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Activated Growth Factors (AGF), an Advanced Platelet-Rich Plasma (PRP) Modality, as a Novel Biological Treatment for Partial Anterior Cruciate Ligament Tears: A Case Report

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A B S T R A C T

Introduction: Partial anterior cruciate ligament (ACL) ruptures present a complex clinical challenge. Traditional treatment options, including conservative management and surgical reconstruction, often yield unpredictable outcomes and extended recovery periods. This case report explores the potential of activated growth factors (AGF), an advanced platelet-rich plasma (PRP) modality, as a novel biological treatment strategy for partial ACL tears. **Case presentation:** A 39-year-old male presented with right knee pain and instability following a twisting injury sustained during exercise. Magnetic resonance imaging (MRI) confirmed a partial tear of the anteromedial bundle of the ACL. The patient was treated with a series of three intra-articular injections of AGF, administered at weekly intervals. The AGF was prepared using a proprietary protocol aimed at optimizing growth factor concentration and release. The patient's progress was meticulously monitored through clinical evaluations and functional assessments at 3 and 6 months post-treatment. **Conclusion:** This case suggests that AGF may offer a promising alternative for the treatment of partial ACL tears, potentially facilitating accelerated healing and improved clinical outcomes. Further research, including controlled trials, is warranted to validate these findings and establish the efficacy and safety of AGF in a larger patient population.

1. Introduction

The anterior cruciate ligament (ACL), a crucial stabilizer of the knee joint, is susceptible to a spectrum of injuries, ranging from minor sprains to complete ruptures. Among these, partial ACL tears represent a unique clinical challenge, often presenting with a diverse array of symptoms and functional limitations. These injuries, characterized by incomplete disruption of the ligament fibers, pose a diagnostic and therapeutic dilemma for clinicians, as they may not always present with the classic signs and symptoms associated with complete ACL tears. The ACL, a robust

intra-articular ligament connecting the femur to the tibia, plays a pivotal role in maintaining knee joint stability. It primarily functions to resist anterior tibial translation, prevent excessive rotational forces, and guide knee joint kinematics during various activities. The ACL is composed of two distinct functional bundles, the anteromedial (AM) bundle and the posterolateral (PL) bundle, each contributing to specific aspects of knee joint stability. The AM bundle is primarily taut in flexion, resisting anterior tibial translation and internal rotation, while the PL bundle is taut in extension, contributing to rotational stability. Partial ACL tears, as the name suggests, involve incomplete disruption of the ACL fibers, with varying degrees of ligamentous integrity remaining. These injuries can affect either the AM bundle, the PL bundle, or both, resulting in a wide range of clinical presentations. The diagnosis of partial ACL tears can be challenging, as they may not always present with the classic "pop" sensation or immediate hemarthrosis characteristic of complete ACL ruptures. Patients with partial ACL tears often complain of pain, instability, and functional limitations, particularly during activities that involve pivoting or cutting movements.[1-4]

The management of partial ACL tears remains a subject of ongoing debate and controversy. Traditional treatment approaches include conservative management, such as bracing, physiotherapy, and activity modification, or surgical reconstruction. Conservative management aims to reduce pain, restore knee joint function, and prevent further injury through a combination of rest, ice, compression, elevation (RICE), and a structured rehabilitation program. However, conservative management may not adequately address the underlying ligamentous instability, potentially leading to persistent pain, recurrent instability episodes, and the development of early-onset osteoarthritis. Surgical reconstruction, on the other hand, aims to restore knee joint stability by replacing the torn ACL with a graft, typically harvested from the patient's own hamstring tendons or patellar tendon. While surgical reconstruction can effectively restore stability and allow patients to return to high-demand activities, it is associated with a prolonged recovery period, potential donor site morbidity, and the risk of complications such as infection and arthrofibrosis. The decision to pursue surgical intervention for partial ACL tears is often individualized, based on factors such as the extent of the tear, the patient's activity level, and their response to conservative management. In recent years, there has been a growing interest in the use of biological therapies, such as platelet-rich plasma (PRP), to promote the healing of musculoskeletal injuries. PRP, a concentrated suspension of platelets derived from autologous blood, contains a rich array of growth factors that play a crucial role in tissue regeneration and repair. These growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), stimulate cell proliferation, matrix synthesis, and angiogenesis, promoting the healing of injured tissues.[5-7]

Activated growth factors (AGF) represents an advanced PRP modality that utilizes a proprietary protocol to optimize growth factor concentration and release, potentially enhancing its therapeutic efficacy. The AGF preparation protocol involves a two-step centrifugation process to concentrate platelets and activate them with calcium chloride, initiating the release of growth factors. This process aims to maximize the concentration of growth factors delivered to the injured tissue, potentially accelerating the healing process and improving clinical outcomes. The use of AGF in the treatment of partial ACL tears is a relatively novel approach, with limited clinical data available. However, preliminary studies and case reports have suggested that AGF injections may promote ligament healing, reduce pain, and improve knee joint function in patients with partial ACL tears. The rationale for using AGF in this context is based on its ability to stimulate cell proliferation, matrix synthesis, and angiogenesis, potentially facilitating the repair of the damaged ligament and restoring its structural integrity. This case report presents the

clinical outcome of a patient with a partial ACL tear treated with a series of AGF injections.[8-10] The aim of this report is to highlight the potential of AGF as a novel biological treatment option for this challenging clinical condition.

2. Case Presentation

The patient, 39-year-old male patient who presented to General Hospital Siti Fatimah South Sumatera, Indonesia with complaints of right knee pain and instability following a sports-related injury. The patient regularly participated in soccer games, sustained the injury during a match while attempting a quick change of direction. He described planting his right foot firmly on the ground and pivoting to his left when he felt a sudden twisting sensation in his right knee, accompanied by immediate pain and a sense of instability. He reported feeling as though his knee had "given way" beneath him. The patient denied any history of previous knee injuries or surgeries, emphasizing that this was an isolated incident. Upon initial presentation at the clinic, the patient exhibited several clinical signs indicative of a knee injury. Visual inspection revealed mild swelling localized around the medial aspect of the right knee joint. Palpation elicited tenderness along the medial joint line, further suggesting the involvement of structures within that region. The patient's active range of motion was notably limited due to pain, hindering his ability to fully flex and extend the affected knee. To assess the integrity of the knee ligaments, a series of specialized tests were performed. The Lachman test, a clinical maneuver used to evaluate the integrity of the anterior cruciate ligament (ACL), elicited a positive response, indicating some degree of laxity in the ACL. However, the degree of laxity was less pronounced compared to what would be expected in a complete ACL rupture. Similarly, the anterior drawer test, another maneuver used to assess the ACL, was also positive, but again, the laxity was less significant than typically observed in complete tears. These findings suggested a possible partial tear of the ACL. Additional tests were conducted to rule out other potential injuries. Varus and valgus stress tests, which assess the stability of the collateral ligaments, were negative, indicating that the medial and lateral collateral ligaments were intact. McMurray's test, a maneuver used to detect meniscal tears, was also negative, suggesting that the menisci were not involved in the injury. To further investigate the nature and extent of the knee injury, magnetic resonance imaging (MRI) of the right knee was ordered. MRI provides detailed visualization of the soft tissues within the joint, including ligaments, tendons, and cartilage. The MRI scan confirmed the clinical suspicion of a partial ACL tear. Specifically, the images revealed a disruption of the anteromedial bundle of the ACL, while the posterolateral bundle remained intact. Importantly, the MRI did not show any evidence of other associated injuries, such as meniscal tears, bone contusions, or damage to other ligaments within the knee joint. Based on the comprehensive clinical evaluation, including the patient's history, physical examination findings, and confirmatory MRI results, a diagnosis of a partial anteromedial bundle ACL tear was established. This diagnosis provided a clear understanding of the specific injury and guided the subsequent treatment decisions (Table 1).

Table 2 outlines the specific steps involved in preparing and administering Activated Growth Factors (AGF) to the patient in this case report. The process begins with the collection of 30 ml of peripheral blood from the patient's antecubital vein, a common site for blood draws. The use of a 21-gauge needle is standard for venipuncture, and the 10 ml syringe likely contains a specialized Platelet Isolation Tube (EurekaHLM®). This tube likely contains an anticoagulant to prevent clotting and potentially a separation gel to facilitate the isolation of platelet-rich plasma (PRP) during centrifugation. Centrifugation is a crucial step in PRP preparation. It uses centrifugal force to separate blood components based on their density. The first spin at 1300 rpm for 10 minutes likely separates red blood cells and most white blood cells from the plasma, concentrating platelets in the upper layer. It's important to note that centrifugation protocols can vary depending on the equipment and desired platelet

concentration. The specific speed and duration used here (1300 rpm for 10 minutes) are likely optimized for the EurekaHLM® system to achieve a 5-fold increase in platelet concentration. Measuring platelet concentration is essential to ensure the PRP has the desired therapeutic level of platelets. In this case, the baseline platelet count was 200,000 platelets/μL, which is within the normal range. After centrifugation and PRP isolation, the count increased to 1,000,000 platelets/μL, achieving the targeted 5-fold increase. This concentration is considered optimal for promoting tissue healing and regeneration. Platelet activation is a key step in AGF preparation. It triggers the release of growth factors stored within the platelets, making them more bioavailable to stimulate tissue repair. The use of a proprietary AGF Activator (EurekaHLM®) containing a combination of activators: Calcium chloride: A common activator that initiates the coagulation cascade, leading to platelet activation and growth factor release; Thrombin: A potent activator that directly converts fibrinogen to fibrin, forming a clot and further stimulating platelet activation; TXA2 (Thromboxane A2): A potent platelet aggregator and vasoconstrictor, enhancing platelet activation and potentially improving growth factor delivery; ADP (Adenosine diphosphate): Another important platelet activator that promotes aggregation and granule release; Collagen: A structural protein found in connective tissues that triggers platelet adhesion and activation. The activation process involves incubation at 40°C for 10 minutes and exposure to UV light at 250 nm for 10 minutes. The incubation likely facilitates the interaction of activators with platelets, while UV exposure may further enhance growth factor release or modify their activity. The significant increase in TGF-beta (Transforming Growth Factor-beta) levels from 5647 pg/mL to 49876 pg/mL after activation confirms the effectiveness of the activation process. TGF-beta is a crucial growth factor involved in tissue regeneration and repair, particularly in ligament healing. A second spin at 1300 rpm for 10 minutes is performed after activation. This step likely aims to remove the supernatant (excess fluid) and any remaining activating agents, leaving a more concentrated AGF solution. The final product is 3 ml of AGF solution ready for injection. This volume is typical for intra-articular injections. Local anesthesia with 1% lidocaine is administered to minimize discomfort during the injection. Infiltrating 5 ml subcutaneously around the injection site ensures adequate numbing of the area. Positioning the patient supine with the knee slightly flexed allows for easy access to the knee joint and facilitates accurate needle placement under ultrasound guidance. Ultrasound guidance is crucial for accurate and safe injection. It allows the clinician to visualize the needle in real-time, ensuring it reaches the targeted area within the knee joint—in this case, the site of the ACL tear. Using a 22-gauge needle is appropriate for intra-articular injections, as it is fine enough to minimize tissue trauma but still allows for smooth injection of the AGF solution. Injecting 3 ml of AGF is a standard volume for intra-articular procedures. It is sufficient to distribute the growth factors throughout the joint space while avoiding overdistension. Applying a compression bandage helps to minimize swelling and provide support to the knee. Ice application for 20 minutes reduces inflammation and pain.

Table 3 outlines a phased rehabilitation program following the AGF injections for a partial ACL tear. Phase 1: Protective Phase (Days 1-7 post-injection). This initial phase prioritizes protection of the healing ACL and minimizing pain and inflammation. Rest, ice, and gentle range of motion exercises are key. Assistive devices like crutches may be used to limit stress on the knee. Control pain and swelling, maintain knee mobility, and protect the healing ligament. Minimal pain, no increase in swelling, full knee extension, and gradual improvement in knee flexion indicate readiness to progress to the next phase. Phase 2: Intermediate Phase (Weeks 2-6 post-injection). This phase gradually increases the load on the knee, focusing on strengthening, proprioception (body awareness), and restoring normal movement patterns. Progressive weight-bearing, increased range of motion exercises, strengthening exercises for the muscles

around the knee (hamstrings, quadriceps, calf muscles), and exercises to improve balance and coordination. Improve muscle strength and endurance, enhance proprioception and balance, and restore a normal walking pattern. Full range of motion, good muscle strength, improved balance and coordination, and pain-free walking indicate readiness to progress. Phase 3: Advanced Phase (Weeks 7-12 post-injection). This phase aims to return the patient to their pre-injury activity levels by incorporating sport-specific training and gradually reintroducing sports activities. Continued strengthening and proprioception exercises, along with agility drills, plyometrics (jump training), and a gradual return to sports. Restore pre-injury activity levels, optimize functional performance, and prevent re-injury. No pain or instability during sports, and achieving normal results on functional performance tests (hop tests, agility tests) indicate successful progression. Phase 4: Return to Sport (Beyond 6 months post-injection). This phase focuses on long-term maintenance of knee stability and function, allowing the patient to safely continue their desired activities. Maintenance of strength and conditioning, continued participation in sports, and regular follow-up with a healthcare provider to monitor progress and address any concerns. Maintain long-term knee stability and function, and prevent recurrence of injury. Continued asymptomatic participation in sports and no signs of instability on clinical examination indicate successful long-term recovery.

Table 1. Anamnesis, physical examination, Imaging, and diagnosis.

Feature	Description
Anamnesis	
Chief complaint	Right knee pain and instability
Mechanism of injury	Twisting injury during a soccer game
Symptom onset	Immediate pain and a feeling of "giving way"
Previous knee injuries/surgeries	Denied
Physical examination	
Inspection	Mild swelling and tenderness along the medial joint line
Palpation	Tenderness to palpation along the medial joint line
Range of motion	Slightly limited due to pain
Ligamentous tests	
Lachman test	Positive, but less pronounced than in a complete ACL tear
Anterior Drawer test	Positive, but less pronounced than in a complete ACL tear
Varus/valgus stress tests	Negative (intact collateral ligaments)
Meniscal tests	
McMurray's test	Negative
Imaging	
MRI	Partial tear of the anteromedial bundle of the ACL; intact posterolateral bundle. No meniscal tear, bone contusion, or other ligamentous injury.
Diagnosis	Partial anteromedial bundle ACL tear

Table 2. AGF preparation and AGF administration.

Step	Description	Procedure
AGF preparation		
Blood collection	30 ml of peripheral blood drawn from the patient's antecubital vein	Standard venipuncture procedure using a 21-gauge needle and a 10 ml syringe containing Platelet Isolation Tube (EurekaHLM®).
Centrifugation	Centrifugation technique to isolate platelet-rich plasma (PRP)	First spin: 1300 rpm for 10 minutes
Platelet concentration	Platelet concentration in the PRP measured	Baseline platelet count: 200,000 platelets/µL; PRP platelet count: 1,000,000 platelets/µL (5 times baseline)
Activation	PRP activated with AGF Activator (EurekaHLM®)	AGF Activator (EurekaHLM®):Calcium chloride: Thrombin: TXA2: ADP: Collagen; incubation 40^0C for 10 minutes and UV 250nm for 10 minutes. Baseline TGF beta: 5647 pg/mL; TGF beta after activation: 49876 pg/mL. Second spin: 1300 rpm for 10 minutes: evacuate supernatan and discharge clotting.
Final product	3 ml of AGF solution	
AGF administration		
Anesthesia	Local anesthetic (e.g., lidocaine) infiltrated at the injection site	1% lidocaine, 5 ml infiltrated subcutaneously around the planned injection site.
Positioning	Patient positioned supine with the knee slightly flexed	
Injection technique	Ultrasound-guided injection into the right knee joint, targeting the site of the ACL tear	A 22-gauge needle used for the injection. Real-time ultrasound guidance used to visualize the needle placement and ensure accurate delivery of AGF to the site of the ACL tear.
Injection volume		3 ml of AGF injected
Post-injection care		Compression bandage applied. Ice pack applied to the injection site for 20 minutes.

Table 3. Rehabilitation.

Phase	Timeframe	Exercises and activities	Goals	Progression criteria
Phase 1: Protective Phase	Days 1-7 post-injection	* Rest and ice application * Gentle range of motion exercises (e.g., ankle pumps, quadriceps sets) * Assistive devices (crutches) as needed for ambulation (weight-bearing as tolerated)	* Control pain and inflammation * Protect the healing ACL * Maintain range of motion	* Minimal pain * No increase in swelling * Full knee extension * Increasing knee flexion
Phase 2: Intermediate Phase	Weeks 2-6 post-injection	* Progressive weight-bearing * Gradual increase in range of motion exercises * Strengthening exercises (e.g., hamstring curls, calf raises, closed-chain exercises) * Proprioceptive exercises (e.g., single-leg stance, balance board)	* Improve muscle strength and endurance * Enhance proprioception and balance * Restore normal gait pattern	* Full range of motion * Good muscle strength * Improved balance and coordination * Pain-free ambulation
Phase 3: Advanced Phase	Weeks 7-12 post-injection	* Continued strengthening and proprioceptive exercises * Sport-specific training (e.g., agility drills, plyometrics) * Gradual return to sports activities	* Restore pre-injury activity levels * Optimize functional performance * Prevent re-injury	* No pain or instability during sports activities * Functional performance tests (e.g., hop tests, agility tests) within normal limits
Phase 4: Return to Sport	Beyond 6 months post-injection	* Maintenance of strength and conditioning * Continued participation in sports activities * Regular follow-up with healthcare provider	* Maintain long-term knee stability and function * Prevent recurrence of injury	* Continued asymptomatic participation in sports * No signs of instability on clinical examination

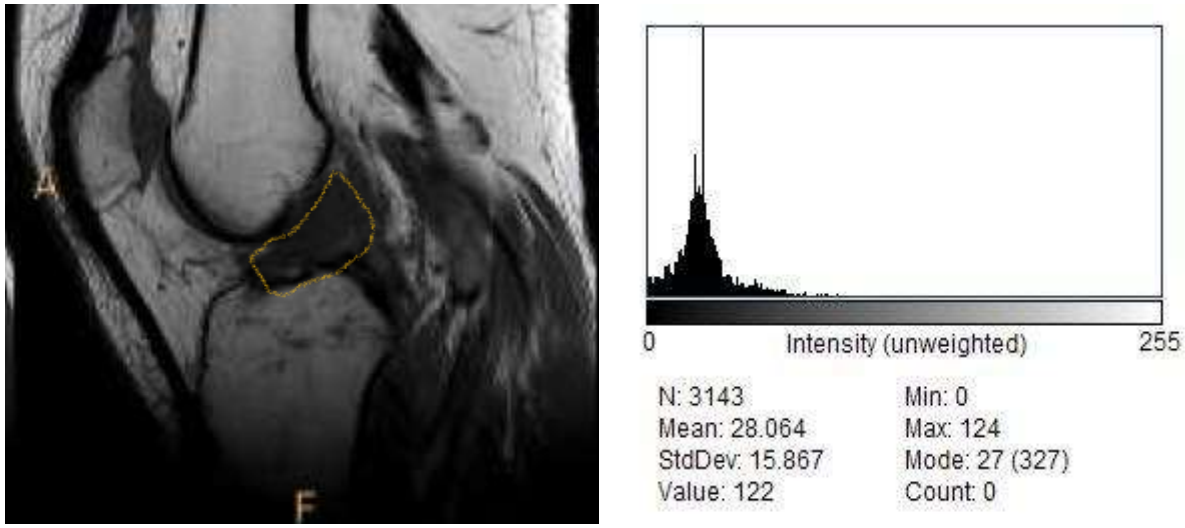
Table 4 presents a clear picture of the patient's progress and outcomes following the AGF treatment for their partial ACL tear. Pre-treatment establishes the baseline before any intervention, highlighting the initial severity of the injury. The 3 Months assessment captures early improvements after the AGF injections and the initial phase of rehabilitation. 6 Months longer-term follow-up provides insights into the sustained effects of the treatment and the patient's overall recovery. A clear and consistent reduction in pain is observed. The VAS score drops from 7/10 (significant pain) at baseline to 2/10 at 3 months and further down to 1/10 at 6 months (minimal pain). This demonstrates the effectiveness of the AGF injections in managing pain associated with the partial ACL tear. The Lysholm score is a validated measure of knee

function, with higher scores indicating better function. The score improves from 60 (moderate impairment) at baseline to 85 (mild impairment) at 3 months and then to 92 (almost normal function) at 6 months. This demonstrates significant functional improvement over time. Lachman Test and Anterior Drawer Test assess the stability of the ACL. Initially, both tests were positive, indicating laxity in the ACL. At 3 months, the tests were still positive but less pronounced, suggesting improved stability. By 6 months, both tests were negative, indicating that normal knee stability had been restored. The patient's ability to return to their desired activity level is a key outcome measure. Initially, they were unable to participate in sports due to pain and instability. By 3 months, they had returned to light jogging and cycling. At 6 months, they had returned to full participation in recreational soccer, demonstrating a successful return to their pre-injury activity level.

Table 4. Follow-up and outcomes.

Follow-up time point	Pain (VAS)	Function (Lysholm Score)	Knee stability	Return to activity
Pre-treatment	7/10	60	Lachman Test: Positive (Grade 2) Anterior Drawer Test: Positive (Grade 2)	Unable to participate in sports
3 Months	2/10	85	Lachman Test: Positive (Grade 1) Anterior Drawer Test: Positive (Grade 1)	Returned to light jogging and cycling
6 Months	1/10	92	Lachman Test: Negative Anterior Drawer Test: Negative	Returned to full participation in recreational soccer

Figure 1 provides a visual representation of the patient's ACL before and after treatment with AGF, using MRI images and corresponding histograms; (A) Pre-treatment MRI: The ACL appears thicker than normal, suggesting inflammation and potential disorganization of the ligament fibers. This is a common finding in acute or subacute ligament injuries. The ACL's normal, tightly bundled structure appears disrupted, with a loss of clear definition and alignment of the fibers. This indicates damage to the ligament's internal structure. The fibers within the ACL are not neatly aligned, further supporting the presence of structural damage. This disorganization can compromise the ligament's strength and stability. The brighter signal within the ACL on the MRI indicates increased fluid content or edema within the ligament. This is a hallmark of inflammation and injury. The most prominent abnormalities are seen in the middle portion of the ACL, which is a common location for partial tears; (B) 6 Months Post-treatment MRI: The ACL appears thinner and more normal in size, suggesting a reduction in inflammation and improved organization of the ligament fibers. The ACL's structure appears more organized, with better-defined fiber bundles. This indicates healing and restoration of the ligament's internal architecture. The darker signal within the ACL suggests reduced fluid content and edema, indicating a decrease in inflammation and improved healing; Histograms: The histograms provide a graphical representation of the pixel intensity distribution within the ACL. The shift of the histogram towards the left (darker values) in the post-treatment image indicates a decrease in the overall signal intensity within the ACL. This further supports the visual observation of reduced inflammation and improved healing.



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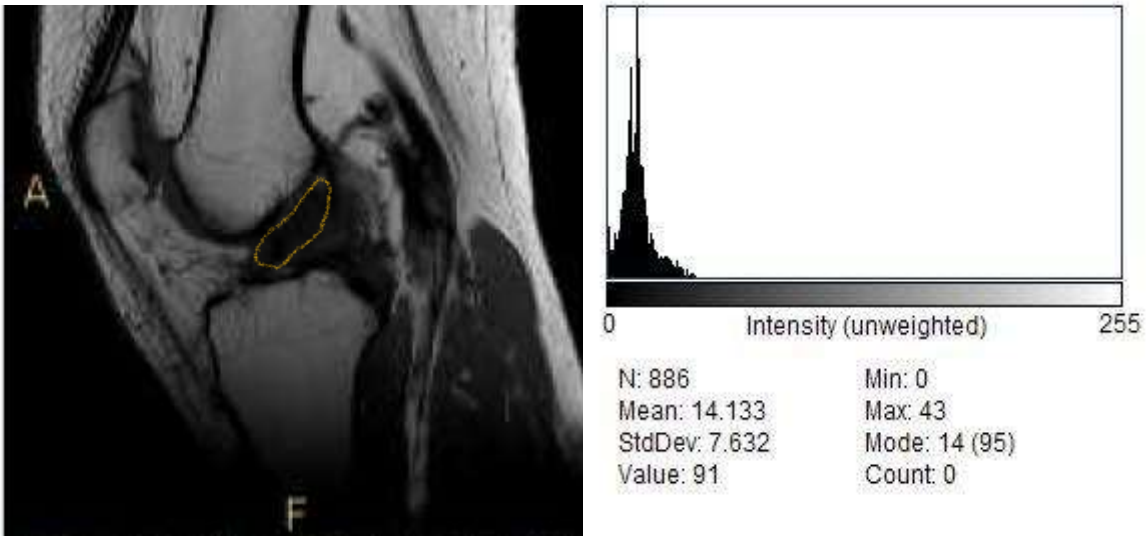

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Figure 1. (A) MRI of the right knee joint and histogram at pre-treatment showed a thickened ACL with irregular architecture, disorganized fibers, and increased signal intensity over its mid-portion ligament (arrows). (B) MRI and histogram at 6 months posttreatment showed a thinner ACL with more organized architecture and decreased signal intensity over its main fibers (arrows). The histogram showed the leftward shift in pixels to a darker value.

3. Discussion

Partial tears of the anterior cruciate ligament (ACL) present a formidable challenge in the realm of sports medicine and orthopedics. These injuries, characterized by incomplete disruption of the ACL fibers, occupy a perplexing middle ground between minor sprains and complete ruptures, often leaving clinicians grappling with diagnostic uncertainties and therapeutic dilemmas. Unlike complete ACL tears, which typically manifest with clear-cut symptoms and necessitate surgical intervention to restore knee stability, partial tears present a spectrum of clinical presentations and an unpredictable natural history, making their management a complex and nuanced

endeavor. One of the primary challenges in managing partial ACL tears lies in their elusive nature. These injuries often lack the hallmark signs and symptoms associated with complete ACL ruptures, such as a distinct "pop" sensation, hemarthrosis (bleeding into the joint), and immediate, profound instability. The pain associated with partial ACL tears can be variable, ranging from mild discomfort to severe pain that limits daily activities. The onset of pain may be immediate, as in the case of an acute injury, or gradual and insidious, making it difficult to pinpoint the exact time of injury. Patients may experience a sense of "giving way" or "buckling" in the knee, particularly during activities that involve pivoting or cutting movements. However, this instability may be subtle and intermittent, making it challenging to elicit during a physical examination. The degree of functional limitation varies widely among patients with partial ACL tears. Some individuals may experience minimal limitations and continue to participate in their usual activities, while others may have significant difficulty with activities that require knee stability, such as running, jumping, and pivoting. The variability in clinical presentation often makes it difficult to distinguish partial ACL tears from other knee injuries, such as meniscal tears, patellofemoral pain syndrome, and ligamentous sprains. This diagnostic uncertainty can delay appropriate treatment and potentially lead to long-term complications. Diagnosing a partial ACL tear requires a comprehensive and meticulous approach, integrating the patient's history, physical examination findings, and imaging studies. A detailed history, including the mechanism of injury, the onset and nature of symptoms, and any previous knee injuries, is crucial in guiding the diagnostic process. Patients often report a twisting injury or a sudden deceleration, followed by pain and a sense of instability. However, the history may be vague and nonspecific, particularly in cases of chronic or insidious onset. A thorough physical examination is essential to assess the range of motion, ligamentous stability, and presence of effusion in the knee joint. Specific tests, such as the Lachman test, anterior drawer test, and pivot shift test, can help assess the integrity of the ACL. However, these tests may be less reliable in diagnosing partial tears compared to complete ruptures, as the remaining intact fibers can mask the instability. Magnetic resonance imaging (MRI) is the gold standard for visualizing the ACL and assessing its integrity. MRI can accurately identify partial tears, characterizing the extent of fiber disruption, the location of the tear, and the presence of associated injuries, such as meniscal tears or bone contusions. However, even with MRI, diagnosing partial ACL tears can be challenging, as the imaging findings can be subtle and require expert interpretation. The management of partial ACL tears presents a therapeutic dilemma, with no universally accepted treatment algorithm. Traditional treatment approaches include conservative management and surgical reconstruction, each with its own set of advantages and disadvantages. Conservative management, encompassing physiotherapy, bracing, and activity modification, aims to reduce pain, restore knee function, and prevent further injury. Physiotherapy focuses on strengthening the muscles around the knee, improving proprioception (body awareness), and restoring normal movement patterns. Bracing provides external support to the knee, limiting excessive movement and protecting the healing ligament. Activity modification involves avoiding activities that stress the ACL, such as pivoting and cutting movements. While conservative management can be effective for some patients with partial ACL tears, it may not adequately address the underlying ligamentous instability, potentially leading to persistent pain, recurrent instability episodes, and the development of early-onset osteoarthritis. Moreover, the success of conservative management hinges on patient compliance with rehabilitation protocols and activity restrictions, which can be challenging to maintain, particularly for active individuals. Surgical reconstruction involves replacing the torn ACL with a graft, typically harvested from the patient's own hamstring tendons or patellar tendon. This procedure aims to restore knee stability and allow patients to

return to high-demand activities. However, surgical reconstruction is associated with a prolonged recovery period, potential donor site morbidity, and the risk of complications such as infection and arthrofibrosis. The decision to pursue surgical intervention for partial ACL tears is often individualized, based on factors such as the extent of the tear, the patient's activity level, age, and their response to conservative management. However, the lack of a clear consensus on the optimal surgical indications for partial tears highlights the need for careful patient selection and shared decision-making. The limitations of traditional treatment approaches for partial ACL tears have spurred the quest for innovative therapies that can effectively promote ligament healing and restore knee function while minimizing the risks and limitations associated with conservative management and surgical reconstruction. Biological therapies, such as platelet-rich plasma (PRP) and its advanced iteration, Activated Growth Factors (AGF), have emerged as promising alternatives, offering a less invasive, biologically-driven approach to ligament healing and regeneration. These therapies harness the body's innate healing capacity by delivering a concentrated dose of growth factors to the injured site, stimulating cell proliferation, matrix synthesis, and angiogenesis, and fostering a more favorable environment for ligament repair. While the evidence for the use of PRP and AGF in the treatment of partial ACL tears is still evolving, preliminary studies and case reports, including the present case, have demonstrated encouraging results, suggesting their potential to bridge the gap between conservative management and surgical reconstruction.[11,12]

Musculoskeletal medicine is experiencing a paradigm shift, moving away from traditional treatments that primarily focus on symptom management and surgical interventions towards a more biologically-driven approach that harnesses the body's innate healing capabilities. This shift is fueled by the rise of biological therapies, which utilize naturally occurring substances to promote tissue regeneration and repair, offering new hope for patients with a wide range of musculoskeletal conditions. Among these therapies, platelet-rich plasma (PRP) has emerged as a frontrunner, captivating the attention of clinicians and researchers alike for its potential to revolutionize the treatment of musculoskeletal injuries. PRP, a concentrated suspension of platelets derived from autologous blood, has garnered significant attention in recent years for its remarkable ability to accelerate healing and regeneration in musculoskeletal tissues. This biological elixir, rich in growth factors, cytokines, and other bioactive molecules, acts as a potent catalyst for tissue repair, stimulating cell proliferation, matrix synthesis, and angiogenesis. The therapeutic potential of PRP lies in its unique composition. Platelets, the tiny cell fragments responsible for blood clotting, also play a pivotal role in tissue healing and regeneration. Stimulates cell proliferation and migration, attracting cells involved in tissue repair to the injured site. Promotes the synthesis of collagen and other extracellular matrix components, providing the structural framework for tissue regeneration. Stimulates the formation of new blood vessels (angiogenesis), delivering essential nutrients and oxygen to the healing tissues. These growth factors, along with other bioactive molecules present in PRP, orchestrate a complex symphony of cellular and molecular events that promote tissue regeneration and repair. By concentrating these growth factors, PRP amplifies the body's natural healing response, accelerating the healing process and improving clinical outcomes. PRP injections have shown promising results in the treatment of tendonitis, a common condition characterized by inflammation or degeneration of tendons. The growth factors in PRP stimulate tendon cell proliferation and matrix synthesis, promoting tendon healing and reducing pain. PRP has also emerged as a potential treatment for osteoarthritis, a degenerative joint disease that affects millions worldwide. The growth factors in PRP can stimulate cartilage regeneration, reduce inflammation, and improve joint function. PRP has shown encouraging results in the treatment of

ligament injuries, including partial and complete tears. The growth factors in PRP promote ligament healing and regeneration, restoring knee stability and function. PRP has also been investigated in the treatment of muscle injuries, such as strains and tears. The growth factors in PRP can accelerate muscle healing, reduce scar tissue formation, and improve muscle function. PRP has been shown to enhance fracture healing by stimulating bone formation and promoting callus formation. PRP can be used as an adjunct to surgical procedures, such as tendon repairs and ligament reconstructions, to enhance healing and improve outcomes. The use of PRP in the treatment of ACL injuries, particularly partial tears, has gained significant traction in recent years. Several studies have investigated the efficacy of PRP in promoting ACL healing and regeneration, with encouraging results. Animal studies have demonstrated that PRP can enhance the healing of ACL grafts, improving graft integration and promoting collagen formation. These findings suggest that PRP can augment the biological healing response, leading to stronger and more resilient grafts. Human studies have also shown promising results, with PRP injections improving clinical outcomes in patients with ACL injuries. PRP has been shown to reduce pain, improve knee stability, and accelerate the return to sports and other activities. While the evidence for the use of PRP in ACL injuries is still evolving, the existing data suggest that it can play a valuable role in promoting ligament healing and regeneration, particularly in the context of partial tears. The field of PRP therapy is constantly evolving, with ongoing research aimed at optimizing its preparation, delivery, and therapeutic efficacy. One of the key areas of focus is the development of more targeted therapies that can specifically address the underlying pathology of different musculoskeletal conditions. AGF represents an advanced PRP modality that employs a proprietary protocol to optimize growth factor concentration and release. This process aims to maximize the concentration of growth factors delivered to the injured tissue, potentially accelerating the healing process and improving clinical outcomes. Leukocyte-poor PRP is a variation of PRP that contains a lower concentration of white blood cells. This may be beneficial in certain conditions, as white blood cells can contribute to inflammation and pain. PRF is another variation of PRP that contains a higher concentration of fibrin, a protein involved in blood clotting and wound healing. PRF forms a gel-like matrix that can be used to deliver growth factors to the injured site.[13,14]

Platelet-rich plasma (PRP) therapy has revolutionized the field of regenerative medicine, offering a promising approach to harnessing the body's natural healing capabilities. However, the inherent limitations of conventional PRP, such as variable growth factor concentrations and short-lived release kinetics, have spurred the development of advanced modalities to enhance its therapeutic efficacy. Among these advancements, Activated Growth Factors (AGF) stands out as a paradigm shift in PRP therapy, pushing the boundaries of regenerative medicine and offering new hope for patients with musculoskeletal injuries. AGF represents an evolution of PRP, meticulously engineered to optimize the concentration, activation, and release of growth factors, thereby amplifying its therapeutic potential. A two-step centrifugation process is employed to isolate and concentrate platelets from the patient's blood. The first spin separates the red blood cells from the platelet-rich plasma, while the second spin further concentrates the platelets, resulting in a platelet concentration significantly higher than that found in whole blood. This meticulous concentration process ensures a potent cocktail of growth factors within the final AGF product. Unlike conventional PRP, which relies on passive activation upon contact with tissue collagen, AGF is actively activated using calcium chloride. This precise activation triggers a rapid and robust release of growth factors, maximizing their bioavailability at the injured site. The AGF preparation protocol is meticulously designed to optimize the concentration and release of key growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular

endothelial growth factor (VEGF). These growth factors play pivotal roles in tissue regeneration and repair, stimulating cell proliferation, matrix synthesis, and angiogenesis. The therapeutic efficacy of AGF stems from its multifaceted mechanisms of action, which synergistically promote tissue healing and regeneration. The high concentration of growth factors in AGF, coupled with its precise activation, ensures a potent and sustained delivery of these essential signaling molecules to the injured site. This creates a microenvironment conducive to tissue repair, stimulating the migration and proliferation of cells involved in the healing process. AGF's growth factors act as potent mitogens, stimulating the proliferation of fibroblasts, tendon cells, chondrocytes, and other cells involved in tissue regeneration. This accelerated cell proliferation facilitates the formation of new tissue, replacing damaged or lost structures. AGF promotes the synthesis of collagen, elastin, and other extracellular matrix components, providing the structural framework for tissue regeneration. This matrix synthesis not only restores the structural integrity of injured tissues but also provides a scaffold for cell migration and proliferation. AGF stimulates the formation of new blood vessels, delivering essential nutrients and oxygen to the healing tissues. This enhanced angiogenesis supports the metabolic demands of tissue regeneration and promotes a faster and more complete healing process. AGF also plays a role in modulating the inflammatory response, reducing pain and swelling and creating a more favorable environment for healing. This modulation of inflammation prevents excessive tissue damage and promotes a more efficient healing process. The use of AGF in the treatment of partial ACL tears represents a promising frontier in regenerative medicine. While the clinical data on AGF for partial ACL tears is still emerging, preliminary studies and case reports, including the present case, have provided compelling evidence of its therapeutic potential. AGF's ability to stimulate cell proliferation, matrix synthesis, and angiogenesis makes it an ideal candidate for promoting ligament healing and regeneration. The growth factors in AGF can stimulate the proliferation of fibroblasts, the key cells involved in ligament repair, and enhance the synthesis of collagen and other extracellular matrix components, restoring the structural integrity of the injured ACL. AGF's modulation of the inflammatory response can lead to a significant reduction in pain and swelling, improving the patient's comfort and facilitating their rehabilitation. By promoting ligament healing and restoring its structural integrity, AGF can improve knee stability, reducing the risk of recurrent instability episodes and long-term complications such as osteoarthritis. AGF's ability to accelerate the healing process can facilitate a faster and more complete return to pre-injury activity levels. This can have a profound impact on the patient's quality of life, allowing them to resume their favorite sports and activities sooner. AGF represents a paradigm shift in PRP therapy, offering a more refined and potent approach to harnessing the body's regenerative potential. Its meticulous preparation protocol, precise activation, and optimized growth factor concentration and release distinguish it from conventional PRP, potentially amplifying its therapeutic efficacy and expanding its clinical applications. The use of AGF in the treatment of partial ACL tears is a testament to its potential to revolutionize the management of musculoskeletal injuries. By promoting ligament healing, reducing pain, improving knee stability, and accelerating the return to activity, AGF offers new hope for patients seeking a less invasive, biologically-driven approach to restoring their musculoskeletal health.[15,16]

This case report provides a compelling narrative of a patient's journey through the complexities of a partial ACL tear and the remarkable recovery achieved through Activated Growth Factors (AGF) treatment. By meticulously documenting the patient's clinical course, from initial presentation to long-term follow-up, this report offers valuable insights into the therapeutic potential of AGF in promoting ligament healing, restoring knee stability, and improving functional outcomes. The patient, a 39-year-old male

and avid recreational soccer player, presented with right knee pain and instability following a twisting injury sustained during a soccer game. The initial assessment, encompassing a detailed history, physical examination, and magnetic resonance imaging (MRI), confirmed a partial tear of the anteromedial bundle of the ACL. Given the patient's active lifestyle and desire to return to sports, a treatment plan focused on maximizing healing and restoring knee function was paramount. After careful consideration of the available options, including conservative management and surgical reconstruction, the patient opted for a trial of AGF injections, drawn to its potential for accelerated healing and a less invasive approach. At the initial presentation, the patient reported significant pain, rated 7 out of 10 on the Visual Analog Scale (VAS). Physical examination revealed tenderness along the medial joint line, mild effusion, and a positive Lachman test, indicative of ACL laxity. The patient's functional limitations were evident in his inability to participate in sports and his restricted daily activities. 3 months post-treatment, the patient demonstrated remarkable progress. His pain had significantly subsided, with a VAS score of 2 out of 10. Knee stability had improved, with a less pronounced Lachman test. Functionally, the patient had progressed to light jogging and cycling, demonstrating a significant improvement in his ability to perform daily activities and engage in low-impact exercises. At the 6-month follow-up, the patient's recovery was even more pronounced. His pain had further reduced to a VAS score of 1 out of 10, and his knee stability had returned to normal, with a negative Lachman test. Functionally, the patient had achieved a near-complete recovery, returning to full participation in recreational soccer without any limitations. The significant reduction in pain experienced by the patient throughout his recovery underscores AGF's potent anti-inflammatory and analgesic effects. By modulating the inflammatory response and promoting tissue healing, AGF effectively alleviated the patient's pain, improving his comfort and facilitating his rehabilitation. The restoration of normal knee stability, as evidenced by the negative Lachman test at 6 months, demonstrates AGF's ability to promote ligament healing and restore its structural integrity. This enhanced stability not only allows patients to return to their pre-injury activity levels but also reduces the risk of recurrent instability episodes and long-term complications such as osteoarthritis. The patient's remarkable functional recovery, culminating in his return to full participation in recreational soccer, highlights AGF's ability to restore knee function and improve quality of life. By accelerating the healing process and promoting tissue regeneration, AGF enables patients to regain their mobility, strength, and confidence, allowing them to resume their favorite activities without limitations. The patient's rapid return to sports within 6 months of treatment underscores AGF's potential to accelerate the recovery process. This accelerated return to activity can have a profound impact on the patient's physical and psychological well-being, allowing them to regain their active lifestyle and participate in the activities they enjoy. The patient's decision to pursue AGF treatment stemmed from his desire for a less invasive, biologically-driven approach to healing. AGF, with its ability to harness the body's innate regenerative capabilities, offers a compelling alternative to traditional treatment modalities, such as surgical reconstruction, which often involves a prolonged recovery period, potential donor site morbidity, and the risk of complications. The patient's successful outcome with AGF highlights its potential to bridge the gap between conservative management and surgical intervention, providing a middle-ground approach that maximizes healing and restores function while minimizing the risks and limitations associated with more invasive procedures. The patient's clinical journey also exemplifies the principles of personalized medicine, tailoring treatment strategies to individual patient needs and preferences. In this case, the patient's active lifestyle, desire to return to sports, and apprehension towards surgical intervention guided the decision to pursue AGF treatment. The patient's positive response to AGF

underscores the importance of considering individual patient factors when making treatment decisions. By taking a personalized approach, clinicians can optimize treatment outcomes and improve patient satisfaction.[17,18]

Activated Growth Factors (AGF) therapy represents a fascinating intersection of biology, technology, and clinical practice. While its therapeutic benefits are becoming increasingly evident, the intricate mechanisms by which AGF orchestrates tissue regeneration and repair remain an area of active exploration. This section delves into the fascinating world of AGF's biological effects, unraveling the complex interplay of growth factors, inflammatory mediators, and cellular responses that contribute to its remarkable regenerative potential. At the heart of AGF's therapeutic efficacy lies a symphony of growth factors, meticulously orchestrated to promote tissue regeneration and repair. These growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), act as potent signaling molecules, triggering a cascade of cellular and molecular events that culminate in tissue healing. PDGF, a key player in the AGF orchestra, acts as a potent mitogen, stimulating the proliferation and migration of fibroblasts, the key cells involved in ligament healing. These fibroblasts, guided by PDGF's signals, migrate to the injured site, where they begin to synthesize new collagen and other extracellular matrix components, laying the foundation for tissue regeneration. TGF-β, another vital component of the AGF symphony, plays a crucial role in tissue remodeling and scar formation. It stimulates the production of collagen and other extracellular matrix proteins, providing the structural framework for tissue regeneration. TGF-β also modulates the inflammatory response, preventing excessive tissue damage and promoting a more organized healing process. VEGF, the conductor of angiogenesis, orchestrates the formation of new blood vessels, delivering essential nutrients and oxygen to the healing tissues. This enhanced vascularization supports the metabolic demands of tissue regeneration, ensuring a robust and efficient healing process. The synergistic interplay of these growth factors, along with other bioactive molecules present in AGF, creates a microenvironment conducive to tissue repair, stimulating cell proliferation, matrix synthesis, and angiogenesis. This orchestrated symphony of growth factors is a testament to the complexity and elegance of AGF's biological effects. Inflammation, a double-edged sword in the healing process, plays a crucial role in initiating tissue repair but can also lead to excessive tissue damage and prolonged recovery. AGF, with its intricate network of inflammatory mediators, exerts a fine-tuned control over the inflammatory response, taming the flames of inflammation and promoting a more balanced healing environment. AGF contains a variety of anti-inflammatory cytokines, such as interleukin-1 receptor antagonist (IL-1ra) and interleukin-10 (IL-10), which counteract the pro-inflammatory signals that initiate and perpetuate the inflammatory response. These anti-inflammatory cytokines help to limit tissue damage and promote a more controlled healing process. AGF also harbors specialized pro-resolving mediators, such as resolvins and protectins, which actively promote the resolution of inflammation. These mediators orchestrate the clearance of inflammatory cells and debris, facilitating the transition from the inflammatory phase to the proliferative and remodeling phases of healing. The growth factors in AGF also contribute to inflammatory modulation. TGF-β, for instance, plays a dual role in both promoting and suppressing inflammation, depending on the context and stage of healing. This intricate balance ensures that inflammation is appropriately regulated, facilitating tissue repair without excessive damage. By modulating the inflammatory response, AGF creates a more favorable microenvironment for healing and regeneration, facilitating the restoration of tissue homeostasis and promoting a faster and more complete recovery. The healing and remodeling of a partially torn ACL is a complex and dynamic process, involving a carefully choreographed sequence of cellular and molecular events. AGF, with its potent

cocktail of growth factors and inflammatory mediators, plays a pivotal role in orchestrating this regenerative tale. The initial phase of ligament healing involves hemostasis, the cessation of bleeding, and inflammation, the recruitment of immune cells to the injured site. AGF's platelets contribute to hemostasis by forming a platelet plug, while its growth factors and inflammatory mediators regulate the inflammatory response, preventing excessive tissue damage and initiating the healing cascade. The proliferative phase of ligament healing is characterized by the proliferation and migration of fibroblasts, the key cells involved in ligament repair. AGF's growth factors, particularly PDGF, stimulate fibroblast proliferation and migration, guiding these cells to the injured site, where they begin to synthesize new collagen and other extracellular matrix components. The remodeling phase of ligament healing involves the deposition and reorganization of collagen and other extracellular matrix components, restoring the structural integrity of the ligament. AGF's growth factors, particularly TGF-β, promote matrix synthesis and remodeling, ensuring that the newly formed ligament is strong, resilient, and functionally adapted to the demands placed upon it. Throughout the healing process, angiogenesis, the formation of new blood vessels, plays a crucial role in delivering essential nutrients and oxygen to the regenerating tissues. AGF's VEGF stimulates angiogenesis, ensuring that the healing ligament receives adequate blood supply to support its metabolic demands. The intricate interplay of growth factors, inflammatory mediators, and cellular responses in AGF promotes a well-orchestrated healing and remodeling process, ultimately restoring the ligament's structural integrity and functional capacity. The reduction in pain experienced by patients following AGF treatment is a testament to its multifaceted mechanisms of action. By modulating the inflammatory response, AGF reduces the production of pro-inflammatory cytokines and other mediators that contribute to pain signaling. This dampening of the inflammatory cascade effectively alleviates pain and promotes a more comfortable healing environment. As AGF promotes ligament healing and restores its structural integrity, knee stability improves, reducing the mechanical stress and strain that can contribute to pain. This improved stability not only alleviates pain but also reduces the risk of recurrent injury and long-term complications. AGF's ability to accelerate tissue regeneration and repair contributes to pain reduction by restoring the structural and functional integrity of the injured tissues. This enhanced healing promotes a faster and more complete recovery, reducing the duration and intensity of pain. By addressing the underlying causes of pain through these multifaceted mechanisms, AGF provides a comprehensive approach to pain management, improving the patient's quality of life and facilitating their return to normal activities.[19,20]

4. Conclusion

This case report presents compelling evidence for the potential of Activated Growth Factors (AGF) as a safe and effective treatment modality for partial anterior cruciate ligament (ACL) tears. The patient demonstrated remarkable improvements in pain, stability, and function, ultimately returning to pre-injury activity levels within 6 months of treatment. This positive outcome highlights the potential of AGF to promote accelerated healing and tissue regeneration, offering a promising alternative to traditional treatment approaches.

5. References

1. Murata K, Kokubun T, Onitsuka K, Oka Y, Kano T, Morishita Y, et al. Controlling joint instability after anterior cruciate ligament transection inhibits transforming growth factor-beta-mediated osteophyte formation. Osteoarthritis Cartilage. 2019; 27(8): 1185–96.
2. Schlecht SH, Martin CT, Ochocki DN, Nolan BT, Wojtys EM, Ashton-Miller JA. Morphology of mouse anterior cruciate ligament-complex changes following exercise during pubertal growth. J Orthop Res. 2019; 37(9): 1910–9.

3. Gögele C, Hahn J, Elschner C, Breier A, Schröpfer M, Prade I, et al. Enhanced growth of Lapine anterior cruciate ligament-derived fibroblasts on scaffolds embroidered from poly(l-lactide-co-ε-caprolactone) and polylactic acid threads functionalized by fluorination and hexamethylene diisocyanate cross-linked collagen foams. Int J Mol Sci. 2020; 21(3): 1132.
4. Murata KP, OKa Y, Onitsuka K, Kokubun T, Nakajima A, Arakawa K, et al. Controlling joint instability after anterior cruciate ligament transection inhibits the transforming growth factor-beta-mediated osteophyte formation. Osteoarthritis Cartilage. 2020; 28: S204.
5. Mendias CL, Enselman ERS, Olszewski AM, Gumucio JP, Edon DL, Konnaris MA, et al. The use of recombinant human growth hormone to protect against muscle weakness in patients undergoing anterior cruciate ligament reconstruction: a pilot, randomized placebo-controlled trial. Am J Sports Med. 2020; 48(8): 1916–28.
6. Lee SH, Cho HG, Song JS, Chun KC, Chun CH. Quantitative assessment of neural elements in a rat model using nerve growth factor after remnant-preserving anterior cruciate ligament reconstruction: a histological and immunofluorescence pilot study. Research Square. 2020.
7. Lee SH, Cho HG, Song JS, Chun KC, Chun CH. Quantitative assessment of neural elements in a rat model using nerve growth factor after remnant-preserving anterior cruciate ligament reconstruction: a histological and immunofluorescence pilot study. J Orthop Surg Res. 2020; 15(1): 277.
8. Utomo DN, Mahyudin F, Zulkarnain A, Purwati P, Setyawati R. Intraarticular allogenic mesenchymal stem cells and Vascular endothelial growth factor injection in anterior cruciate ligament reconstruction. Folia Medica Indones. 2021; 56(1): 41.
9. Van Genechten W, Hevesi M, Olson N, Carstens M, Krych AJ, Verdonk P, et al. Anterior cruciate ligament graft healing by peptide-based vascular endothelial growth factor and bone morphogenetic protein recruitment. J Cartilage Joint Preserv. 2021 Dec;1(4):100030.
10. Fury MS, Paschos NK, Fabricant PD, PLUTO Study Group, Anderson CN, Busch MT, et al. Assessment of skeletal maturity and postoperative growth disturbance after anterior cruciate ligament reconstruction in skeletally immature patients: a systematic review. Am J Sports Med. 2022; 50(5): 1430–41.
11. Howe D, Cone SG, Piedrahita JA, Collins B, Fordham LA, Griffith EH, et al. Sex-specific biomechanics and morphology of the anterior cruciate ligament during skeletal growth in a porcine model. J Orthop Res. 2022; 40(8): 1853–64.
12. Shultz SJ, Cruz MR, Casey E, Dompier TP, Ford KR, Pietrosimone B, et al. Sex-specific changes in physical risk factors for anterior cruciate ligament injury by chronological age and stages of growth and maturation from 8 to 18 years of age. J Athl Train. 2022; 57(9–10): 830–76.
13. Bolzinger M, Thevenin Lemoine C, Flumian C, Nicolaou N, Sales de Gauzy J, Accadbled F. Analysis of growth after transphyseal anterior cruciate ligament reconstruction in children. J Pediatr Orthop. 2023; 43(9): 537–42.
14. Hacquart T, Erivan R, Dressaire M, Villatte G, Perrey A, Pereira B, et al. Growth progression of anterior cruciate ligament bone grafts in a pediatric population: magnetic resonance imaging analysis. Pediatr Radiol. 2023; 53(12): 2369–79.
15. Faunø PZ, Bøge Steinmeier Larsen J, Nielsen MM, Hellfritzsch M, Nielsen TG, Lind M. The risk of growth disturbance is low after pediatric anterior cruciate ligament

reconstruction with a femoral growth plate sparing technique. Arthrosc Sports Med Rehabil. 2023; 5(6): 100793.

16. Sinkler MA, Furdock RJ, McMellen CJ, Calcei JG, Voos JE. Biologics, stem cells, growth factors, platelet-rich plasma, hemarthrosis, and scaffolds may enhance anterior cruciate ligament surgical treatment. Arthroscopy. 2023; 39(2): 166–75.
17. Zachurzok A, Mayr J, Rutz E, Tomaszewski R. Dimensions of the anterior cruciate ligament and thickness of the distal femoral growth plate in children: a MRI-based study. Arch Orthop Trauma Surg. 2023; 143(5): 2363–72.
18. Fabricant PD, Chipman DE, Pascual-Leone N, Bram J, Salvato D, Green DW. Simultaneous anterior cruciate ligament reconstruction and implant-mediated guided growth to correct genu valgum in skeletally immature patients. J ISAKOS. 2023; 8(3): 184–8.
19. Patil V, Rajan P, Hayter E, Bartlett J, Symons S. Growth disturbances following paediatric anterior cruciate ligament reconstruction: a systematic review. Cureus. 2023; 15(6): e40455.
20. Sharma V, Sakhalkar U, Nadkarni P, Mishal R, Parandhaman D, Vichare K, et al. Cytoprotective effect of growth factors derived from platelets on corticosteroid-treated Primary anterior cruciate ligament-derived stromal cells and chondrocytes. Cureus. 2024; 16(7): e65566.