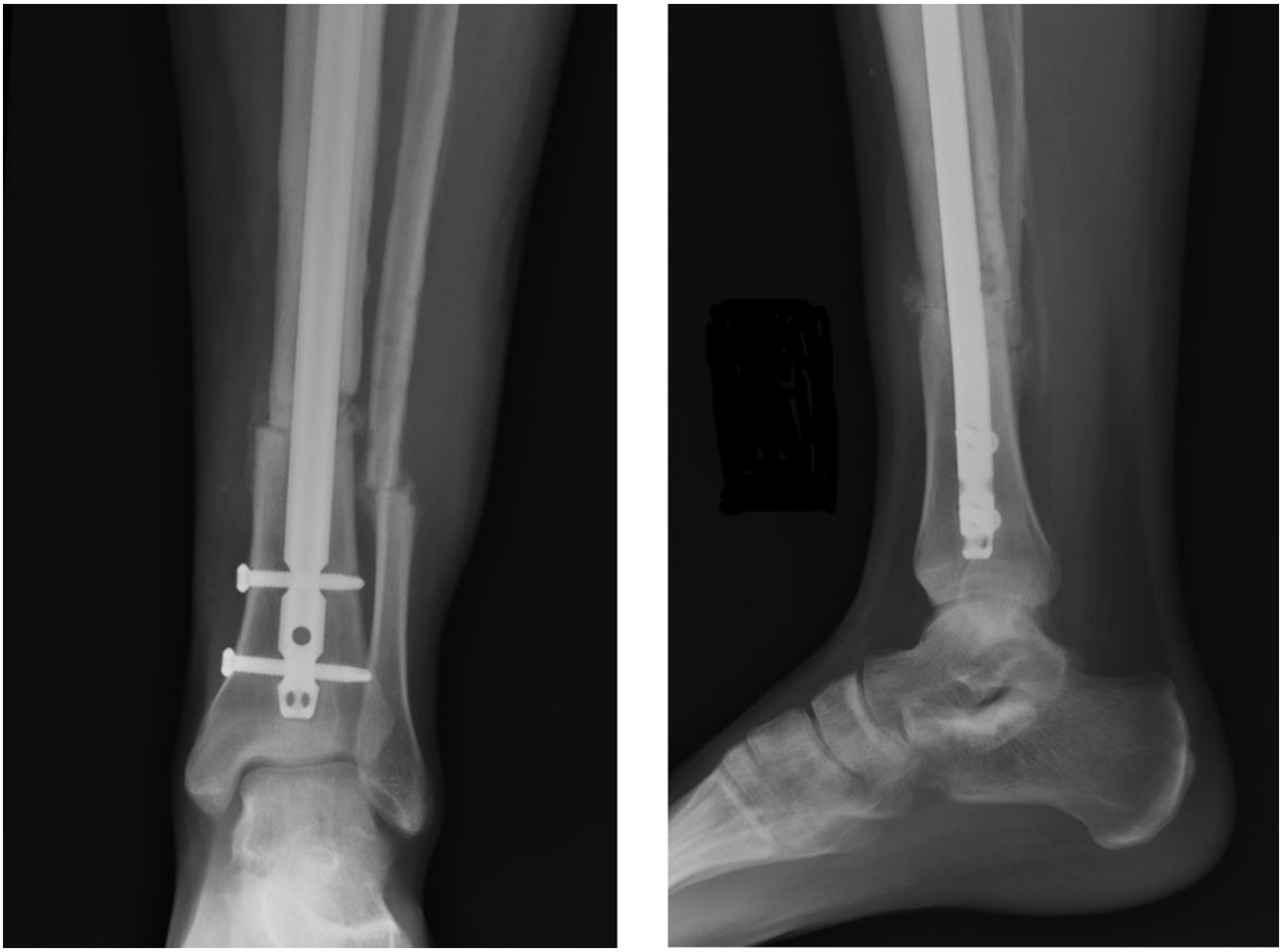

Figure 4. Anterior-posterior and lateral radiographs demonstrating callus formation of tibia after revision surgery.

time of surgery; at least 2 positive intraoperative specimens with the same organism; or microorganisms identified on histopathologic stain of deep tissue. Routinely used serum inflammatory markers including WBC count, ESR, and CRP are categorized as only suggestive criteria for definition of a fracture-related infection [14]. Support for placing inflammatory markers in the category as only suggestive for infection is found in a more recent paper by Brinker et al [15]. They examined 211 consecutive nonunions and found inflammatory biomarkers to be poor predictors for the diagnosis of infection [15]. The positive predictive value of WBC, ESR, and CRP in diagnosing infection as the cause of nonunion in their study was 0.20, 0.29 and 0.33, respectively [15].

Culture of microorganisms obtained from the site of nonunion remain the gold standard for diagnosis and are required to select effective antimicrobial treatment. If possible, all preoperative antibiotics should be held for 2 weeks before obtaining new cultures [16]. Multiple samples should be collected from the bone-implant interface, and cultures of deep tissue are preferred to swabs of the area [16].

However, antibiotics are an adjunct to the definitive orthopedic management of an infected nonunion. Bone must be debrided until bleeding viable tissue is present at the resection margins [17]. All nonviable tissue and infected implants are resected to limit substrate for the formation of microbial biofilm [17].

Initial treatment of the fracture may require placement of an external fixator frame. Antimicrobial impregnated devices can be placed temporarily within the surgical site in the form of beads, coated nails, or cement blocks [18]. Surgical care for the fracture and any associated soft tissue injury continues in stages, after systemic treatment with antibiotics, and exchange and removal of any temporary fixation devices. Nonabsorbable antibiotic delivery systems may behave as a foreign body after elution of the antibiotic is complete and are usually removed [17]. Final orthopedic management may include repeat internal fixation, bone grafting, or bone transport [18].

CONCLUSIONS

In the setting of fracture nonunion, infection should always be considered as a potential etiology, particularly when the initial injury was an open fracture. In the absence of obvious clinical signs such as pyrexia, erythema, and wound drainage, patients may present with pain and tenderness at the fracture site and pain with weight bearing. Inflammatory markers are poor predictors of infected nonunion, but diagnosis is suggested radiographically by minimal bridging callus at the fracture site. Culture data are needed for an accurate microbiologic diagnosis. Successful management of infected nonunion requires a multidisciplinary approach with correction of inhibitors to fracture healing (smoking cessation, glucose control), systemic therapies (targeted antibiotics and vitamin D replacement), and local surgical intervention (removal of infected hardware, bone and soft tissue), followed by definitive fixation to ensure fracture healing and eradication of infection.

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