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Original Article

Return to the original sport at only 3 months after an Achilles tendon rupture by a combination of intra-tissue injection of freeze-dried platelet-derived factor concentrate and excessively early rehabilitation after operative treatment in a male basketball player: A case report

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ABSTRACT

Background: Achilles tendon rupture is one of the most common serious injuries in athletes. Various studies to accelerate the healing process of the Achilles tendon have been performed as it takes a longer time to repair the tissue compared to other tendons. Here, we report a case of an acute Achilles tendon rupture in a male basketball player treated by a combination of an intra-tissue injection of freeze-dried platelet-derived factor concentrate, which included a platelet-derived growth factor with an early rehabilitation protocol after the operative treatment to facilitate the biological healing of the injured tendon tissue. To the best of our knowledge, this case is the first instance that enabled the athlete to return to original sport activity at only 3-months after the injury.
Case report: A 23-year-old male basketball player who belonged to a university basketball team sustained an Achilles tendon rupture during running in a training match. The remaining time period until the final tournament of the university league as a senior player was only 3 months. The patient received a combination of an intra-tissue injection of freeze-dried platelet-derived factor concentrate and early rehabilitation protocol after operative treatment. Surgery was performed 4 days after the injury and the early rehabilitation protocols were applied postoperatively. A freeze-dried platelet-derived factor concentrate was injected into the ruptured site of the Achilles tendon under ultrasound guide at 4 weeks postoperatively. The patient could return to play at the pre-injury level without any symptoms and disfunctions at 3 months after surgery. At two years postoperatively, the patient could play basketball without symptoms or rerupture.
Conclusions: We reported a case of an Achilles tendon rupture which was treated by a combination of intra-tissue injection of freeze-dried platelet-derived factor concentrate and an early rehabilitation protocol after the operative treatment. The patient could return to play basketball at the pre-injury activity level at only 3-months after the injury, suggesting that the role of applying excessively early rehabilitation of mechanical loading could facilitate tendon tissue healing when combined with an intra-tissue injection of freeze-dried platelet-derived factor concentrate.

Abbreviations: ATRs, Achilles tendon ruptures; PRP, Plate-rich plasma; TGF-β, Transforming growth factor-β; VEGF, Vascular endothelial growth factor; PDGF, Platelet-derived growth factor; IGF, Insulin growth factor; b-FGF, Basic fibroblastic growth factor; FD-PFC, Freeze-dried platelet-derived factor concentrate; T2-STIR, T2 weighted short tau inversion recovery; MRI, Magnetic resonance imaging.

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1. Introduction

Treatment for Achilles tendon ruptures (ATRs) generally divide between conservative and operative treatments [1,2]. Conventionally, it has been common to apply immobilization and non-weightbearing for several weeks as a rehabilitation protocol in the either conservative or operative treatment [3–5]. Recently, several studies have suggested the advantage of an early rehabilitation protocol including early weight-bearing and early range of motion in both treatments [5–8]. These studies have suggested that the early rehabilitation protocol compared to the conventional rehabilitation protocol improved the restoration of functional properties of tendon tissue more rapidly, which could lead to earlier return to work and sport. A recent meta-analysis has compared the clinical outcomes of conservative and operative treatments for ATRs when the early rehabilitation protocol was applied [9]. According to this report, the rates of re-rupture was similar between both treatment methods, however, it concluded that operative treatment might lead to faster return to work and sport than conservative treatment. Therefore, in terms of treatment for athletes, it is recommended that the combination of operative treatment and an early rehabilitation protocol is indicated for Achilles tendon ruptures in our clinical practice [10].

Regenerative therapy using biological materials in orthopedic sports medicine have increased in recent years [30]. Among these biological materials, platelet-rich plasma (PRP) is widely used for various conditions in sports medicine, because this material possesses advantages such as the ease of preparation with less burden on the patient and its relative safety in terms of side reactions and rejections [22]. PRP is rich in various growth factors that are expected to promote tissue repair and accelerate the healing process in various conditions [19–22]. It can release growth factors including transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), insulin growth factor (IGF), and basic fibroblastic growth factor (b-FGF), all which serve important roles in tissue regeneration. Some clinical studies have investigated the effect of PRP in treating ATRs, however, there are currently little evidence to prove its effectiveness [25–27].

Freeze-dried platelet-derived factor concentrate (FD-PFC) is prepared as a decellularizing PRP and preserved using a freeze drying method [15]. It has been validated by Araki J et al. [16] that PFC can formulate rich growth factors, especially PDGF-BB, which is part of the PDGF growth family and it has been reported by Pan et al. [17] that the purified freeze drying methods of PRP products is a suitable technique that can preserve bioactivities and growth factor counts [18]. For these reasons, FD-PFC is expected to promote tissue repair, however, there are no reports that use FD-PFC in treating ATRs.

Here, we report a case of an Achilles tendon rupture in a male basketball player who was treated by a combination of surgical treatment, an early functional rehabilitation protocol, and additional injection of FD-PFC and returned to play basketball at the pre-injury levels at 3-months after the injury. Written informed consent was obtained from the patient for publishing this report.

2. Case report

A 23-year-old male basketball player who belonged to a university basketball team sustained an Achilles tendon rupture during running in a training match. The remaining time to the final tournament of the university league as a senior player was only 3 months. Therefore, the combination of operative treatment and additional intra-tendon tissue injection of FD-PFC was applied to enable him to return to play basketball as early as possible.

The operation was performed under general anesthesia at 4 days after the injury. The patient was placed in the prone position. An air tourniquet was used for the operation. After an approximately 7-cm mild curved skin incision was placed along the medial side of the Achilles tendon, the fascia was incised to the same length as the skin incision. The ruptured Achilles tendon was confirmed, and the tendon was repaired by a combination of the modified side-locking loop suture technique using USP No.5 braided polyblend suture material (FiberWire, Arthlex, Naples, Florida, USA) as a core suture and cross-stich technique using USP No.2 monofilament as a peripheral suture reported by Imade et al. (Fig. 1) [11]. After the fascia was repaired, the wound was sutured.

The process of preparing FD-PFC begins with the extraction of 49 ml of autologous blood to prepare PRP, which was prepared by centrifugation and then PFC was prepared according to a method described by Araki et al. [16] and was subsequently freeze-dried and powdered. In order to create a solution for injection into the knee joint, the FD-PFC was dissolved in 6 ml of physiological saline. The prepared FD-PFC was dissolved in 3 ml of saline and injected into the sutured site of the Achilles tendon under ultrasound guide at 4 weeks postoperatively (Fig. 2).

The postoperative rehabilitation was performed according to a report by Miyamoto et al. [10]. Postoperatively, immobilization with a cast or a splint was not applied, while active and passive range of motion exercises on the ankle of the operated side was initiated one day after surgery. Partial weight bearing was initiated at postoperative day 4 because the active dorsiflexion angle of the operated side was 0° or more, and full weight bearing was initiated without crutches at 4 weeks postoperatively. Leg heel raising exercises and muscle strengthening exercises were initiated at 6weeks, jogging was allowed at 8 weeks postoperatively. At 12 weeks postoperatively, the patient was permitted to return to play basketball after confirming no symptoms, no difference in the circumference of the lower leg between the operated side and the unaffected side, and that the abnormal intensity at the repaired site of the Achilles tendon improved in the T2 weighted short tau inversion recovery (T2-STIR) on magnetic resonance imaging (MRI) (Fig. 3). The patient could return to play at the pre-injury level at 3 months after surgery. At two years postoperatively, the patient was playing basketball at the recreational level without symptoms and rerupture.

3. Discussion

Treatment options for ATRs in high activity athletes generally have been either conservative treatment or operative treatment, however, the optimal treatment is still under debate [1,2]. The time it takes to return to play after ATRs is an issue that athletes must consider when deciding either to pursue an operative treatment or not, as ATRs usually take longer to heal in comparison with others tendon injuries [12]. Therefore, various studies on treatment to accelerate the healing process in the Achilles tendon have been performed.

Conventionally, a late rehabilitation protocol with immobilization for several weeks after sustaining the injury has been applied in treatment for ATRs [3–5]. However, several animal experiments and meta-analyses have recently suggested that an early rehabilitation protocol including early weight-bearing and early range of motion exercises provides the beneficial effects on tendon healing [5–8,13,14]. In animal experiments, early rehabilitation provided more rapid improvement in functional properties of the tendon than continuous immobilization, accelerated restoration of load to failure and reduced tendon deflection [13,14]. Pneumaticos et al. [13], investigating the effect of early mobilization after Achilles tendon repair in rabbit models showed that early mobilization

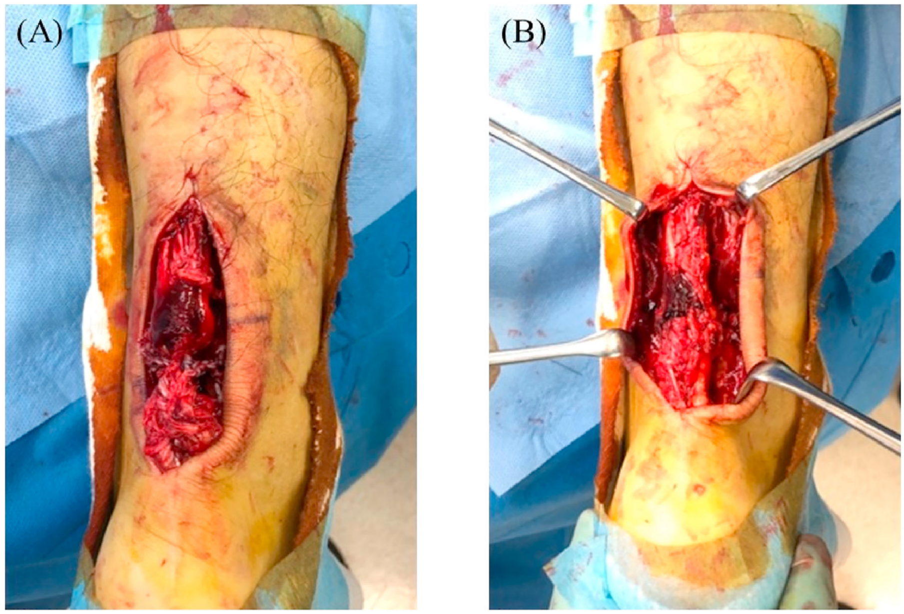

Fig. 1. The ruptured Achilles tendon was confirmed (A), and the tendon was repaired by a combination of the modified side-locking loop suture technique using USP No.5 braided polyblend suture material as a core suture and cross-stich technique using USP No.2 monofilament as a peripheral suture (B).

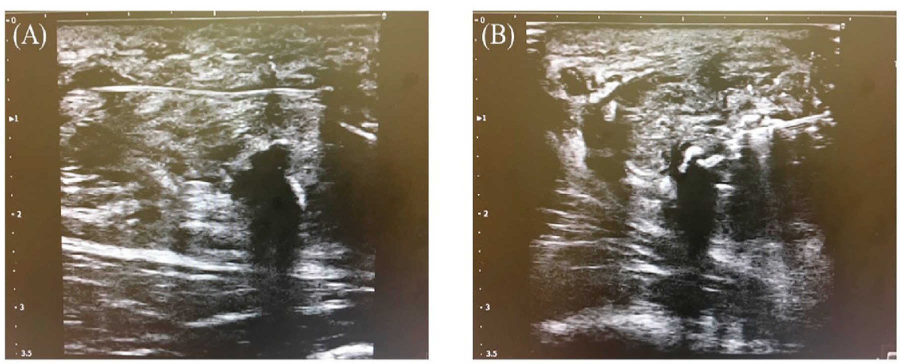

Fig. 2. After confirming the sutured site of the Achilles tendon with the long-axis image (A) and the short-axis image (B) under ultrasound, the prepared FD-PFC was dissolved in 3 ml of normal saline and injected into the site.

restored the functional properties of the tendons more rapidly than continuous immobilization. Palmes et al. [14] also reported that early mobilization led to fundamental changes in the biological process of tendon healing, resulting in accelerated restoration of load to failure and reduced tendon deflection in a mouse model. Similarly, several meta-analyses of clinical outcomes of the treatment of ATRs suggested that early rehabilitation improved the functionality more and enabled earlier return to work and sport than late rehabilitation with prolonged immobilization [5–8].

In comparison of the clinical outcomes of conservative treatment and operative treatment for ATRs in applying early rehabilitation, Willits et al. [19] analyzed 144 patients (seventy-two treated conservatively and seventy-two treated operatively) in a randomized control study and suggested that the rates of re-rupture, range of motion of the affected ankle and calf circumference were not significantly different between the two groups. Meta-analysis, according to Soroceanu et al. [9], also showed that there was no difference in the rate of rerupture, the strength, and the circumference between conservative and operative treatments. However, this meta-analysis investigation showed that patients who were treated operatively returned to work sooner than those who received conservative treatment. Therefore, in terms of treatment options of ATRs for athletes, we generally recommend a combination of operative treatment and an early rehabilitation protocol for Achilles tendon ruptures in our clinical practice.

PRP is an autologous blood product, which is rich in various bioactive proteins such as VEGF, IGF, b-FGF, PDGF, platelet-derived epidermal growth factor, TGF-β and epidermal growth factor [19–21]. These bioactive proteins are expected to promote tissue repair and accelerate the healing process in various conditions [22]. Numerous studies have been conducted to investigate the effect of PRP for treatment of ATRs in recent years [23–27]. Several animal experiments have provided evidence of the beneficial effects of PRP, which include increase in strength, vascularity and better tissue organization in the Achilles tendon [23,24]. However, the use of PRP for Achilles tendon ruptures is still controversial in clinical studies [25–27]. De Carli et al. [25] investigated the effect of addition of PRP in ATRs treated operatively. They compared a PRP group (15 patients surgically treated with addition of PRP both during surgery and 14 days after surgery) and a control group (15 patients surgically

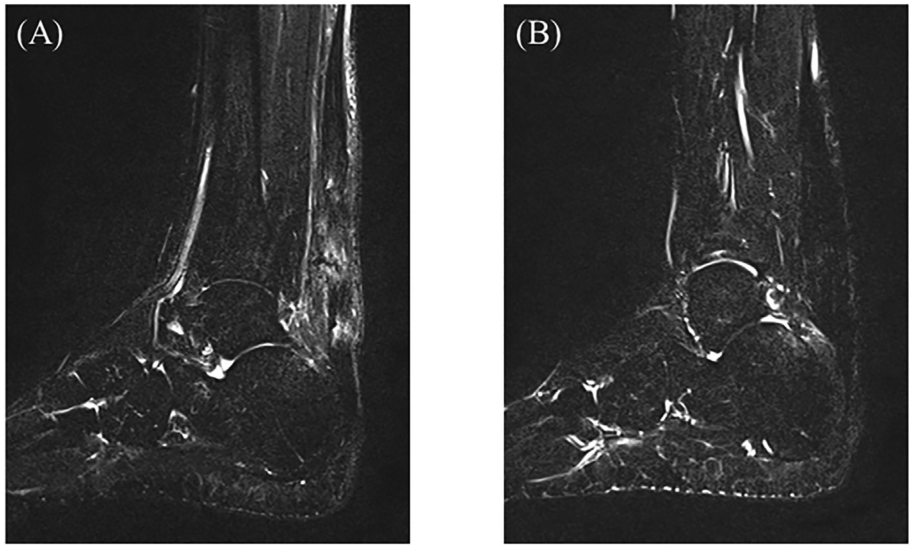

Fig. 3. The abnormal intensity at the repaired site of the Achilles tendon at pre-injection of FD-PFC in T2-STIR of MRI (A) improved at 12 weeks after the operation (B).

treated without addition of PRP) and demonstrated that there were no significant differences in structural and functional results between the two groups. Schepull et al. [26] performed a randomized trial to investigate the effect of PRP for ATRs, showing that PRP was not useful for operative treatment of ATRs. On the other hand, Sanchez et al. [27] reported better outcomes in using PRP for ATRs treated with operative treatment and that the use of PRP improved thickness in the treated tendons and enabled earlier return to sport. These clinical studies provided different results using different postoperative rehabilitation protocols. De Carli et al. [25] and Schepull et al. [26] applied a total of 5–7 weeks of immobilization using a walker brace or a short leg cast. On the other hand, Sanchez et al. [27] applied immobilization for only 2–3 weeks. These results suggest that applying an excessively early rehabilitation would be necessary in the tendon tissue healing process.

FD-PFC is prepared by decellularizing PRP and preserving it by a freeze drying method [15], and is rich in various growth factors such as VEGF, b-FGF, PDGF, TGF-β and epidermal growth factor. Araki et al. [16] have firstly introduced the optimized preparation method of PFC and further performed hematological analysis in PRP, PFC and their intermediates. In this report, the platelet concentration (x 10^4/μl) and the PDGF-BB concentration (ng/mL) were much higher in PFC than in PRP (the platelet concentration was 51.4 ± 7.15 in PRP, 415 ± 50.1 in PFC and the PDGF-BB concentration was 6.79 ± 1.73 in PRP, 157.9 ± 16.0 in PFC). PDGF-BB is a part of the PDGF growth family and expected help the tendon healing process because it has mitogenic, chemotactic and angiogenetic properties [28]. Several studies have investigated the effects of growth factors on tenocyte proliferation which is an important factor in the tendon healing [28,29,33–36]. These studies have shown that PDGF-BB promotes tenocyte proliferation most among various growth factors, and further promotes tenocyte proliferation in combination with other growth factors such as b-FGF and IGF. In addition, PDGF-BB may also stimulate the production of other growth factors such as IGF and indirectly promote tendon healing [29]. Furthermore, it has been reported that the preservation technique by freeze drying maintains bioactivities of growth factors for a longer time than fresh PRP [17,18]. Given these advantages of FD-PFC, it is expected to promote tendon healing more effectively.

To the best of our knowledge, this case is the first instance that enabled an athlete to return to play basketball at the pre-injury activity level only 3-months after the injury. According to previous *in vivo* and *in vitro* research, in cases that lacked physiological mechanical loading in progenitor cells or fibroblast at the tendon tissue injured site, it failed to gain the mechanical property of the tendon tissues in the process of tendon tissue remodeling due to an increased production of catabolic proteolytic enzyme such as matrix metalloproteinase [31,32]. Taking this phenomenon into consideration, the role of applying excessively early rehabilitation as mechanical loading might facilitate and accelerate tendon tissue healing when combined with growth factors such as an intra-tissue injection of FD-PFC. As a limitation, this was a case report and there is a necessity to elucidate the capability of PDGF in FD-PFC with mechanical loading.

4. Conclusion

We reported a case of an Achilles tendon rupture, which was treated by a combination of intra-tissue injection of FD-PFC and an early rehabilitation protocol after operative treatment. The patient could return to play basketball at the pre-injury activity level only 3-months after the injury, suggesting that the role of applying an excessively early rehabilitation as a mechanical loading could facilitate a tendon tissue healing with a combination of an intra-tissue injection of FD-PFC.

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