Chapter 10
Regenerative Medicine for Hand and Wrist Pain

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Osteoarthritis

Osteoarthritis (OA), or degenerative joint disease (DJD), just as it can affect any other joint in the body, can affect the hand and wrist. Currently, the treatments typically performed are palliative and analgesic and range from conservative to surgical management. Nonpharmacologic interventions include joint protection techniques, use of splints, assistive devices to perform ADLs, and physical modalities. Pharmacological interventions include topical or oral medications [1]. Although the American College of Rheumatology (ACR) does not recommend intra-articular injections [1], they are often used in patients refractory to other treatments.

The prevalence of carpometacarpal (CMC) joint arthritis in men is 21–27% and in women 24–29% [2]. CMC arthritis can result in pain, weakness, and deformity [3]. Nonpharmacologic and pharmacologic treatments should be attempted first, including a thumb spica splint and/or hand therapy [4]. Modalities such as heat, ice, transcutaneous electrical stimulation, and therapeutic ultrasound can be used. If nonpharmacologic treatment fails, then pharmacologic treatment can be attempted.

Pharmacologic treatment consists of oral or topical medications and injections. Oral medications include acetaminophen or paracetamol, various anti-inflammatories (NSAIDs, steroids), neuropathic agents (gabapentin, pregabalin), SSRIs (duloxetine), and glucosamine chondroitin. Topical medications available include capsaicin, lidocaine, and diclofenac. These agents are available in various preparations like patches, gels, or ointments. Injections that are available are steroid and viscosupplementation injections, although evidence of their effectiveness is lacking [4].

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If these nonpharmacologic and pharmacologic treatments fail, surgery remains an option. Per Vermeulen et al., there are eight common surgical procedures performed for CMC arthritis, but one has not been demonstrated to be superior to the others [3].

With the advent of regenerative medicine techniques, there is treatment available that can potentially regenerate or heal arthritic cartilage and bone. At this time, no studies have been carried out on the effects of platelet-rich plasma (PRP) or stem cell therapy on hand or wrist OA. However, there are studies looking at the effects of stem cell therapy and PRP on hip and knee OA.

Intra-articular PRP injections have been shown to be efficacious for knee arthritis; therefore, intra-articular PRP injections for CMC joint arthritis could be efficacious as well. Dai et al. performed a meta-analysis that included ten studies looking at PRP for knee osteoarthritis versus saline or viscosupplementation [5]. Thus study showed that PRP and viscosupplementation had similar outcomes regarding pain relief and functional improvement at 6 months postinjection. However, at 12 months postinjection, PRP demonstrated greater pain relief and functional improvement. Furthermore, PRP demonstrated greater pain relief and functional improvement when compared to saline at 6 and 12 months postinjection [5].

Similarly, stem cell use has demonstrated positive outcomes in several studies for knee OA; therefore, its use for wrist/hand OA may be beneficious as well. Jayaram et al. reviewed studies that looked at the efficacy of bone marrow-derived stem cells (BMSC) and adipose-derived stem cells (ADSC) on knee OA in animal and human models [6]. Several studies demonstrated regeneration and improvement in knee joint cartilage quality after intra-articular injection with BMSCs; this was determined by magnetic resonance imaging, gross examination, and histologic examination. Along with improvement in cartilage quality, BMSC decreased the rate of joint damage and cartilage degeneration. Pain improvement after injection with BMSC was seen in individuals as well [6]. Intra-articular injection with ADSCs was also shown to slow knee OA progression by slowing the rate of cartilage degeneration. Pain and function improved after ADSC treatment as well [6].

Mesenchymal stem cells, such as BMSCs and ADSCs, and PRP injections have consistently demonstrated a high safety profile when used for musculoskeletal conditions, such as OA. Additionally, studies on knee OA have demonstrated efficacy; therefore, these interventions, with the right protocol, could potentially be applied to CMC joint arthritis as well.

Tendinopathies

In addition to being beneficial for OA in the hand and wrist, regenerative medicine can be of benefit when treating different tendinopathies in the hand and wrist. Common tendinopathies in the hand and wrist are De Quervain's, intersection syndrome, extensor carpi ulnaris tendon injury, and trigger finger or stenosing tenosynovitis.

De Quervain's tenosynovitis is due to overuse and is the result of thickening of the first extensor retinaculum at the wrist. It occurs due to repetitive movement of the abductor pollicis longus (APL) and extensor pollicis brevis (EPB) tendons as they pass through the first dorsal compartment of the wrist under the first extensor retinaculum [7]. On physical examination, one will find tenderness to palpation in the first dorsal compartment with possibly local swelling. Finkelstein's test is performed by placing the thumb inside a clenched fist and ulnar deviation at the wrist. The test is considered positive if it reproduces pain over the radial styloid. Currently, conservative management consists of oral anti-inflammatories, topical cream, thumb spica splint, occupational therapy, and sono-guided steroid injection to the first dorsal compartment if pain and functional impairment is severe enough. If conservative management fails, surgical opening of the first dorsal compartment is an option [7].

Intersection syndrome is another overuse disorder of the wrist and another cause of pain. This disorder results in pain in the dorsal forearm approximately 4–8 centimeters proximal to Lister's tubercle [8]. Friction between the APL and EPB tendons and the extensor carpi radialis brevis and longus (ECRB and ECRL) tendons results in inflammation and pain. Swelling and pain can be seen at the site of intersection between these tendons. Crepitus at the site has been described, along with pain that worsens with activity and use. It is a clinical diagnosis, but ultrasound and/or MRI can be performed for confirmation. Conservative management should be attempted first with rest, analgesia, and immobilization. In some cases, this may not be enough to reduce the inflammation, and a sono-guided tendon sheath steroid injection is warranted. Saline hydrodissection to reduce the adhesions has been described as an interventional treatment as well [9].

Another common overuse injury in the hand/wrist is extensor carpi ulnaris (ECU) tendinopathy. This pathology is commonly found in athletes who use sticks, bats, or clubs [10]. The ECU is in the sixth extensor compartment of the wrist. Unlike the other five compartments, the sixth compartment is found along the ulna, not the radius. Another unusual characteristic of the ECU is that it is not housed exclusively by the extensor retinaculum; there is also an ECU tendon sub-sheath. There are two types of ECU tendinopathy that can occur. One is a constrained tendinopathy – the ECU is being compressed within the ECU tendon sub-sheath. The other type is an unconstrained tendinopathy; this involves subluxation or dislocation of the tendon [10].

Clinically, on exam, one will find weakness of the ECU and tenderness to palpation over the dorsal-ulnar aspect of the wrist. Many individuals describe the pain as a burning sensation. There is rarely a history of trauma or specific injury to the wrist for individuals with a constrained tendinopathy. Those who have an unconstrained tendinopathy will typically have a history of a hypersupination injury with ulnar deviation and flexion of the wrist. Swelling can be seen along the sixth dorsal compartment of the wrist. The diagnosis of an ECU injury is made clinically, but often concomitant injuries such as triangular fibrocartilage (TFCC) tears occur as well. Therefore, ordering an MRI to further delineate any concomitant injuries and to assess the status of the tendon is advisable [10]. Management of an

ECU tendinopathy is dependent upon the type of tendinopathy – constrained versus unconstrained. In constrained tendinopathies, the goal of treatment is to avoid rupture of the tendon and further deterioration of the ECU tendon. In unconstrained tendinopathies, the goal of treatment is to stabilize the ECU tendon and to re-establish normal, anatomical alignment. Immobilization with a splint for 2–3 weeks, oral or topical anti-inflammatories, and occupational therapy are the initial treatment for constrained tendinopathies. The splint should hold the forearm in pronation with the wrist extended and in slight ulnar deviation. If indicated, a sono-guided steroid injection to the tendon sub-sheath can be performed. If all of the above treatments fail, one can consider surgical release of the tendon. In unconstrained ECU tendinopathies, open reduction and reconstruction are typically advised [10].

Trigger finger, or stenosing tenosynovitis, is another common tendinopathy of the hand. It has a prevalence of 2–3% of the population. Individuals present with locking and pain of the involved digit. A palpable nodule can be felt as well. Individuals can have trigger finger of just one to several fingers, and it can appear unilaterally or bilaterally. Management begins with conservative treatment with occupational therapy and hand use (occupational and ADLs) modification if needed. If symptoms persist, a sono-guided steroid injection into the tendon sheath under the A1 pulley can be performed. If symptoms persist after a steroid injection, surgical release of the A1 pulley can be considered [11].

Although regenerative medicine in the treatment of overuse injuries in the wrist and hand has not been substantially documented at the time of writing this text, there is literature regarding the use of PRP specifically in other overuse injuries. The use of PRP to treat patellar tendinopathy has been documented in case series and small randomized controlled trials [12]. Mainly due to lack of protocol standardization for aspirate preparation or injection technique (infiltration with or without needle tenotomy), there is still controversy in the use of PRP for soft tissue injuries [13]. Nevertheless, Mautner et al. did a retrospective study on the efficacy of sono-guided tenotomy and PRP injection in patients with chronic tendinopathy: lateral and medial epicondylitis, patellar tendonitis, Achilles tendonitis, rotator cuff tendonitis, hamstring tendonitis, and gluteus medius tendonitis [14]. They demonstrated a moderate (>50%) improvement in pain after ultrasound-guided PRP injections for chronic tendinopathy. The pathology of tendinosis is similar regardless of location. Therefore, it can be reasonably expected that PRP will be efficacious in chronic tendinopathies in the hand, but more research is warranted. Additionally, stem cell use for tendinopathies has not been studied, and its use in other more common tendinopathies like rotator cuff injury is currently not advised [15].

Ligamentous Injuries

Two important ligamentous injuries that can occur in the hand and wrist are scapholunate ligament and ulnar collateral ligament (UCL) injuries. The scapholunate ligament is one of the interosseous membranes of the wrist. Scapholunate ligament

injuries typically occur with a fall onto an outstretched hand. These injuries are commonly seen concomitantly with a distal radius fracture, perilunate dislocation, or a scaphoid fracture. Alternatively, they can be seen as an isolated injury [16]. Acute scapholunate injuries present with acute swelling over the anatomical snuff-box and radiocarpal joint. Individuals with a scapholunate injury will experience weakness and pain, as well as instability. Treatment of acute static scapholunate ligament dissociation is surgical, with closed reduction and pinning or with open reduction and repair of the ligament. Acute partial ligaments injuries without any of the collapse deformities are best treated in a short-arm thumb spica cast for at least 6 weeks [16, 17].

Similarly, UCL injury, Skier's thumb, or Gamekeeper's thumb is an injury that affects the stability of the medial aspect of the first MCP joint where first- and second-degree tears can be treated with immobilization with a short-arm thumb spica cast for 4 weeks. After 2 weeks, the cast can be changed, and if the patient is pain free, a removable splint can be used and ROM exercises started. A non-displaced avulsion fracture can be treated with a cast for 4–6 weeks. Operative treatment should be considered if the avulsion fracture is greater than 10–15% of the articular surface, if displacement is more than 2–3 millimeters, or if angulation is present [18, 19]. There are no studies or case reports on the use of regenerative interventions for this type of injuries, but theoretically they might be beneficial, especially in partial tears where nonsurgical treatment is preferred.

Other Soft Tissue Injuries

A common wrist pathology is carpal tunnel syndrome (CTS) or median neuropathy at the wrist. CTS can lead to paresthesia in the thumb, index finger, middle finger, and radial side of the fourth finger. In extreme cases, individuals can have thenar weakness [20]. Conservative management consists of nighttime splinting, oral medications, and occupational therapy. If these treatments fail, then a sono-guided steroid injection can be attempted. Cases refractory to conservative management or those with evidence of axonal injury can be referred for surgical decompression.

Now, with the advent of regenerative medicine, there is an additional option for individuals suffering from CTS. The scientific evidence has demonstrated mixed results on the efficacy of PRP as treatment for CTS. Malahias et al. and Özçakar et al. demonstrated additional benefit from a single PRP injection into the carpal tunnel when compared to night splints and activity modification-only group [21, 22]. On the other hand, Raeissadat et al. found that although safe, in short term, PRP plus splint is not more effective than splint in reducing pain, symptom severity, and functional status in mild and moderate carpal tunnel syndrome [23]. As previously seen in other pathologies, PRP seems to be safe, but its efficacy in treating most MSK conditions is still questionable; however, it is still a viable treatment option before having to consider surgery in conditions such as CTS.

Another common wrist pathology is triangular fibrocartilage complex (TFCC) injury. The TFCC stabilizes the distal radioulnar joint. It consists of the ulnotriquetral ligament, meniscal homologue, articular disc, dorsal radioulnar ligament, volar radioulnar ligament, ulnolunate ligament, and ulnar collateral ligament. Injury to the complex results in ulnar-sided pain and instability to the distal radioulnar joint [24]. It is commonly seen in athletes who use bats, clubs, or rackets. Individuals report a deep aching pain, a clicking with pronation-supination of the forearm, and pain with gripping. MRI should be obtained if TFCC injury is suspected to delineate extent of injury and to look for any concomitant injuries. As previously mentioned, ECU injuries can be seen with TFCC injuries. Nevertheless, the gold standard for diagnosis is wrist arthroscopy. Active individuals with suspected TFCC tears should undergo wrist arthroscopy for possible debridement of central tears or repair of peripheral tears [25]. Like in other pathologies in the hand and wrist, there is no evidence in the literature for the use of regenerative medicine interventions on TFCC injuries, but it is a possible alternative to surgery.

Conclusion

There is very limited scientific evidence of efficacy of regenerative medicine interventions for the treatment of hand and wrist injuries. The main reason for this is lack of studies focused in this anatomic area. Nevertheless, there is some evidence for PRP and stem cells for similar pathology, OA, tendinopathy, and ligamentous injury, in other areas of the body that has consistently demonstrated a high safety profile but mixed results on positive outcomes. These procedures seem to be safe; therefore they can be recommended as an alternative to patients refractory to proven conservative modalities who do not want to undergo surgery.

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