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Ulnar nerve dysfunction at the elbow after platelet-rich plasma treatment for partial ulnar collateral ligament injuries

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Background: Platelet-rich plasma (PRP) has been used for the treatment of partial ulnar collateral ligament (UCL) tears of the elbow in throwing athletes. Very few studies have focused on the complication profile of PRP in this application.The purpose of this study was to discuss the complication of ulnar nerve fibrosis and resulting cubital tunnel syndrome after a PRP injection for a partial UCL injury.
Methods: A retrospective review of 3 high-level baseball players who underwent a PRP injection for treatment of their partial UCL injury was completed. All 3 were noted to have an asymptomatic subluxing ulnar nerve at time of presentation. Their postinjection course is discussed, and the complication of cubital tunnel syndrome highlighted.
Results: All 3 players developed cubital tunnel syndrome with significant fibrosis surrounding their ulnar nerve.
Conclusion: PRP injections for the treatment of partial UCL injuries of the elbow may place some patients at risk of developing postinjection cubital tunnel syndrome from increased fibrosis around the ulnar nerve. This complication may be more likely to develop in patients who present with a subluxing ulnar nerve.

Injuries involving the ulnar collateral ligament (UCL) at the elbow have increased over the last ten years. Injury to the UCL is caused by a valgus stress across the elbow joint and is oftentimes seen in overhead throwing athletes. The late cocking and acceleration phases, during the throwing motion, place great stress across the UCL and can lead to microscopic tears in the ligament.[5,16] Although surgical reconstruction is often necessary for mid-substance tears to allow for return to play, conservative treatment remains the recommended initial plan for partial tears. The success rate of nonoperative management of these injuries varies throughout the literature, with the reported return to play rates varying from 42% to 84%, with most authors utilizing a rehabilitation protocol that included rest followed by a gradual strengthening and throwing program.[12,13,22] In the hopes of improving the success rate of nonoperative management for these injuries, many have begun to use orthobiologics in the treatment of their patients with partial UCL tears. Platelet-rich plasma (PRP) has been utilized to treat partial UCL tears with the hope of achieving better healing of the ligament and faster return to preinjury status.

PRP is autologous blood that has been centrifuged down to separate out the platelets which contain growth factors and cytokines.[2] There is leukocyte-rich PRP (PRP_{LR}), which contains leukocytes and has proinflammatory effects, and there is leukocyte-poor PRP (PRP_{LP}), in which the leukocytes have been removed and has anti-inflammatory effects.[10] A study by Podesta et al used PRP_{LR} injections and guided physical therapy regimens to treat partial tears. They showed an 88% return to play at an average of 12 weeks.[21] The reported improvement seen with the addition of PRP is believed to be due to the ability of platelets to release multiple growth factors and cytokines. The alpha granules in platelets contain a concentrated source of growth factors, specifically vascular endothelial growth factor, transforming growth factor (TGF-β), insulin-like growth factor, fibroblastic growth factor, and epidermal growth factor.[11] These growth factors play important roles in cell proliferation, chemotaxis, cell differentiation, and angiogenesis to enhance healing at the injection site. Although the use of PRP to treat partial UCL tears appears promising, most studies have not examined the potential adverse effects associated with its use.

Institutional review board approval was not required for this study.

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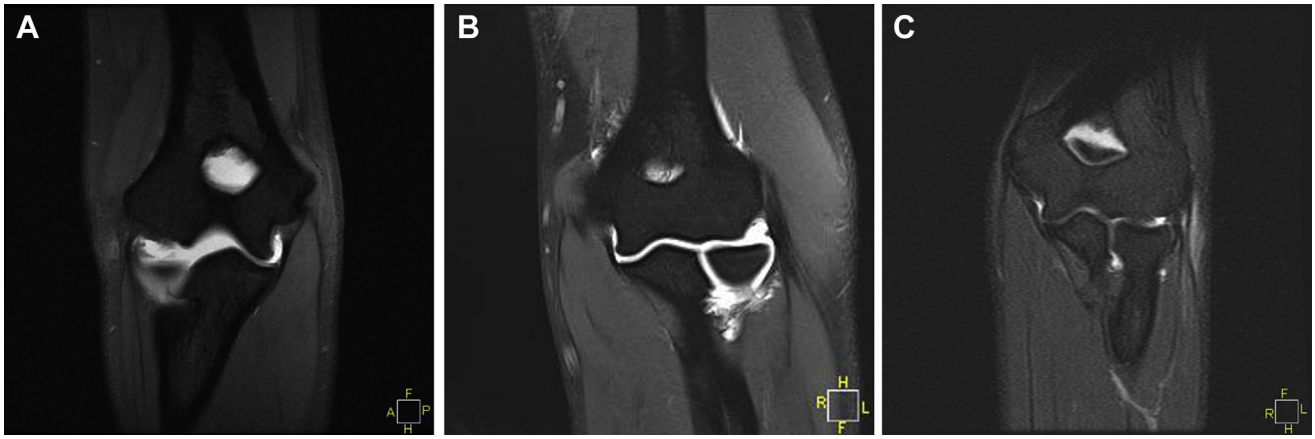

Figure 1 (A–C) MRI arthrogram images of the 3 patients showing disruption of the proximal insertion site of the ulnar collateral ligament.

Many series looking at the application of PRP for partial UCL tears report few if any complications, with mild swelling and tenderness being cited.[7,9,21] However, most reports do not include long-term follow-up, which may yield a higher incidence of adverse findings. Furthermore, recent publications have seemed to dim the initial enthusiasm for the use of PRP in partial UCL injuries.[4] Therefore, acknowledgment of a higher possible complication rate must be taken into consideration when treating these athletes. The purpose of our article is to present a case series of PRP induced ulnar nerve dysfunction at the elbow after treatment of a partial UCL injury. A commonly found sequence of events supported by characteristic findings on history and examination will be presented, along with a proposed etiology and treatment. The fact that the patients in our series did show healing of the UCL though must be stressed, and suggestions on the use of PRP to avoid ulnar nerve dysfunction will be made.

Cases

After a waiver was granted by the institutional review board, a retrospective chart review was performed for patients who had undergone a PRP injection for a partial UCL tear and subsequently developed ulnar nerve neuritis. We identified 3 patients who met these criteria and received a PRP injection between 2017 and 2019.

All patients were young males, with an average age of 17.7 years old. None of the patients had any underlying comorbidities, were smokers, or were on any antiplatelet or anti-inflammatory medications. They were all collegiate level baseball players who had similar initial presenting symptoms, which included pain at the medial elbow and a decrease in their throwing velocity. In addition, they all had positive examination findings consistent with a UCL injury on valgus stress of the elbow. Interestingly, all 3 patients were also noted to have a subluxing ulnar nerve on initial physical examination; however, none of the patients had any ulnar nerve symptoms at rest or after a trial of throwing. No ulnar nerve paresthesia or weakness was noted on examination. Each patient underwent an MR arthrogram to verify injury to the UCL. In each of the 3 patients, a partial injury was seen at the proximal insertion site of the UCL (Fig. 1, A–C).

After a trial of conservative therapy failed to relieve their symptoms, they all elected to undergo a PRP injection. Approximately 60cc of autologous blood was drawn from the contralateral antecubital fossa. The Arthrex Angel System (Arthrex, Naples, FL, USA) was used to spin the whole blood down to separate out the PRP from the platelet poor plasma and red blood cells. Immediately after obtaining the PRP, a sterile preparation of the medial elbow was completed and approximately 5cc of PRP_{LP} was injected around the proximal UCL tear site under fluoroscopic visualization. No additional activating agents were added to the concentrate before injection. To ensure consistent placement of the injection, palpation of the medial epicondyle and aiming the needle from distal to proximal toward the proximal UCL attachment was completed. All of the injections were completed by a single surgeon. The platelet concentration was approximately 1145.3 ± 488.4 x $10^3/\mu L$ (range 1633.7-656.9 x $10^3/\mu L$). After PRP injection, a sterile bandage was placed on the injection site and the arm placed into a sling. All patients were instructed to avoid NSAIDs for 2 weeks after injection to not affect the platelet's healing potential. After the injection, the patients underwent 2 weeks of rest and gentle range of motion followed by a graduated rehabilitation program, described by Podesta et al.[21] This included starting formal physical therapy at week 2, focusing on range of motion, and avoiding valgus stress to the elbow. By week 5, strengthening and valgus loading were initiated. At week 8, an interval throwing program was started with a goal of return to play by week 12.

Each patient completed the directed rehab program and felt like their symptoms were improving. However, all 3 patients were seen back in clinic after PRP injection, with symptoms consistent with ulnar nerve dysfunction. All 3 patients had intermittent numbness and tingling in the ring and small fingers, with a positive Tinel's sign and elbow flexion test. In addition, once the patients presented with signs of cubital tunnel syndrome, it was noted on examination that their ulnar nerve was no longer subluxing but was now adherent and tender in the cubital tunnel. The 3 patients presented with these ulnar nerve signs at 7 months, 6 months, and 8 months, respectively.

The decision was made to perform surgery for each patient to release their cubital tunnel. Intraoperative findings were universal for all 3 patients, with pronounced fibrosis surrounding the ulnar nerve and neurodesis of the ulnar nerve to the floor of the cubital tunnel. In addition, all were noted to have an intact and stable UCL, with no disruption of the proximal insertion site. Neurolysis of the ulnar nerve and anterior subfascial transposition was completed (Fig. 2, A–C). Postoperatively patients underwent a graduated rehabilitation program. All 3 were able to return to their preinjury level of sport with full relief of symptoms.

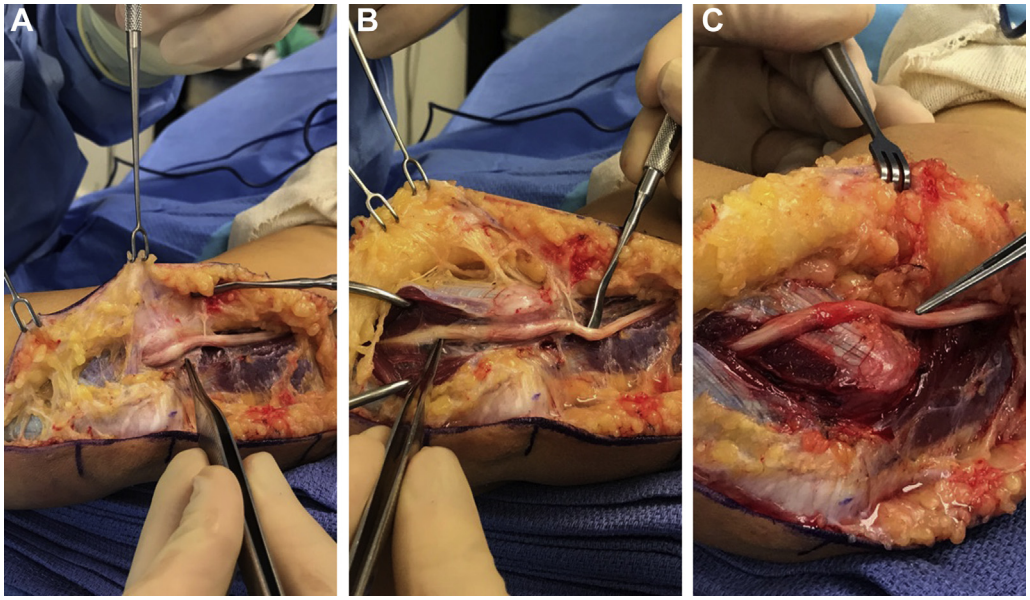

Figure 2 (**A**–**C**) Intraoperative images demonstrating significant fibrosis surrounding the ulnar nerve after the cubital tunnel has been released (**A** and **B**) and the ulnar nerve following neurolysis and anterior subfascial transposition (**C**).

Discussion

The popularity of PRP in treating musculoskeletal injuries has increased over the last 2 decades with laboratory evidence supporting its use in the treatment of muscle and tendon injuries.[1,8] Similarly, clinical studies have also shown promising results with PRP in a variety of conditions.[14,21] Combined with an increase in the development of marketed devices, which has enabled the use of PRP injections in the outpatient and office setting to be feasible, it is easy to see why its popularity has increased.[6] Initial studies, looking at the outcomes of PRP for the treatment of partial UCL injuries of the elbow, demonstrated improved outcomes compared with conservative treatment of these injuries alone.[7,9,21,22]

Surgical repair and reconstruction of the UCL after an injury has shown good results, with reported return to play at over 90%.[18,23,24] The downside of surgical management of these injuries is the long rehabilitation process, with most players returning to play at around 13 months.[18] The initial study by Rettig et al, looking at the nonoperative treatment of partial UCL injuries demonstrated that return to play could be much quicker with their patients returning at an average of 6 months. However, only 42% of their patients were successful with this treatment plan.[22] The addition of PRP offers a potential therapeutic agent to help speed up the healing process. By implementing a nonoperative treatment plan with focused rehabilitation and introducing a PRP injection, Podesta et al had an 88% return to play rate.[21] In a similar study, Deal et al demonstrated a 96% return to play when using a nonoperative treatment approach, which included a PRP injection along with an off-loading brace and an integrated rehabilitation program.[7] Dines et al reported that patients who received a PRP injection for a partial UCL tear 73% had good or excellent results. Interestingly, the higher the level of competition the patient was involved in, the better they did after PRP therapy. This was likely due to the increased resources and time the professional and collegiate players were able to spend with therapists.[9] Overall, the use of PRP for UCL injuries has shown good short-term clinical results; however, more recent literature has not been as promising.

In a recent study, which utilized the Major League Baseball Health and Injury Tracking System, a total of 544 players were found to have been treated nonoperatively for UCL injuries; of these players, 133 received PRP injections.[4] A matched comparative study was completed that demonstrated a 54% overall return to play rate. The authors also reported that players who received PRP had a longer delay in return to throwing compared with the no PRP group and a delay in return to play.[4] This recent study brings in to question the effectiveness of PRP treatment for partial UCL injuries in high-level athletes and dims the very favorable results of earlier studies. Despite the varied results, most of the studies reported a very low complication rate after injection. The only complications reported in any of the studies examining PRP in partial UCL injuries were cases of localized soft tissue swelling occurring at the site of application immediately after injection.[7,21] Likewise, very few reports detailing the possible risks of PRP injections have been discussed in the literature with most being case reports of extreme inflammation or synovitis.[17,20] A closer examination of patients symptoms after a PRP injection may lead to an increase in reported incidences.

The 3 patients in our study all had a subluxing ulnar nerve on their initial evaluation. After PRP injections, they initially felt that their symptoms were improving; however, all 3 went on to develop ulnar nerve paresthesias in their hands and had positive clinical examination findings of cubital tunnel syndrome. They were taken back to decompress the cubital tunnel and a significant amount of fibrosis surrounding the ulnar nerve was present, which was likely leading to their neuritis. It is important to note that on close examination of the UCL, after the ulnar nerve was anteriorly transposed, the ligament appeared healed without any disruption of the fibers at their attachment sites. It is possible that the increased concentration growth factors helped the ligament heal but also caused the fibrosis to develop in our 3 patients. Studies have shown that high concentrations of TGF-β1 can lead to the development of tissue fibrosis.[19] Recent studies investigating the effects of TGF-β blocking agents such as Losartan and Suramin have promising *in vitro* and animal results with decreasing fibrosis in skeletal muscle.[3,15] It is possible that administering an antifibrotic agent, such as Losartan after a PRP injection, may decrease the risk of developing ulnar nerve issues secondary to fibrosis formation. Of course, clinical and *in vivo* studies will need to be completed to

verify its effectiveness. In addition, it is possible that the patients were at a higher risk of developing postinjection complications due to their subluxing ulnar nerves. It may be worth consideration to avoid PRP injections in this patient population due to the increased possibility of postinjection ulnar nerve issues.

Conclusion

As the field of orthobiologics continues to grow and the use of PRP continues to broaden, it is important to remain aware of the possible adverse risks it may pose. The possibility of PRP induced ulnar nerve dysfunction of the elbow in partial UCL injuries should be recognized, especially in the throwing athlete with a pretreatment asymptomatic subluxing ulnar nerve.

Conflicts of interest

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