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Case Report

Streptococcus mitis septic arthritis after leucocyte-rich platelet-rich plasma injection for the knee osteoarthritis: A case report

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ABSTRACT

A 62-year-old female patient having comorbidities of hypertension, hyperlipidemia, obesity, peptic ulcer, and bilateral Grade II knee osteoarthritis was admitted with a complaint of knee pain. An intra-articular leukocyte-rich platelet-rich plasma (LR-PRP) injection was administered to both knees after clinical and laboratory examinations. Three days later, the pain increased and synovial effusion developed in her left knee. The patient was diagnosed with *Streptococcus mitis*-induced septic arthritis. Clinical and laboratory improvement was obtained with immediate ceftriaxone treatment in addition to irrigation and debridement. This is the first case report in the literature describing septic arthritis developing after intra-articular injection LR-PRP injection.

Keywords: Osteoarthritis, platelet rich plasma, septic arthritis.

Intra-articular injections are commonly practiced in the treatment of knee osteoarthritis, as they lack the potential systemic adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs).[1] The most common injection therapies are corticosteroids, platelet-rich plasma (PRP), and viscosupplementation such as hyaluronic acid,[2] and it has been suggested that intra-articular PRP injections are more effective than hyaluronic acid injections.[2-4] The PRP is an autologous derivative of whole blood and has anti-inflammatory properties, it reduces pain and improves clinical function.[2] It is also a safe procedure and has negligible adverse effects.[5,6] To date, no case report has been reported in the literature regarding septic arthritis with intra-articular leukocyte-rich (LR) PRP (LR-PRP) injections. Herein, we present a case with bilateral knee osteoarthritis in whom septic arthritis developed only in the left knee after intra-articular LR-PRP injection.

CASE REPORT

A 62-year-old female patient having comorbidities of hypertension, hyperlipidemia, obesity, peptic ulcer, and bilateral knee osteoarthritis was admitted with chronic knee pain without a history of trauma. She was treated with physical therapy and NSAIDs six months ago; however, her pain did not resolve. She benefited from PRP injections administered to both knees two years previously, although she was unable to report the exact number of injections or the type of PRP. No history of infection or surgery was noted in the previous one year. A physical examination revealed mild genu varum, mildly antalgic gait, normal range of motion,

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and palpable crepitus during passive motion. There was no warmth or soft-tissue swelling, although there was tenderness over the joint line. Grade II osteoarthritis was detected according to the Kellgren-Lawrence criteria in radiological examinations of both knees. She had no fever, and vital functions such as blood pressure, pulse, and respiratory rate were normal on admission. Her physical examination including range of motion, motor and sensory evaluation was normal in all extremities. Laboratory evaluations were normal (erythrocyte sedimentation rate [ESR] 10 mm/h, C-reactive protein [CRP] 3 mg/L, white blood cell count [WBC] 6.5×10^3 with a differential of 53.1% neutrophils, 33.2% lymphocytes, 8% monocytes). An intra-articular LR-PRP injection was performed using a 21-G needle for both knees with the superolateral approach, with the patient lying in the supine position with her knees in full extension. Povidone iodine (10%) was used three times for skin preparation, and the skin was allowed to dry before injection. The physiatrist washed her hands and wore sterile gloves during the procedure. The injection site was covered with a sterile bandage after the procedure. To prepare the PRP, a 20 mL venous blood sample was drawn into two 10-mL vacutainer tubes containing either 1 mL of 0.106 M sodium citrate for preparing PRP. The blood sample was, then, centrifuged for 8 min at 1500 g resulting in the three following layers: the inferior layer was composed of erythrocytes, the intermediate layer was buffy coat, and the superior layer was made up of plasma. A long needle was attached to a 5 mL Luer-Lok™ syringe (Becton Dickinson, New Jersey, USA) and 4 mL PRP was collected by sticking the long needle into the PRP tube above the erythrocyte layer. The PRP was carried to the re-suspension tube and gently shaken for 30 sec to suspend the platelets. The buffy coat layer, consisting of platelets, was then gently aspirated into a syringe in a volume of 2 mL for each knee. The patient was advised to avoid strenuous or prolonged weight-bearing activities for two days after treatment.

Three days later, the patient presented to the clinic with increased pain. Physical examination revealed warmth, moderate effusion, and a limitation of range of motion in the left knee joint. Laboratory evaluations showed an elevated ESR of 56 mm/h, CRP of 218 mg/L, and an elevated WBC count of 13.3×10^3 with. a differential of 70.4% neutrophils, 17.8% lymphocytes, and 10.5% monocytes. Due to a concern for infection, arthrocentesis was performed under a sterile technique. Analysis of the synovial fluid demonstrated 45 to 50 WBC/mm^3, with a negative Gram stain and also cultures of the synovial fluid were negative. The patient was given symptomatic treatment (i.e., NSAIDs, cold application, rest) and was followed for three days. Arthrocentesis was repeated in the patient whose symptoms persisted. The synovial analysis showed 8,000 WBC/mm^3 and *Streptococcus mitis (S. mitis)* production in the culture. The patient was suspected as having septic arthritis and was referred to the orthopedics clinic. Intraoperatively, an inflamed synovium was noted. Surgical irrigation with the use of sterile normal saline and debridement with synovectomy was performed, followed by a four-week course of intravenous ceftriaxone. The patient had significant improvement in pain and function, her inflammatory markers returned to normal, and there were no signs of infection. She was discharged on Day 19 of hospitalization with oral amoxicillin and clavulanic acid for an additional 15 days. The patient was followed for six months on a monthly basis, and no signs of infection were observed. At one-year postoperative follow-up, the patient had persistent knee pain with radiographic evidence of osteoarthritis. A written informed consent was obtained from the patient.

DISCUSSION

This case demonstrates that septic arthritis should be considered after intra-articular PRP injection. Within one week after the injection, limited effusion developed in the left knee, there was no fever, and the synovial fluid culture was negative. However, *S. mitis* was isolated from a culture obtained during the second arthrocentesis. The PRP has been shown to promote cell recruitment, proliferation, and angiogenesis resulting in a reduction in the critical regulators of the inflammatory process and a decrease in the expression of inflammatory enzymes.[2,5,7] The researchers conclude that the use of PRP injections in degenerative knee osteoarthritis is efficacious based on quality of life measures and visual analog scale pain scores, with negligible adverse events.[4,7,8] Although the most adverse events reported are pain, stiffness, syncope, dizziness, headache, nausea, gastritis, sweating, and tachycardia, there are no severe complications such as septic arthritis reported in the literature, and all events self-resolved in days.[4,6] Moreover, it is suggested that there are more adverse effects with PRP, when the solution is prepared with the double-centrifugation technique, compared to the single method.[7] The *S. mitis* is anaerobic, Gram-positive coccus, and one of the alpha-hemolytic species of streptococcus. Although it is thought to have low

pathogenicity and virulence, it is known to cause pleuropulmonary infections,[9] small bowel infections secondary to malignancy,[9] orthopedic surgery infections,[10] infectious endocarditis,[11] and septic arthritis.[12] In a retrospective analysis of cases of septic arthritis, *S. mitis* was detected in the synovial fluid culture analysis of three patients who underwent intra-articular hyaluronic acid and corticosteroid injections (only *S. mitis* in one patient, *S. mitis*/*Actinomyces odontolyticus* in one patient, *S. mitis*/*S. gordonii* in one patient).[12] The *S. mitis* is commonly found in the oropharynx, skin, gastrointestinal system, and female genital system flora.[13] Additionally, *S. mitis* strains mainly cause infections in patients with neutropenia, and patients with neutropenia may be more likely to have serious infections.[14] However, the presented patient had no recent dental procedures, other identified sources of infection or malignancy, or neutropenia on investigation. Intra-articular injections are invasive procedures, and there are absolute and relative contraindications.[2] However, there was no contraindication for the PRP injection for our patient. Additionally, all routine infection prevention procedures were followed carefully during her procedure, as emphasized.[15] Thus, her infection was unusual, particularly given the organism identified. Although both knees were injected with LR-PRP, the reason for developing septic arthritis only in the left knee could not be explained.

In conclusion, no septic arthritis cases due to intra-articular LR-PRP injection have not been reported to date. To the best of our knowledge, this is the first case report of *S. mitis* septic arthritis developing in a single knee following bilateral intra-articular LR-PRP. Although intra-articular PRP injections have been reported to be safe and have few adverse effects, this case demonstrates the need for microbiological research, and laboratory analyses, particularly for neutropenia. In patients with progressive pain and a swollen joint after intra-articular PRP injection, it is important to consider septic arthritis, to use appropriate antibiotic treatment, and perform debridement, if necessary, and to maximize long-term outcomes, as long-lasting infections can cause permanent damage to the joint.

Declaration of conflicting interests

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