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Tissue Guided Regeneration with Platelet Rich Plasma and Resorptive Collagen Membrane in Case of Chronic Osteomyelitis of Tibia

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Abstract

Background: Chronic osteomyelitis is a serious and difficult complication in open fractures, occurring in about 20% of cases. Treatment approach must be multidisciplinary with surgical basis. At the end of the classical eradication of the infection, there is often a large bone defect. Guided tissue regeneration (GTR) with allogeneic platelet gel, autologous cancellous bone graft and resorptive collagen membrane is one of the possibilities how to bridge bone defect.

Patients: 26 year old male patient, suffered from chronic osteomyelitis. The therapy for osteomyelitis was started and after two months osteomyelitis was healed, soft tissue defect was grafted with surralis flap. GTR with allogeneic platelet gel and autologous cancellous bone graft and resorptive collagen membrane was performed to fill the defect.

Results: The essential idea of this therapy was to combine the healing capacities of platelet-derived growth factors and osteogenic stem cells and the modeling capacity of the platelet gel. After 4 months of GTR therapy the graft was incorporated, the bone defect was fully bridged and full weight-bearing capacity was achieved. Using resorptive collagen membrane, healing capacities of tissue increased.

Conclusions: The aim of our treatment approach, with GTR by allogeneic platelet gel, autologous and bone graft combined with collagen resorptive membrane can improve and shorten the treatment outcome.

Keywords: Tissue guided regeneration; Allogeneic platelet gel; Autologous cancellous bone graft; Resorptive collagen membrane; Osteomyelitis

Introduction

Multidisciplinary treatment approach to osteomyelitis and wound infection after open bone fracture

Bone infection, osteomyelitis, in the area of the fracture is one of the most serious complications that need long and demanding therapy. Untreated or inappropriately treated can lead to amputation. It occurs in about 2% of closed fractures postoperatively and even in a higher - 20% of open fractures.

Every operative treatment of bone fractures is accompanied with the possibility of infection of the operative wounds. In a healthy organism, tissue is well perfused and can handle the initial infection, while in open fractures; wounds are contaminated, accompanied by damage to the soft tissue. In case of bone damage, necrosis may occur. Similarly, it may also occur in case of closed fractures. Infection may occur hematogenously, with spread of infection from septic foci, often being polymicrobial, most commonly caused by *Staphylococcus aureus*, *Pseudomonas aeruginosa* or Enterobacteriae [1,2]

Chronic osteomyelitis is the most often complication of open fractures that has disturbance of cortical blood supply due to injury and is contaminated. Therefore it represents the origin of infection. It is diagnosed by a positive microbiological test result and by clinical picture of a fistula with leakage of pus for more than 6 weeks, with no systemic symptoms and minor local symptoms. Diagnostic procedures are microbiological test results, histology, bone biopsy, X-ray, scintigraphy, fistulography, ultrasound, magnetic resonance imaging [1]

Its treatment is still difficult and no evidence-based guidelines exist. First line treatment is with antibiotics, based on antibiogram of the isolated pathogenic bacteria. Therefore surgery plays a major role in the treatment process. There are many novelties being used in surgical treatment, such as musculoskeletal tumour surgery, intramuscular flap and GTR [1,3,4]. The treatment approach must be multidisciplinary with surgical basis [4,5].

Classic osteomyelitis treatment is basically surgical with radical necrectomy of the bone and soft tissue sequestrectomy, followed by filling the dead space, introduction of local and systemic antibiotic therapy and stabilization of the fracture and/or bone defect with an external fixator. An advantage of external fixation with or without the Ilizarov technique is making the contact between the bone fragments without intervention into the infected area and minimal impairment of soft tissue. Necrectomy has decisive influence on the outcome of the treatment, as it allows removal of hematoma, damaged tissue, sequesters and foreign bodies, which are a potential source of

infection. At the next step, when infection is eradicated and fracture is healed, deficit of both soft tissue and bone becomes a major problem. Deficit of soft tissues is often solved by methods of reconstructive surgery (flap) and filling of large bone defect using spongioplastics, drainage or antibiotic beads. Another possible way of reconstructing the bone deficit is using GTR which uses the allogeneic platelet gel, autologous cancellous bone graft and resorptive collagen membrane, the basic idea of which is to heal the tissue with potential growth factors derived from platelets and osteogenic progenitor cells [3,4,6-8].

This method is combined by adding the patient's own bone or alternative heterologous osteoinert, osteoinductive or osteoconductive materials, the best being the one containing all the elements necessary for successful healing; osteogenic potential of the cells' signalling molecules and osteoconductive bone matrix, which is found in one's own bone graft. Heterologous materials are most often only bioconductive or inert and accelerate bone formation. GTR was first described in 1959 and first developed by Melcher in 1976, who found the need to exclude unwanted ingrowth of cells at the site of bone defects, thereby allowing the growth of the desired tissue – in the case of bone surgery, this means the bone [4,9]. In 1982 GTR was first used in periodontal surgery [4].

Principles of Tissue Guided Regeneration and its use in Surgery

The basic principle of GTR is based on the fact that the different cellular components in the tissues have different speeds of migration or ingrowth in the wound or in case of bone surgery, the bone defect during the healing process. With a mechanical barrier, in this case collagen resorbable membrane, we prevent fibroblasts and other soft tissue cells to prematurely in grow into the bone defect area, since it is known that cells with osteogenic potential migrate more slowly [10]. Allogeneic platelet gel, which represents a source of growth factor, was proven to be just as efficient and safe to use as autologous for the regeneration of defects of long bones [8,11]. Autologous bone graft is being used as a gold standard of GTR, with disadvantage that patient has to undergo additional operations and having risk for all the accompanied complications.1 Therefore alternative graft materials are being investigated. Materials that are in use are heterologous, xenografts, autologous and allogeneic [3,4,12]. Which type of graft we decide to use depends on the reason for its use, therefore clinical picture, age and mobility of the patient [13]. Out of heterologous material, the most investigated is bovine, but also porcine bone grafts are in use. The aim of tissue engineering is to provide better materials and its efficiency with less side effects [14,15]

The essential idea of this therapy was to combine the healing capacities of platelet-derived growth factors and osteogenic stem cells and the modeling capacity of the gel [3,6,10,14]

Patient and Method

Chronic osteomyelitis after open fracture of distal cruris

26 year old male, sustained high energy open fracture of distal cruris with steel wire (Figure 1). He was urgently operated – necrectomy of bone and soft tissue, revision of wound and external fixation was performed (Figure 2A). After 2 weeks when there was no clinical or laboratory signs of infection, the conversion of external fixator to tibial nail was performed (Figure 2B). Skin defect was covered with Tiersch transplant. Four months later he was admitted back to the hospital with clinical signs of infection; fever, high temperature and erythema in the area of Tiersch. Osteomyelitis was diagnosed.

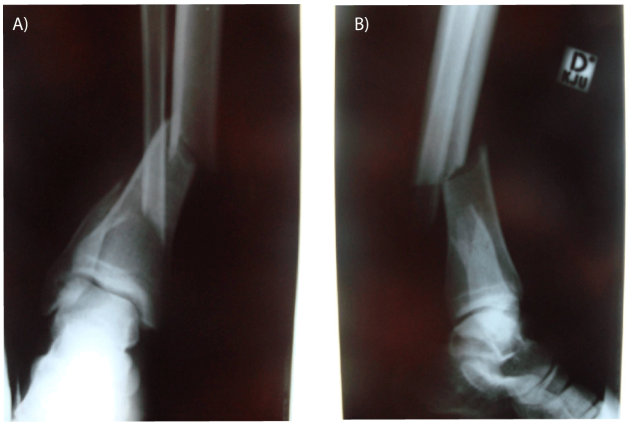

Figure 1: Fracture of right distal cruris.

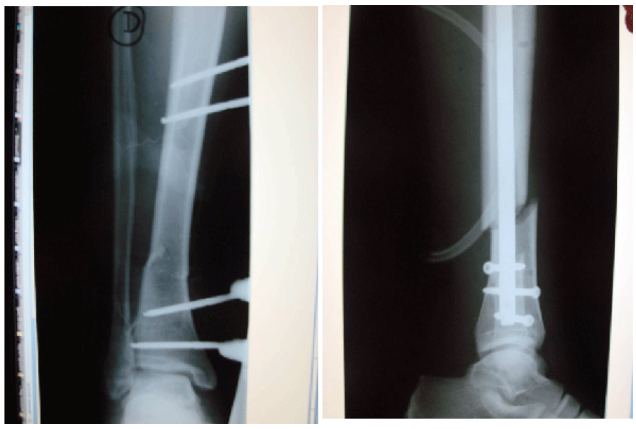

Figure 2: Stabilization of the fracture with external fixator immediately after injury (A). Removal of the external fixation and osteosynthesis of the tibia with intramedullary nail (B).

In the process of therapy all known methods were used. Primary treatment was surgical. Intramedullary nail was replaced with external fixator, radical necrectomy of bone and soft tissue was performed, negative pressure suction was changed every three days. Tissue was taken and sent to microbiology and histology. Staphylococcus Aureus resistant to penicillin was isolated, and according to anti-biogram therapy with Vancomycin was started intravenously for six weeks, following by per os Trimethoprim-sulfamethoxazole antibiotic for further four weeks.

In two months of intensive treatment, chronic osteomyelitis was healed and soft tissue defect was grafted with surralis flap (Figure 3). One month later we performed spongioplasty, we used GTR with allogeneic platelet gel, autologous cancellous bone graft and resorptive collagen membrane (Figure 4). The allogeneic platelet gel was ABO- and RhD-matched, leukocyte-depleted and irradiated.

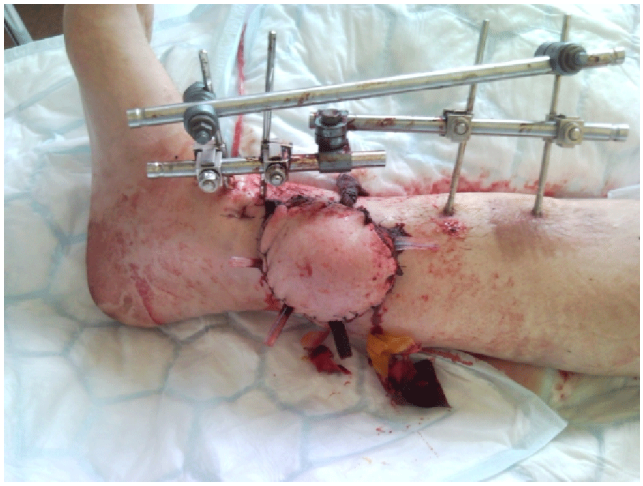

Figure 3: Soft tissue defect covered by the Surralis flap, bone defect of the tibia was stabilized with external fixator.

A few days after the procedure, the patient was released to home care, with external fixator and instructions for appropriate care of the fixator. Because of better control of the patient's treatment, he was commissioned for check-ups once a week. He was monitored by having regular X-rays, to detect progress of overgrowth of the bone defect. After 8 weeks, when X-ray detected that overgrowth of the bone defect was in progress, the patient was advised that he can lay the operated leg on the ground.

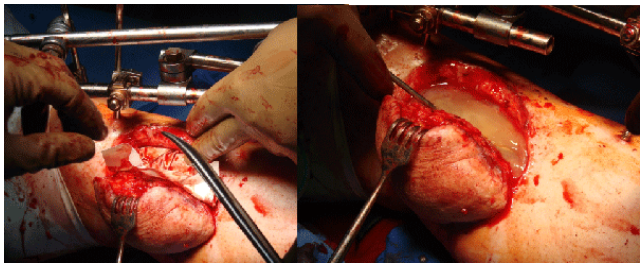

Figure 4: Guided Tissue Regeneration, resorptive collagen membrane (A) and allogeneic platelet gel (B).

Fourteen weeks later, the graft was fully incorporated, external fixator was removed, the bone defect was fully bridged and full weight-bearing capacity was achieved at week. During the treatment patient had no side effects. Because of the non-union of the fibula four months later he was operated and corrective osteotomy and osteosynthesis of the fibula was performed. After three and a half years of follow up patient is without pain, able to deal with daily and sport activities, without symptoms of infection recurrence (Figure 5).

Figure 5: X-ray of the cruris after the end of the therapy.

Discussion

Guided tissue regeneration is well known in oral surgery and is making an entry into orthopaedic trauma surgery [3-5,11]. In bone surgery pseudarthrosis and unhealed fractures after osteosynthesis represent a major problem that requires re-surgery. In re-osteosynthesis usually an approach called spongioplasty is used. This additional invasive procedure to get a patient's own spongiosa is associated with pain, longer hospitalization and rehabilitation time with increased possibility of infection in this region [3,15]. Therefore new methods, that are patient friendly are being studied. The use of autologous cancellous bone for the treatment of the pseudarthrosis of long bone fractures, together with allogeneic platelets has already been described [3,11]. An addition in our case was the use of heterologous resorbable collagen membrane. It has osteoconductive features, meaning it resorbs with time, made of high consistency dense collagen fibers, with the advantage that it can be shaped into the desired size. It represents a mechanical and biological barrier, which protects the graft and provides better healing. In time, collagen membrane is replaced by new tissue and bone, that it stimulates to produce [3,11,16] Best graft to use must be osteogenic, osteoinductive and osteoconductive [13].

This case report indicates that the clinical use of GTR with the platelet gel and spongioplasty with resorbable collagen membrane, that represents a mechanical and biological barrier, may be used in a patient with extensive bone defect after chronic osteomyelitis. The purpose of resorbable collagen membrane is to prevent premature ingrowth of soft tissue cells into bone defect area and consequently osteoblasts, which need more time to migrate, to do their work and grow over the defect.

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