Exuberant inflammatory reaction as a side effect of platelet-rich plasma infiltration for treating one case of tendinopathy

Short title : Inflammatory reaction after PRP infiltration

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Abstract:

Platelet-rich plasma (PRP) contains a large quantity of growth factors, which may enhance tendon healing processes. Local infiltration of PRP represents a relatively new treatment for tendinopathies. To date, no side effects have been reported after infiltration of PRP to treat tendinopathy. We reported a case of exuberant inflammatory reaction after one infiltration of PRP to treat jumper's knee in a type 1 diabetic patient who was 35 years old. Injections of PRP must be proposed after careful consideration for patients with morbidity risks linked to insulin-dependent diabetes.

Keywords: platelet rich plasma, side effect, tendinopathy

Introduction:

Platelet-Rich Plasma (PRP) contains a large quantity of growth factors (i.e. Plateled-Derived Growth Factor, Insulin like Growth Factor 1, Vascular Endothelial Growth Factor, basic Fibroblast Growth Factor, etc...) which may enhance tendon healing processes by promoting matrix synthesis and wound healing [1]. (PRP = Platelet-Rich Plasma) To our knowledge, even though this treatment is subject to controversy regarding its effectiveness and there is no consensus for the use of PRP therapies in tendinopathies, no side effects were reported in literature [1].

Case report:

We report the case of a 35-year-old type 1 diabetic patient with right upper patellar tendinopathy that had persisted for more than 6 months. This case of tendinopathy was resistant to all of the typical conservative treatments that were applied (non-steroidal anti-inflammatory drugs, physical therapy, eccentric reeducation, shock wave therapy). His diabetes was well controlled (glycated hemoglobin: 45 mmol/mol).

(PRP = Platelet-Rich Plasma) In our clinical experience, we realized around fifty infiltrations for various tendinopathies. (PRP = Platelet-Rich Plasma) None of the other patients (none of them were diabetic) we treated with PRP infiltration developed any side effects. (PRP = Platelet-Rich Plasma) The PRP was obtained with an apheresis machine (COM.TEC and kit CS5L, Fresenius-Kabi, Bad-Homburg, Germany), offering us a reproducible PRP from the autologous blood of each patient. (PRP = Platelet-Rich Plasma) The patient benefited from an intratendinous infiltration of 6 mL of PRP (8.10^5 platelets/mm^3, almost no red or white blood cells) in loco dolenti, at the apex of the patella (in 3 sites), after a carefully disinfection with povidone-iodine, but without local anesthesia. Immediately following the infiltration, local cryotherapy was performed for 15 minutes. Typically, a standardized program of sub-maximal eccentric rehabilitation should be started 1 week after infiltration. (CRP = C-reactive protein; WBC = white blood cells) However, the patient experienced

local swelling with erythema, increased heating and pain, which appeared just underneath the patella, without biological inflammatory syndrome (CRP 0.3 mg/L, WBC 8420/mm^3). In absence of septic general symptoms, no blood or wound culture were made. (MRI = Magnetic Resonance Imaging) At 2 weeks post-infiltration, a greatly increased Doppler signal in a thicker tendon was observed by ultrasounds compared to that before infiltration (Fig. 1), but there was no sign of infection demonstrated by either MRI (Fig. 1) or CT: no sign of septic center, septic collection or osteitis. However, the local inflammation did not decrease after a 3-week treatment of oral diclofenac 75 mg, local cryotherapy and application of ketoprofen, and adjunct use of colchicine 1 mg. Thus, an insidious infection was suspected, even though there was no evidence of biological inflammatory syndrome or sign of infectious lesion on imagery examination. Antibiotic therapy (rifampicine 600 mg + minocycline 100 mg, twice a day), was initiated for three months. Due to a lack of improvement via imaging and clinical examination (persistence of a local swelling with erythema, increased heating and pain, in an anxious patient), a 3-phase bone scintigraphy was performed (Fig. 2). The results suggested the presence of a complex regional pain syndrome type 1 (CRPS1). (CRPS1 = complex regional pain syndrome 1) The patient benefited from classical physical therapy for CRPS1 and concomitant class-2 pain killers. (PRP = Platelet-Rich Plasma) The evolution was favorable after 6 months of treatment, and the pain decreased to a level similar to that before the infiltration of PRP.

Discussion:

(PRP = Platelet-Rich Plasma) PRP is a relatively new treatment for tendinopathies; there is neither general agreement nor formal clinical evidence for its effectiveness. However, this treatment may be helpful for chronic tendinopathies resistant to typical treatments [1]. (PRP = Platelet-Rich Plasma) To our knowledge, no side effects have been reported in the literature following injection of PRP to treat tendinopathies [1]. (PRP = Platelet-Rich Plasma) Only one case report described the

development of dense exuberant synovitis of the subacromial space after acromioplasty and postoperative PRP injection in a 66-year-old man [2].

Our patient was a type 1 diabetic; it is well known that these patients are at an increased risk of developing comorbid pathologies and have compromised immune systems [5]. (PRP = Platelet-Rich Plasma) In our case, the patient developed an exuberant local inflammatory reaction one week after the infiltration of PRP. (PRP = Platelet-Rich Plasma) This inflammation was probably initiated by locally released growth factors by the platelets whose action was too wide for a diabetic patient, even though the platelet concentration in PRP did not exceed 3-4 times that of the blood, and did not contain any leukocytes nor lymphocytes. (PRP = Platelet-Rich Plasma) Indeed, if the PRP was contaminated with these cells, which can cause tissue damage and an increased inflammatory reaction, the side effect observed in our patient could have been greater [8].

In only a single case, it is very hard to attribute causality to the patients diabetes. (CRPS1 = complex regional pain syndrome 1) In the same way, it is very difficult to rule out the microcrystalline and infectious origins of this exuberant inflammatory reaction and attribute it the the diagnostic of CRPS1. However, it is clearly not the intended outcome of this treatment. (PRP = Platelet-Rich Plasma) Thus the formal etiology of this adverse reaction after a local injection of PRP remained unclear, but the type 1 diabetes could have been a contributing factor.

(PRP = Platelet-Rich Plasma) In conclusion, even though PRP infiltration represents a new and promising treatment for tendinopathy, more studies are needed both to verify its clinical efficacy and standardize its use. Moreover, implementing this innovative treatment requires caution because of potential adverse events. Thus, the balance between benefits and risks must be carefully evaluated before using this treatment, especially in patients with type 1 diabetes.

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Fig. 1: a. Sagittal section of the knee, MRI T2 sequence. The upper part of the tendon is thicker, with a heterogenic aspect and visible hypersignal of the surrounding tissue. b. Longitudinal ultrasound of the patellar tendon in which the upper part is thicker and presents a great deal of vascularization observed by the color Doppler.

Fig. 2: Suspicion of complex regional pain syndrome type 1 (CRPS1) of the right knee via 3-phase bone scintigraphy.