Plasma Rich in Growth Factors to Treat an Articular Cartilage Avulsion: A Case Report

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ABSTRACT

SÁNCHEZ, M., J. AZOFRA, E. ANITUA, I. ANDÍA, S. PADILLA, J. SANTISTEBAN, and I. MUJIKA. Plasma Rich in Growth Factors to Treat an Articular Cartilage Avulsion: A Case Report. *Med. Sci. Sports Exerc.*, Vol. 35, No. 10, pp. 1648–1652, 2003. **Introduction:** The application of an autologous plasma rich in growth factors is beneficial in restoring connective tissues, as shown by clinical evidence in oral surgery and more recently in arthroscopic anterior cruciate ligament reconstruction and two cases of ruptured Achilles tendon in professional athletes. This is attributed to the slow delivery of growth factors from harvested platelets that have been activated by endogenous thrombin promoted by the addition of calcium chloride. **Purpose:** This case report describes a new application of this therapy in the arthroscopic treatment of a large, nontraumatic avulsion of articular cartilage in the knee of an adolescent soccer player. **Methods:** After arthroscopic reattachment of the large (>2 cm) loose chondral body in its crater in the medial femoral condyle, autologous plasma rich in growth factors was injected into the area between the crater and the fixed fragment. **Results and Conclusion:** Despite the extremely poor prognosis of the case, complete articular cartilage healing was considerably accelerated, and the functional outcome was excellent, allowing a rapid resumption of symptom-free athletic activity. This technique opens new perspectives for human tissue regeneration. **Key Words:** PRGF, KNEE ARTHROSCOPY, TISSUE REGENERATION, FUNCTIONAL RECOVERY

Avulsions of articular cartilage are not uncommon among athletically active children and adolescents. As in cases of osteochondritis dissecans, the medial femoral condyle of the knee joint is the most commonly affected area, and although the etiology of this condition remains speculative, repetitive microtrauma is considered to be associated with it (1,12,22,25). Patients with open distal femoral physis usually have a more favorable prognosis for healing with nonoperative treatment, but not all lesions in the skeletally immature patient heal without operative intervention, and surgical treatment is indicated for detached lesions (2,8,12,20,27). Given its lack of blood supply, lymphatic drainage, or neural elements, articular cartilage possesses a limited capability to regenerate after significant mechanical destruction of the cells and collagen scaffold (6,7,18). Recent reports in animal models suggest that the process of cartilage healing *in vivo* may be improved by growth factors, which are small proteins synthesized both by local cells at the injury site and by infiltrated blood-borne inflammatory cells. These factors stimulate cell proliferation, migration, differentiation, and matrix synthesis and can affect chondrocyte metabolism, chondrogenesis, and improve cartilage healing *in vivo* (7,9,10,14,17,18,26).

Growth factors could therefore be considered suitable tools to enhance cartilage repair. However, the most appropriate way to use these growth factors is not known. Our work is based on the use of an autologous plasma rich in growth factors (PRGF) obtained from the patient's own blood by means of a simple procedure. Our hypothesis is that the presence of PRGF in the surgical site accelerates the regeneration of local tissues by a mechanism that reproduces the initial physiological steps of tissue repair: upon activation, platelets aggregate producing a clot, and secrete a variety of cytokines, including adhesive proteins and growth factors such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), insulin-like growth factor I (IGF-I), and epidermal growth factor (EGF). These substances act on local cells inducing specific responses.

Until now, autologous PRGF has been shown to enhance and accelerate soft tissue repair and bone regeneration in the preparation of future sites for dental implants (3,4), and to enhance postsurgery healing and remodeling of anterior cruciate ligament grafts (23) and ruptured Achilles tendons in professional athletes (unpublished observations). These successful clinical results, along with the above-mentioned observations from animal models, provided a rationale for the application of PRGF in a case of arthroscopically treated

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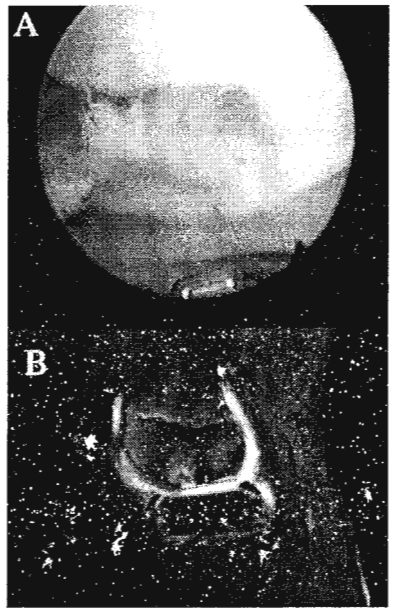

FIGURE 1—(A) Arthroscopic image of the crater lesion in the medial femoral condyle; (B) MRI scan showing the chondral lesion, which did not extend into the subchondral area.

avulsion of articular cartilage in the knee joint, in an attempt to accelerate articular cartilage healing and complete functional recovery.

The purpose of this report was to describe a novel application of autologous PRGF in the arthroscopic treatment of a large, nontraumatic avulsion of knee articular cartilage, which appeared to be effective in enhancing and accelerating healing, hence functional recovery, in an adolescent soccer player. In conformance with the policy of the American College of Sports Medicine, the subject's parents provided written informed consent to undergo and publish the following medical procedures, which were approved by the Ethics Committee of the Universidad del País Vasco-Euskal Herriko Unibertsitatea.

CASE REPORT

At presentation, a 12-yr-old soccer player reported feeling a sudden sharp pain and locking of his right knee during a training session. After clinical evaluation and MRI he was diagnosed with a large, nontraumatic avulsion of knee articular cartilage. The lesion was located in the medial femoral condyle (Fig. 1), and a large (>2 cm) loose chondral body was detected in the intercondylar fossa area (Fig. 2).

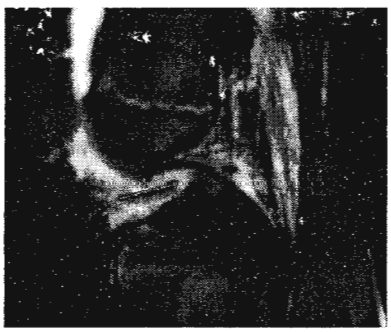

FIGURE 2—MRI scan showing the large (>2 cm) loose articular cartilage body.

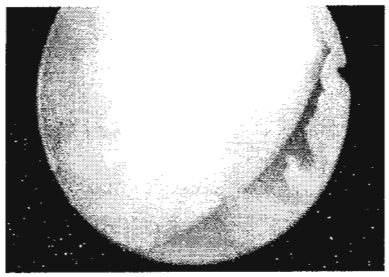

FIGURE 3—Arthroscopic image of the chondral fragment reattached and fixed to its bed in the medial femoral condyle with five biodegradable pins.

METHODS

Forty milliliters of venous blood were withdrawn by venous puncture from an antecubital vein 20–30 min before surgery and administration of anesthesia. Blood was collected on 5-mL tubes containing 3.8% (w/v) trisodium citrate, then centrifuged at 1800 rpm for 8 min (PRGF System II, BTI, Vitoria-Gasteiz, Spain). The 0.25-mL fractions located immediately above the erythrocytes were collected from each tube and transferred to sterile tubes. Fifty microliters of $CaCl_2$ at 10% (w/v) were added per 1-mL fraction of platelet-enriched plasma. This preparation was injected (see below) with no delay to allow the self-assembling of the fibrin just in the gap between the fragment and its bed, providing a supportive scaffold during the healing process to facilitate tissue maturation.

Surgical procedure. Knee arthroscopic surgery was performed under general anesthesia and using the usual portals. After debridement of the crater with a curette, the loose chondral fragment was placed in its bed with a push rod then fixed with five 40 mm × 1.3 mm Ø biodegradable pins (Orthosorb® Resorbable Pin, De PuyACE Medical Company, Warsaw, IN) (Fig. 3). The full-thickness loose chondral fragment had no bone attached to it and was flexible. It fit perfectly in its bed after careful removal of a layer of initial scar tissue in its deep face with a shaver. Next, the knee was vacuumed, and a hole was drilled through the reattached chondral fragment with a Kirschner wire. Approximately 2.0 mL of the activated PRGF preparation (as described above) were then injected through the hole and into the area between the crater and the fixed fragment, filling up any existing mismatch between the crater and fragment and sealing the edges of the reattached fragment. Prophylactic treatment with antibiotics and antithrombotics was established after surgery.

Postoperative management and follow-up. Postoperatively, the patient was allowed to walk using elbow crutches, but he was maintained nonweight-bearing for 4 wk, wearing a knee brace with limited range of motion. Two weeks after surgery (Fig. 4), physical therapy was initiated,

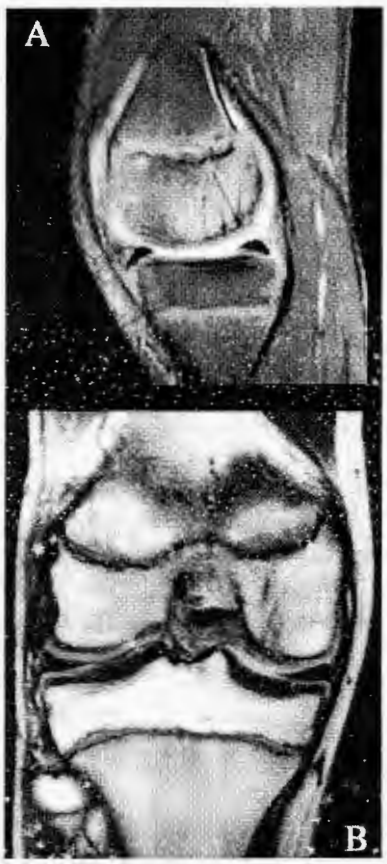

FIGURE 4—Sagittal (A) and coronal (B) MRI scans showing the excellent degree of reattachment of the chondral fragment into the articular cartilage 2 wk after the arthroscopic intervention.

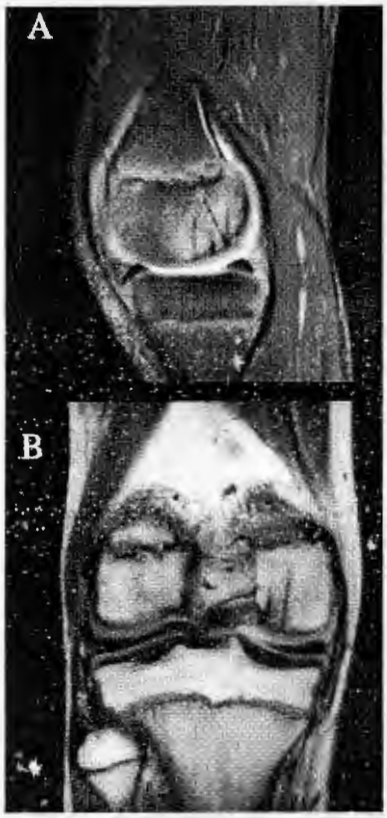

FIGURE 5—Sagittal (A) and coronal (B) MRI scans showing almost complete continuity between the reattached chondral fragment and the articular cartilage 6 wk after the arthroscopic intervention.

with range-of-motion exercises without axial loading. Weeks 4–8 after surgery were supposed to be of partial weight-bearing with elbow crutches. However, compliance with activity restriction was problematic, and by the sixth week after surgery, the subject could not be prevented from running and actively participating in games and sports in school (Fig. 5), even though he was not allowed to take part in formal soccer training. Unloaded stationary bicycling and strengthening exercises without axial loading were included in the recovery process between weeks 9 and 18 after surgery. The subject was allowed back in formal training with his teammates 18 wk after surgery (Fig. 6). At the time of writing, 38 wk after surgery, the subject was fully involved in training and competition without any recurrent symptoms.

DISCUSSION

The prognosis for healing after reattachment of a loose articular cartilage fragment is less favorable when the lesion is large (>2 cm in diameter), it does not extend into the vascularized subchondral area, and the fragment is purely articular cartilage and lacks subchondral bone (7,12,15,18,20,25). In this report, we have described our observation of enhanced articular cartilage healing, which led to accelerated functional recovery, by applying PRGF in a case of arthroscopically treated avulsion of articular cartilage with less favorable prognosis. The observed healing process and reattachment of the chondral body was outstanding, given that the usual operative treatment indicated for this type of lesion would have required fragment removal and crater drilling, curettage, mosaicplasty, rigid internal fixation, or autologous chondrocyte transplantation (12,25,27). Unfortunately, the long-term results of fragment excision have been described as extremely poor, even in patients treated before skeletal maturity (2), and potential disadvantages of the other operative treatments include creation of fibrocartilaginous channels, damage to the articular cartilage, donor site morbidity, and uneven articular congruence fit (12,27). The observed functional outcome was also excellent, with complete functional recovery and symptom-free resumption of normal athletic activity 18 wk after surgery. Even though this should be viewed as a preliminary report and the results cannot be unquestionably attributed to the application of PRGF based on a single case with a relatively short follow-up period, the application of PRGF could represent an interesting new technique to enhance the healing of a detached piece of articular cartilage.

Ability to repair articular knee lesions is dependent on cellularity and on the rate of matrix turnover per chondrocyte. Cell density could be enhanced considerably by local delivery of growth factors by chemotaxis and/or mitosis of local and attracted cells. Recent studies in tissue engineering have provided experimental evidence of the role of IGF-I, PDGF, TGF-β, EGF, and bFGF in chondrocyte proliferation

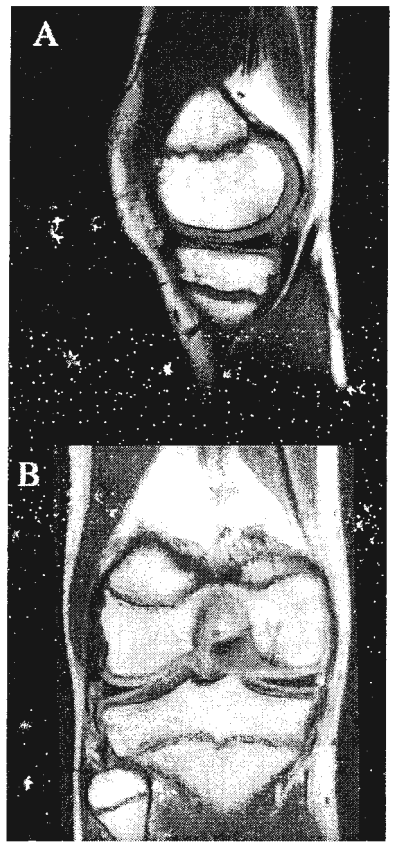

FIGURE 6—Sagittal (A) and coronal (B) MRI scans showing complete reattachment of the chondral fragment and perfect continuity of the articular cartilage 18 wk after the arthroscopic intervention.

(5,11,16,19). As cells cannot grow in an empty space, it is very important to provide a scaffold that could maintain cells adhered in the defect during the healing process. Fibrin could act as a supportive matrix and promote further tissue maturation (21). Furthermore, if this scaffold is soaked in active biological agents that are capable of inducing matrix production, such as growth factors (11), all these favorable circumstances taken together may potentially enhance the regeneration of cartilaginous tissue. *In vitro* studies show that three-dimensional systems are required for chondrocyte function and that interaction of the cell with its surrounding environment has a major effect in cell metabolism (13,24). In this respect, the fibrin scaffold soaked with a physiologically designed combination of growth factors may interact with the local cells and other cells attracted by chemotaxis and control cell repair mechanisms.

Consequently, to take advantage of the repair and regenerative potential of these substances, we have associated the use of growth factors and arthroscopic surgery to treat this large avulsion of articular cartilage with less favorable prognosis. This novel strategy consists of using the autologous fibrin as a three-dimensional carrier of growth factors and adhesive proteins contained in platelets. We have designed a simple and reproducible protocol to provide a natural source of growth factors that are greatly involved in repair processes. The PRGF preparation is easily obtained and manipulated, and the only concern is that once activated with calcium chloride it must be applied without delay to allow "*in situ*" self-assembling of the fibrin net and preservation of growth factor activity (3). In addition to a high concentration of growth factors, this preparation exhibits no antigenic capacity and preserves the integrity of platelets, which release the contents of alpha granules after activation of the concentrate (4).

CONCLUSIONS

In conclusion, the new application of PRGF-assisted regenerative technique could have contributed to enhance and accelerate articular cartilage healing after arthroscopic treatment of a large, nontraumatic avulsion of knee articular cartilage in an adolescent soccer player. This PRGF therapy is easy to implement, requires only about 40 mL of autologous blood, and the risk of disease transmission or antigenic reaction is nonexistent as autologous blood is not mixed with any other component of animal or human origin. Even though the present preliminary results need to be confirmed in a large cohort of patients, this PRGF-assisted tissue regeneration technique opens new perspectives in the area of human tissue regeneration and could become a valuable tool to treat a wide range of musculoskeletal injuries. Refinement of the PRGF technique and its further clinical applications as a potential stimulator in tissue repair are at present being evaluated by the authors.

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