

Review Article

A Gout Flare Caused by the Administration of Platelet Rich Plasma: A Clinical Case

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Abstract

The therapy with Platelet Rich Plasma (PRP) administered in degenerated or injured musculoskeletal tissues is a new and promising regenerative treatment option. Traditionally, it is considered that as PRP represents an autologous (to the patient) blood product, the potential for serious side effects is neglectable. Consequently, it is important that any significant negative consequences are well described. We present a fifty-five years old male patient, complaining of pain and stiffness in his right ankle joint due to multiple traumas during his earlier sport career. He had no any contraindications and PRP was injected intraarticularly under ultrasound guidance. On the next day, the patient developed an intensive pain and swelling in the regions of the right ankle and the dorsum of the right foot. The acute phase reactants were elevated and there was no leukocytosis. On ultrasound examination, there was an effusion in the tibiotalar and talonavicular joints. Arthrocentesis was performed and the microscopic examination revealed the typical needle shaped monosodium urate crystals inside the joint fluid and no bacteria. Consequently, the diagnosis of acute gouty flare was made (the patient has a history of gout, but did not have any flares in the past two years). As PRP concentrate contains naturally many proinflammatory molecules, we speculate that some of them may activate the macrophages that residue normally in the synovium and the capsule of the injected joint. The activated macrophages further may react to the MSU crystals deposited there, leading to the development of a gouty flare. In conclusion, the possibility of a flare should be explained to gouty patients, candidate for PRP treatment.

Keywords: Platelet Rich Plasma; Gout; Flare

Introduction

The Platelet Rich Plasma (PRP) therapy offers a new and potentially revitalizing option in the treatment of degenerative rheumatic diseases. Since its first conceptualizing in the 1990s, this method was increasingly used in the rheumatological and orthopaedic medicine practice [1]. Traditionally, it is considered that as the PRP represents an autologous (to the patient) blood product, the potential for any side effects or negative consequences of this treatment virtually does not exist. Consequently, it is very important that any significant side effects are described and distributed to the knowledge of the physicians practicing this therapeutical method.

In the current clinical case, we describe an intensive gout flare, directly connected with the administration of PRP for an ankle joint osteoarthritis and ligamentous injury.

Case Description

Fifty-five years old male patient was consulted due to constant pain and stiffness in his right ankle joint. He is an ex professional comparator in sport orienteering and he relate his ankle complaints with multiple traumas and sprains of the ankle supporting

ligaments throughout his sport career and to the substantial weight gain in the recent years. The patient has tried multiple courses of physiotherapy treatments, but he still needs frequent intake of NSAIDS for his pain. At clinical examination, the patient has limited range of motion in his right tibio-talar joint, pain on palpation along the joint line, as well as pain on varus and valgus stress of the ankle. The X rays showed osteoarthritis of the right tibio-talar joint with narrowing of joint space and subchondral osteosclerosis. The ultrasound of the right ankle showed non-uniform thinning of the cartilage along with ligament pathology (thickened and hypoechoic talo-fibular, deltoid and calcaneo-fibular ligaments), no synovitis or joint effusion were evident. At the laboratory tests there are no signs of inflammation, the number of platelets in the peripheral blood meets the requirements for a PRP treatment.

After discussion on the therapeutic options, the patient was offered a treatment of his ankle condition with PRP injections, which the patient accepted and signed an informed consent form. The standard procedure for this treatment at our institution was followed: 22 ml of venous blood was drawn out in a 25 ml sterile system for platelets separation that was prefilled with a 3 ml of 1% sodium citrate. After that, the system was placed in a centrifuge and spined double times (respectively 8 and 3 minutes) at 3500 RPM according to the manufacturer instructions (SWS, South Korea). The PRP produced by this process was transferred in a 5 ml sterile syringe and then injected under ultrasound guidance intraarticularly in the patients' right tibio-talar joint, as well as periarticular along the predefined damaged ligaments. Aseptic conditions were maintained all through the procedure. There were no any side effects reported and the patient left the clinic with an advice to restrain from greater physical activity the following days.

On the next day, the patient called the clinic and complained of a very intensive pain, swelling and feeling of warmth in the regions of the right ankle and the dorsum of the right foot. He could barely walk due to the pain. The patient was invited to the clinic. On the clinical examination there was a substantial swelling in the right ankle and foot, the overlaying skin was warm, the area was tender and painful on palpation, the range of motion in the tibio-talar and talonavicular joints - decreased. According to the patient, the current symptoms resembled very much the gout flares that he has experienced before, but not in the last two years when there were no attacks.

The ultrasound examination showed effusion in patient's right tibiotalar and talonavicular joints with the presence of hyperechoic amorphous material in the fluid, as well as subcutaneous oedema. The laboratory results revealed elevated levels of the CRP and ESR, no leukocytosis and borderline serum uric acid. The diagnosis of an acute crystal arthritis flare gout was made. In the differential diagnostic plane, the possibility of septic iatrogenic arthritis was discussed but there was no fever, systemic signs, leukocytosis. Anyway, an ultrasound guided arthrocentesis with aspiration of the synovial fluid was carried out. The sample was examined under polarized light microscope and the typical needle shaped MSU crystals were seen (Fig. 1-3). The fluid was also sent for a microbiological study and no bacteria growth was detected. A therapy with colchicum was initiated, the patient advised to follow RICE regimen and to report any worsening of the condition. In one week, the symptoms gradually improved and the patient returned to work and resume everyday activities.



Figure 1: Patient's swollen right ankle joint, note normal metatarsophalangeal joints.

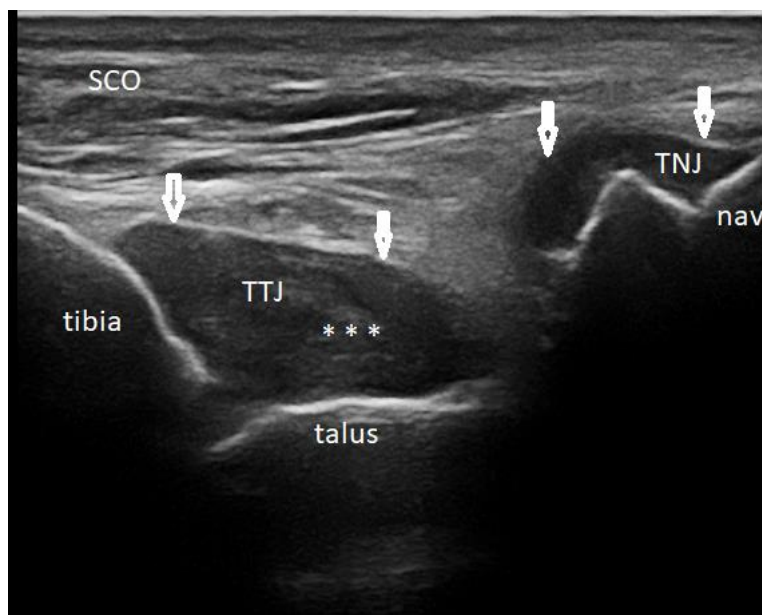


Figure 2: Longitudinal ultrasound image across the right ankle joint showing effusion in the Tibiotalar (TTJ) and Talonavicular (TNJ) joints (arrows), note the hyperechoic material inside the effusion in the tibiotalar (asterisks) and the Subcutaneous Oedema (SCO).



Figure 3: Needle shaped MSU crystals from the patient's tibiotalar joint effusion under light microscopy.

Discussion

The uric acid arthritis (gout) is the most frequent among the crystal induced arthritis. It is caused by accumulation and deposition of Monosodium Urate (MSU) crystals in the articular and periarticular tissues. Gout is a frequent disease, for example it was found to affect 3,9% of the population in the USA [2]. The typical course of the disease includes sudden acute flares of pain which are followed by symptomless period with variable length (sometimes years as in the present patient). The flares are caused by different stimuli- stress, dehydration, diet mistakes, infections, all of which could decrease the stability of the intratissue MSU deposits. The recognition of the naked MSU crystal by Toll-like receptor, which are normally involved in triggering innate host defence responses to infectious pathogens, was recently discovered to be a primary trigger of the inflammatory tissue reactions associated with gouty arthritis. Thus, macrophages can recognize and contact with the MSU crystals, get activated and start an intense and rapid inflammatory reaction [3]. During the flare, the affected joints are extremely painful, swollen and hot, making septic arthritis the main differential diagnosis consideration. The treatment of the acute flare is with colchicum, corticosteroids, ACTH, NSAIDs, IL 1 blockers, RICE regimen [2,3]. In our case, the medical treatment included only colchicum and RICE, as NSAIDs and corticosteroids are known to interfere negatively with the regenerative capabilities of the PRP (1), while IL 1 blockers are not available in our country.

The PRP therapy is part of the conception of the so-called Orth biologic medications which are administrated to promote tissue regeneration [4]. The proteomic analysis showed that the activated platelets can release up to 3000 bioactive proteins [5]. They regulate in a synergetic way numerous molecular pathways included in the chemotaxis, cell proliferation and specialization, neo angiogenesis and synthesis of the extracellular matrix. Some of these bioactive molecules, although important in tissue repairment are proinflammatory in nature [5,6].

Traditionally, the PRP treatment is considered safe, with minimal risk of side effects, provided that good aseptic environment and technic of intervention are implemented. In the literature the main side effect described is postprocedural pain with various intensity, but generally short-lived [7].

Our literature search in PubMed did not revile any reports on gout flares following PRP administration. Yet, we think that, in our patient the PRP application could have caused the observed intensive gout flare due to several possible mechanisms. Firstly, some of the proinflammatory molecules, contained naturally in the platelet concentrate may activate the macrophages that

residue normally in the synovium and the capsule of the injected joint. These activated macrophages then may react to the MSU crystals deposits that are presented in the articular and periarticular tissues of the patient. This interaction may lead to further and sustained macrophages activation and development of a true gout flare. On the other hand, the low-grade inflammation that always follows the intraarticular/ periarticular degranulation of the injected large number of platelets during the PRP administration, could cause destabilization of the disposable MSU crystals, their contact and interaction with the macrophages and eventually to an acute crystal flare. In addition, it is known that sometimes small sport or hobby related injuries of the foot may provoke a flare in gout patients. As in trauma there is some intratissue bleeding, the mechanism of developing a flare due to a traumatic episode and due to PRP administration could be similar.

Conclusion

To the best of our knowledge, this is the first report of a gout flare as a direct consequence of a PRP concentrate administration. The affected joint was the same that was injected with the PRP. Considering the growing popularity, availability and usage of PRP treatment among physicians dealing with musculoskeletal problems, it is mandatory that any significant side effects of this therapy is marked and described. In our case, we believe that there was a direct relation between the administrated PRP injection to the patient's ankle joint and ligaments and the acute gout flare affecting the same that joint. Although the evolution of this side effect was favourable, it still caused considerable pain, anxiety and limitations in the daily life of the patient, as well as required additional time and resources from the treating physician. Knowing the possibility of causing an acute flare, the treatment with PRP should be administrated carefully in patients with known diagnosis of gout (although currently asymptomatic) and the possibility of a flare explained to them. In addition, a colchicum prophylaxis could be considered in high risk (i.e., those with recent or numerous flares) gout patients scheduled for a PRP treatment.

Conflict of Interest

The authors have no conflict of interest to declare.

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