Case1 Biceps Tendinopathy Farrah Jawad

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A 30 year old right hand-dominant male presented to clinic with a six month history of bilateral elbow pain. The pain was over the antecubital fossa and the medial aspect of both elbows. It started insidiously and he noticed it mainly after kickboxing. He had been kickboxing since the age of 15. He had no new changes with his training. He used to box three times a week, weight train twice a week and was a keen runner. He would tend to feel the pain after weight training. He had to stop boxing due to the pain. He also reported wearing long shirt sleeves gives him pain over the antecubital fossa. He has some stiffness of the elbows for around 30 minutes particularly in the morning. There was no swelling. He sometimes experienced painless clicking with the elbows. He had increased the weights with his weight training somewhat before symptoms started but otherwise there was no other significant change in his usual routine. He had no neck pain and no paraesthesia of the upper limbs. He had been wearing bilateral elbow supports for four months which he found helpful.

Past Medical History:

Nil.

Medications:

Finasteride.

Social History:

He was a trader.

Physical Examination:

There was normal range of movement of both elbows in all planes. Resisted elbow flexion gave slight discomfort but there was good strength. There was tenderness of both biceps tendons bilaterally. Resisted wrist flexion bilaterally had good power with no pain. The rest of the examination was unremarkable.

Investigations:

Radiographs were requested to evaluate both elbows. These appeared normal with normal alignment, joint space, no evidence of soft tissue calcification or bony abnormality.

Ultrasound scanning of the elbows using a GE Logiq E9 ultrasound machine showed features of tendinopathy of the biceps tendons close to their insertion over the radial heads. There was a loss of normal fibrillar pattern but with no obvious tear. There was no obvious neovascularity. The features were in keeping with tendinopathy.

Impression:

Biceps tendinopathy of both elbows.

Plan:

He was advised to modify his training to avoid aggravating his symptoms greater than 4/10 pain on a visual analogue scale (VAS). He was referred for an assessment by a physiotherapist to formulate a programme of exercise to treat his tendinopathy, including eccentric biceps curls and resisted supination with a Theraband. He underwent weekly assessments by the physiotherapist and his exercises were adjusted and progressed.

Clinical course:

He was then reviewed after six weeks of physiotherapy. He reported improvement but continued to have residual symptoms. The patient expressed an interest in platelet-rich plasma (PRP) injections as his friend had a good outcome with this for a musculoskeletal problem. It was explained that the evidence for the benefit of PRP is mixed and that if he wished to pursue this as a potential option, further imaging could be arranged to confirm the diagnosis to ensure there was no other potential cause for his pain. It was explained that tendinopathy can sometimes take some time to resolve and that it is not uncommon for it to go on for many months. PRP injection, its potential merits and risks were discussed with him.

Subsequent magnetic resonance imaging (MRI) scan of both elbows was in keeping with a low grade distal biceps insertional tendinopathy and mild peritendinitis with no obvious tear seen. The rest of the structures of both elbows appeared normal.

Based on these findings and the patient's wishes, he was referred to a colleague who performs ultrasound-guided injections of PRP to the biceps tendon insertion.

The injection was performed under clean conditions with written consent and ultrasound guidance. 10ml of whole blood was taken from the patient which was then centrifuged using a Regen lab system for five minutes. 6ml of clear, straw-coloured platelet rich plasma was then harvested. 2ml of 2% Lidocaine was infiltrated from the skin to the distal biceps insertion in the left antecubital fossa followed by 3ml of PRP to the tendon and peritendinous region. This was then followed by a similar procedure (same volumes) to the biceps insertion via a radial tuberosity approach. There were no immediate complications and good infiltration of the tendon and peritendinous tissue was achieved. The patient was advised to look out for any signs of infection and to contact the medical practitioner immediately in the event of any concerns.

The patient was then reviewed three weeks later. He reported a significant improvement in his symptoms, with pain at the left elbow rated at 1 to 1.5 out of ten (previously 3/10). With regard to the right elbow he reported pain at 2/10 (previously 3/10). He was keen to consider a second injection to the distal biceps insertion which was performed exactly as the previous injection under clean conditions with written consent and ultrasound guidance. 4ml of 2% lidocaine was injected via a radial tuberosity approach from the skin to the distal biceps. 6ml of straw-coloured, platelet-rich plasma was harvested from 10ml of whole blood which had been centrifuged using a Regen Lab system for five minutes. 4ml of platelet-rich plasma was injected to the tendon insertion and peritendinous region. There were no immediate complications and good infiltration of the tendon.

The patient was encouraged to arrange a review appointment two weeks post-injection for consideration of a second injection to the elbow if required. To date he has had two PRP injections to the right distal biceps tendon and one to the left. He reports his symptoms are improved and that pain does not exceed 2/10 post-exercise. He continues with his exercise-based programme of rehabilitation with his physiotherapist.

The issue of informed consent and patient choice

Consent to treatment is a vital component of ethical medical practice. Consent must be voluntary, informed and the patient must have capacity to make the decision (nhs.uk, 2019). This means that a patient must not be coerced into making a particular decision. A patient must be supplied with the information as to what the treatment entails, what the intended benefits and potential risks are, and if there are any side effects. In this case, it was explained to the patient that the evidence for PRP injection is mixed and that guidance from the National Institute of Health and Care Excellence (NICE) states that autologous blood injections (including techniques to harvest PRP) do not seem to cause harm but that evidence for their efficacy is still limited (Nice.org.uk, 2013). NICE also states that where such injections are undertaken, clinical outcomes should be audited and reviewed (Nice.org.uk, 2013). A patient must also have the capacity to make an informed decision which means understanding what the treatment entails, be able to weigh up the potential advantages and disadvantages of undergoing the treatment and being able to retain the information.

The Faculty of Sport and Exercise Medicine state in their Professional Code document (Fsem.ac.uk, 2016) that clinicians should “be extremely cautious about giving personal endorsement to methods, products or equipment which do not have a robust peer-reviewed evidence base” and that “where there is a lack of evidence in support of a novel treatment this should be communicated to the patient.”

In this scenario, the patient made an informed decision to pursue PRP injection as a treatment modality as he felt it was unlikely to do him harm and he wished to try something different to see if this might make a difference to his persistent symptoms.

The role of imaging in the diagnosis of insertional biceps tendinopathy

Ultrasound is considered the gold standard for evaluating tendons (Grassi et al., 2000). Ultrasound involves no radiation, is quick, dynamic and can be interpreted in real time by the sonographer. Ultrasound scanning can be performed quicker than an MRI scan (the average time for which is up to 15 minutes vs 30 minutes). Ultrasound can be very helpful in evaluating structures of the elbow but the main disadvantage may be the presence of anisotropy particularly with evaluation of the distal biceps brachii tendon which is prone to this phenomenon at its insertion (Tagliafico, Bignotti and Martinoli, 2015).

There are various techniques which can be adopted to view the distal biceps tendon, including anterior, medial, lateral and posterior approaches. It is possible to use all four to add to the information gleaned from performing the ultrasound scan of the distal biceps tendon (Tagliafico, Bignotti and Martinoli, 2015). To view the tendon anteriorly, the elbow should be extended and maximally supinated. The tendon can be identified in short axis, then with the probe flipped 90 degrees, viewed in long axis. It is usually necessary to increase probe pressure distally to help view the distal part of the tendon as this is the area prone to anisotropy. To view the tendon laterally, the patient should have their elbow flexed at 90 degrees, maximally supinated, and the tendon viewed longitudinally by placing the probe over the lateral arm. The brachioradialis can act as an acoustic window. Medially, the same technique for viewing the distal biceps tendon can be adopted but by placing the probe over the medial arm. In this position, the pronator teres acts as an acoustic window. Posteriorly, the tendon can be viewed with the probe applied to the proximal forearm in a transverse plane with the forearm maximally flexed and pronated. The tendon can be seen to move in this position when supinating and pronating the forearm (Tagliafico, Bignotti and Martinoli, 2015).

Magnetic resonance imaging (MRI) has excellent specificity and sensitivity in the detection of tendinopathy, partial and complete tears of the long head of biceps tendon (Fitzpatrick and Menashe, 2018 and Giuffrè and Moss, 2004). T2-weighted or short tau inversion recovery (STIR) sequences are helpful in assessing tendons. Axial, sagittal and a FABS (flexed elbow, abducted shoulder, supinated forearm) view can be obtained to aid the diagnosis of distal biceps tendon tears (Giuffrè and Moss, 2004). The FABS view is obtained with the patient prone with the shoulder abducted 180°, with the elbow flexed to 90°, and the forearm supinated. This position allows a longitudinal view of the distal biceps tendon (Giuffrè and Moss, 2004). MRI is useful in assessing complete tears of the distal tendon, particularly in measuring the degree of tendon retraction and the quality of the remaining tendon for repair (Falchook et al., 1994 and Fitzgerald et al., 1994).

<u>Ultrasound-guided injection to the distal biceps tendon insertion</u>

Ultrasound-guided injections are overall more accurate than landmark-guided injections (Daniels et al., 2018). To inject the distal biceps tendon insertion, a posterior approach is favoured in order to avoid vascular structures and the following steps are taken:

- The patient is seated with the arm resting at 90 degrees of flexion and the forearm pronated.
- The transducer is placed in longitudinal section over the biceps tendon at its insertion onto the radial tuberosity.
- The needle is inserted at 45 degrees to the transducer from anteromedial to posterolateral direction.
- The injection can be made peritendinously +/- fenestration of the tendon insertion itself (Resteghini, 2018).

The role of PRP injection in general

Platelet-rich plasma is a mixture of platelets and growth factors derived from the centrifugation of whole blood. PRP is thought to enhance regeneration of tendons by releasing platelet-derived growth factors, cytokines and other proteins which may stimulate and moderate the inflammatory response (Andia, Rubio-Azpeitia and Maffulli, 2015, Galatz et al., 2015, Hudgens et al., 2016), with effects on cellular proliferation and collagen synthesis. Activation of cell adhesion molecules and promotion of fibroblast migration by PRP may also promote tendon healing (Alsousou et al., 2009).

A systematic review and meta-analysis looking at the changes in VAS scores in the short- and long-term of patients injected with PRP for rotator cuff injuries and lateral epicondylitis showed that PRP significantly improved VAS scores compared with control groups (Chen et al., 2017). The systematic review did not include or exclude the different types of PRP in their analysis, the number of injections, the dosage used or the preparation method used. There are four main variations in the different types of PRP that can be harvested (see table 1) (Mishra et al., 2012). This variety of PRP products poses a challenge in study design as the different types of PRP may not all be equal in terms of what they may or may not do. There is no consensus on which PRP is the best to use, and there is evidence that platelet concentrations greater than five times that of normal serum may have deleterious effects on tendon healing (Dhillon et al., 2014). Chen et al found that there was extensive variability in the methods by which PRP was prepared and injected, adding to the heterogeneity of the studies included in the review (including differences in the way clinical outcomes were measured between included studies, patient-only blinding or unblinded studies).

Table 1 (Mishra et al, 2012). Sports Medicine classification of PRP.

	White blood cells	Activation?	Platelet concentration (x that of serum)
Type 1	Increased	No activation	A – 5x or < B - <5x
Type 2	Increased	Activated	A – 5x or < B - <5x
Type 3	Minimal or no WBCs	No activation	A – 5x or < B - <5x
Type 4	Minimal or no WBCs	Activated	A – 5x or < B - <5x

There is in vitro evidence that human tenocyte proliferation increases when cultured in PRP (McCarrel and Fortier, 2009, de Mos et al., 2008, de Mos et al., 2009). In vivo application of PRP in tendon injuries appears to promote angiogenesis, generation of fibrovascular callus and might have catabolic effects on traumatised areas of tendon (de Mos et al., 2008). In Chen et al's systematic review, the authors considered saline injection, dry needling, autologous blood injection and corticosteroid injection all to be appropriate controls – but these differing injectates and dry needling all involve introduction of a needle which may itself have a placebo effect. A large, double-blind randomised controlled trial looking at the effects of hyaluronic acid versus PRP injection for knee osteoarthritis did not show any differences in patient outcome between the two injectates (Filardo et al., 2015). Again, these results may be due to the variations in types of PRP, its dosing and administration, or the introduction of a needle alone as a possible placebo effect. Dry needling of a tendon may stimulate tendon healing and the addition of PRP to this technique may have a synergistic effect (Stenhouse, Sookur and Watson, 2013).

Overall, the use of PRP appears to be safe with no significant adverse events reported in Chen et al's systematic review and meta-analysis of 1937 unique patients treated with PRP. PRP seemed to provide short and long-term relief of tendon and ligament injuries, in particular rotator cuff injuries and common extensor origin tendinopathy. It is, however, difficult to draw definitive conclusions on PRP as there is heterogeneity between the studies and a lack of standardisation in the use of PRP (Chen et al., 2017). There is potential for a placebo effect with the use of PRP, as the response to a placebo is independent of IQ, meaning that every individual may be subject to a placebo effect (Doherty and Dieppe, 2009), and the magnitude of the effect is determined by what patients are told about the treatment and therefore their expectations (Filardo and Kon, 2015).

The role of PRP injection in distal biceps tendinopathy

A PubMed search using the criteria "platelet rich plasma AND distal biceps tendinopathy" generated six publications from 2012 to 2018 respectively. One paper discussed the management of elbow tendinopathies in general and only discussed the potential use for PRP in common extensor tendinopathy (Taylor and Hannafin, 2012). Two of the remaining five papers were low-powered cohort studies (Barker et al., 2015 and Sanli et al., 2014), the third was a letter response to Barker et al's paper, (Gosens and Funk, 2015), the fourth was a descriptive review (Kwapisz et al., 2018) and the fifth was a single case report (Mautner, Stafford and Nguyen, 2015). There is limited evidence for the use of PRP injection in distal biceps tendinopathy, based on these low powered studies and low levels of evidence. Low powered studies in particular make it difficult to infer anything at all from the results due to the possibility of a type II error.

Sanli et al in their small study of twelve patients with distal biceps tendinopathy injected with three microliters of leucocyte-rich PRP found that all of them showed a statistically significant improvement in pain and functional outcome, and in some cases, significant improvement in isometric muscular strength. These patients all had a single ultrasound-guided PRP injection only. The study was not double blinded or controlled, and they used three different PRP preparation systems between patients in their study. The patients in Sanli et al's study were also given an eccentric exercise programme to complete post-injection which may have affected outcomes. Nevertheless, at the median follow-up of 47 months, all patients reported significant improvements in pain and functional outcome, with no adverse events reported and no recurrence of symptoms (Sanli et al., 2014).

Similarly, Barker et al in their low powered study of six patients were also injected with a single PRP injection (Type 1B PRP according to the Sports Medicine PRP Classification System). The authors state that "no specific physiotherapy was employed" but it is not clear whether they mean that physiotherapy treatment was not standardised or whether it did not take place post-injection. Four patients symptoms resolved completely within 6 weeks of injection and two patients had two injections in total with resolution of their symptoms. All six patients reported improvements post-injection and said they would consider another injection in the event of symptom recurrence. The patients were followed up at a minimum of one year and the improvement in symptoms appeared to be maintained. A lack of control group is a major limitation in this study (Barker et al., 2015).

Ultrasound-guided PRP injection appears to be safe with no adverse effects reported in the limited available studies. It is possible that in these studies, symptoms may have eventually settled with conservative treatment in time, however it is important to note that patients included in the studies had months of symptoms and some had rapid improvement in their symptoms with PRP injection, which was sustained after one year (Barker et al., 2015).

Summary

Clinicians are obligated to provide patients with balanced accounts of the evidence available when it comes to using injection therapies in the clinical setting to enable patients to make informed choices about their management. Decision-making should be patient-centred and clinicians should stay up to date with regards the evidence for injection therapies so that frank discussions can take place between patient and clinician. There is mixed evidence for the efficacy of PRP injection in general and the quality of the evidence for its use in biceps tendinopathy is low. In vitro and in vivo evidence for PRP on tenocytes is encouraging in its positive effects on tendon healing but large scale, double-blinded, randomised controlled trials with standardisation of the types of PRP used will add to the evidence base in this area. It is possible that there is a placebo effect, however symptomatic improvement and lack of adverse effects can be considered as positive outcomes regardless of how PRP works. A greater issue will be the cost of the PRP injection; whether or not it is cost-prohibitive for self-funding patients in the private sector, whether there is sufficient evidence for insurance companies to authorise funding or whether the National Health Service will fund PRP injection in the future.

In this scenario, the patient reports symptomatic improvement in his distal biceps tendinopathy, at least in the short term, after several months of symptoms with no improvement with conservative management strategies.

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