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Case Report

Adverse event following platelet rich plasma injection for the management of early Osteoarthritis of knee – A report of 4 cases

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ABSTRACT

Background: Osteoarthritis is the leading cause of chronic disability affecting more than 80% of people over the age of 55. Several treatment options are there for early Osteoarthritis (OA) knee, like- rest, ice, brace, NSAIDs, intra-articular corticosteroid, Intra-Articular Hyaluronic Acid (IAHA), and intra-articular platelet-rich plasma (PRP) injection. Growth factors in PRP (PDGF, IGF, VEGF) promote matrix synthesis, cell growth, and migration, thus facilitating protein transcription. Several studies regarding PRP injection in the management of OA knee support this line of management without any documented complications of PRP at the knee joint.

Case Report: We report 4 cases of acute inflammation related to PRP injection for the treatment of OA knee. Two patients developed mild inflammation which was treated with oral medication on an outpatient basis. Another two patients developed moderate to severe inflammation which warranted surgical intervention.

Conclusion: Intraarticular PRP injection has been reported in the literature as a successful modality of treatment in OA knee without any significant adverse effect. We are reporting four cases of adverse events following intraarticular PRP injection. Two cases were mild inflammations while the other two were moderate to severe. All four patients recovered and the outcome was satisfactory compared to the pre-injection status. The exact cause for the reaction after PRP injection in the knee is not known. Further study is needed for the cause of the inflammatory reaction.

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1. Introduction

Osteoarthritis (OA) is a degenerative noninflammatory joint disease. Osteoarthritis is the leading cause of chronic disability affecting more than 80% of people over the age of 55. Symptomatic OA of the knee has a prevalence of 22% to 39% in India.¹ OA is a multifactorial entity, involving multiple causative factors like trauma, mechanical forces, inflammation, biochemical reactions, and metabolic derangements.² Osteoarthritis is due to an imbalance between the destructive

and reparative or synthetic processes of the articular cartilage. But the source of pain is mainly derived from changes to the non-cartilaginous components of the joint, like the joint capsule, synovium, subchondral bone, ligaments, and peri-articular muscles.^{2,3} Even though OA is noninflammatory, the synovial fluid has been found to contain multiple inflammatory mediators including plasma proteins prostaglandins (PGE₂), leukotrienes (LKB₄), cytokines (TNF, IL1 β , IL6, IL15, IL17, IL18, IL21), growth factors (TGF β , FGFs, VEGF, NGF), nitric oxide, and complement components.^{4,5} Several treatment options are there for early OA knee, like- rest, ice, brace, NSAIDs,

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intra-articular corticosteroid, Intra-Articular Hyaluronic Acid (IAHA), and intra-articular platelet-rich plasma (PRP) injection.

Growth factors in PRP (PDGF, IGF, VEGF) promote matrix synthesis, cell growth, and migration thus facilitate protein transcription. The supra-physiological release of platelet-derived growth factors directly at the site of diseased cartilage, may stimulate the natural regenerative signaling cascade and enhance the healing of tissue with further mediation of the anti-inflammatory response.⁶ PRP has some advantages too, like it is autologous, natural, safe, activates a normal healing process. In a clinical update by Cook et al., they have suggested that PRP should be the first choice in the management of early OA knee.⁷ Several studies regarding PRP injection in the management of OA knee support this line of management without any documented complications of PRP at the knee joint. In this case series, we report 4 patients with mild to moderate inflammatory reactions following PRP injection.

2. Case Summary

2.1. Case 1

A 45-year female presented to orthopedic OPD with right knee pain and swelling for one year. The pain increased with walking and cross-legged sitting. There is no history of any preceding trauma. On examination right knee crepitus was present. She was advised standing X-ray of her right knee. She was diagnosed with right knee OA (Ahlback grade 2). Intraarticular autologous Platelet-rich plasma injection was given in the right knee. The next day of the procedure patient presented to OPD with the complaint of increased swelling, pain, and redness of the right knee. On examination, there was increased local temperature and the knee was tender on palpation. But she did not develop any effusion at the inflamed knee.

She was advised to rest, immobilization, knee brace and ice pack application (RICE protocol) along with tablet aceclofenac. After three days of supportive treatment, the patient's ESR, CRP were still raised. So, prophylactic broad-spectrum antibiotic (Tab. linezolid) was prescribed. Regular OPD-based follow-up was done. The inflammation subsided within one week. At six weeks follow up the patient showed a significant reduction in pain and improved functional outcome as compared to pre-procedure status.

2.2. Case 2

A 55-year male presented with bilateral knee pain (right more than left) for 2 years. Following clinical and radiological evaluation he was diagnosed with bilateral OA knee - Ahlback grade 2 on the right side. Initially, he has advised lifestyle modification, physiotherapy, and analgesics for 6 weeks. But the patient revisited OPD without any improvement. Then the patient was prepared

for PRP injection after counseling and informed consent.

After PRP injection in the right knee patient presented to OPD on post-procedure day one with complaints of increased swelling, pain, and redness of the right knee. On examination, the patient had a local rise of temperature and tenderness. The acute inflammation of the right knee subsided on rest, local application of ice pack, oral analgesics, and prophylactic antibiotics. At six weeks follow-up, patient was doing better when compared to pre-injury status.

2.3. Case 3

A 52 year male patient presented to OPD with pain in the left knee for one year. After a thorough clinical and radiological examination, a diagnosis of left knee OA (Ahlback grade 2) was made. After proper counseling and informed consent, intraarticular PRP injection was administered in the left knee.

The patient presented to the OPD on the following day with complaints of pain not relieving on oral analgesics, swelling, and redness. On examination local temperature was raised, the knee was tender and there was effusion of the joint. The patient was admitted to the hospital for further management.

The pain and effusion did not subside following immobilization, ice packs, and intravenous analgesics for 72 hours. Arthrocentesis was performed which yielded 30ml of yellow clear viscous fluid. The fluid was sent for gram staining and culture which came negative. The patient was managed with intravenous antibiotics (Linezolid, clindamycin), analgesics, jones compressive bandage, and immobilization for one week and discharged after the subsidence of inflammation and effusion. At six weeks follow up there were no signs of inflammation and the patient had a good functional outcome.

2.4. Case 4

A 48-year female, a known case of osteoarthritis of the bilateral knee, previously managed conservatively with analgesics and physiotherapy presented to OPD with pain in the left knee. She was counseled and prepared for autologous intraarticular PRP injection in the left knee after informed consent. She presented to the emergency ward of our hospital on the evening of the procedure with severe pain, swelling, and redness of the left knee. On examination, there was a local rise of temperature, tenderness, effusion, and painful range of motion of the left knee.

Arthrocentesis was performed and 50 ml of yellow clear fluid was aspirated and sent for culture. She was admitted and intravenous analgesics and antibiotics were started. The aspirated fluid did not yield any growth. As the pain and effusion did not subside following intravenous medication arthrotomy and debridement were planned. The patient

underwent arthroscopy, debridement, and synovectomy of the left knee. Intraoperatively no pus collection was noted but the synovium was found to be hypertrophied and inflamed. She recovered without any postoperative complications

3. Discussion

Osteoarthritis knee is a degenerative joint disease where several inflammatory markers have been found in the synovial membrane of the knee joint. Literature showed many established treatment options for the management of early OA knee. Many studies have reported satisfactory results with intraarticular injection of PRP for OA knee. Most of these studies report no or only mild adverse events following PRP injection that is usually self-limiting. Taniguchi et al in a clinical trial for intra-articular PRP injection for the treatment of OA knee observed only minor adverse events in 73% of patients but all symptoms resolved within 48 hours.⁸ Sanchez et al, in a randomized clinical trial between PRP and Hyaluronic acid(HA), found the incidence of mild adverse events to be similar between the two groups and limited to 48 hours.⁹ In another randomized controlled trial comparing PRP and HA, Filardo et al. observed a higher incidence of minor reactions such as pain following injection in the PRP group than the HA group. They considered proteases and reactive oxygen released from WBCs as the cause of acute reaction following PRP.¹⁰ In our study out of 34 patients, 2 patients had a mild inflammatory reaction and 2 patients had moderate to severe reaction. In the latter 2 cases, the synovial fluid analysis yielded no growth after culture excluding any infective etiology.

Patel et al reported acute adverse events such as dizziness, syncope, tachycardia, headache, and nausea at the time of injection, but none too severe to cause concern.¹¹ We have not found such adverse events in our study but keeping the patient under observation following intraarticular injection is recommended.

All these studies report that the adverse events if any subside within days and do not have any long-term effect on the outcome. Our study also supports this observation as all 4 patients had good functional outcomes at 6 months follow up.

4. Conclusion

Most of the literature on PRP reports only mild self-limiting adverse events following PRP injection. We have reported 4 adverse events following PRP injection in 32 patients, 2 being mild and 2 moderate to severe. Our study supports the observation that adverse events following PRP injection do not affect its long-term results. The exact cause for the reaction after PRP injection in the knee is not known. Some researchers have postulated proteases and reactive oxygen from WBCs as the cause but further research is needed.

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6. Conflict of Interest

The authors declare they have no conflict of interest.

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