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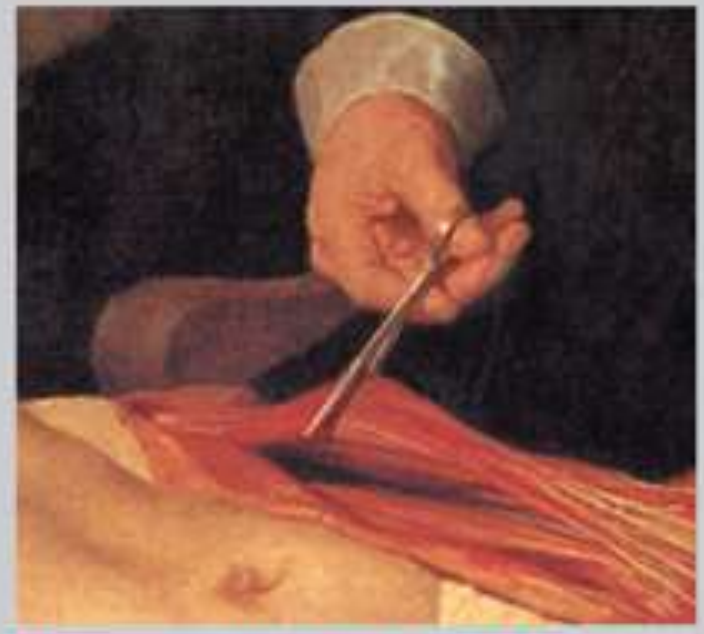

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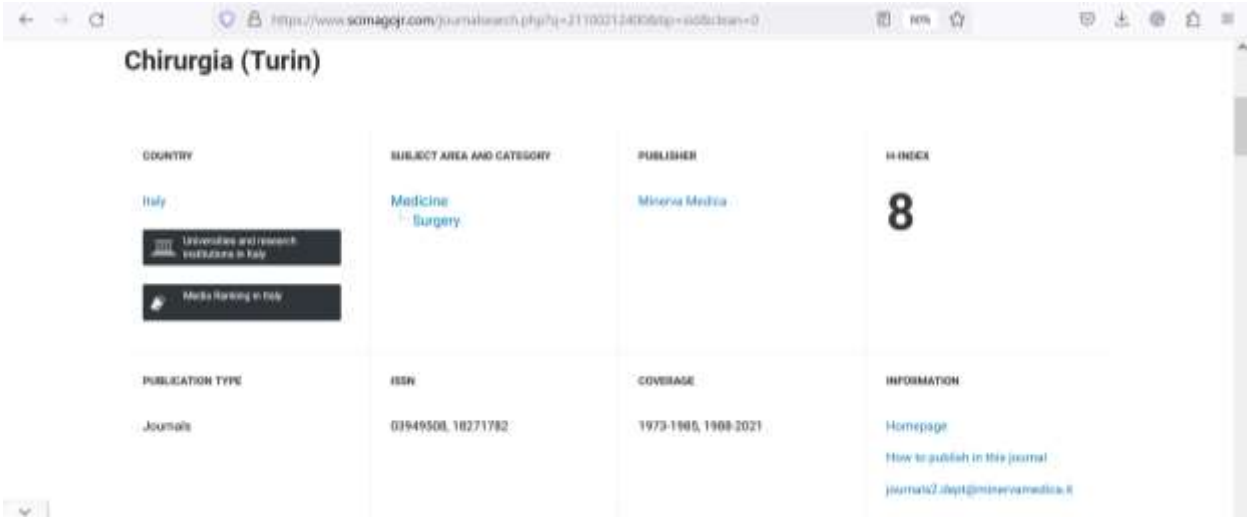
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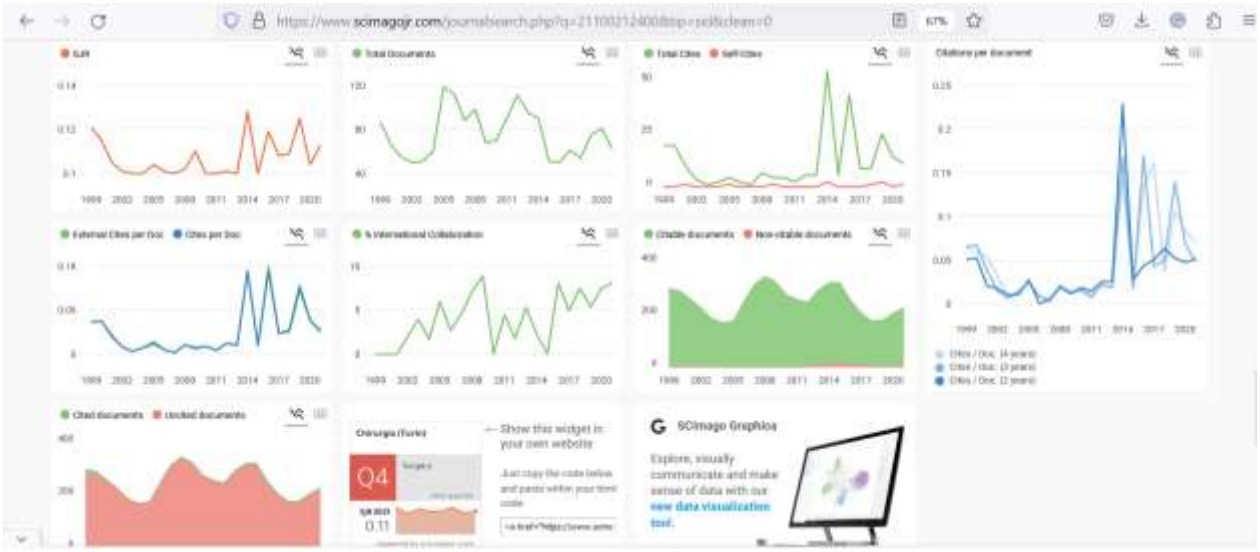
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CASE REPORT

USG guided-intra-articular platelet-rich plasma injection of knee-osteoarthritis patient

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ABSTRACT

Osteoarthritis is a degenerative joint disease with multiple risk factors. Knee osteoarthritis causes morning stiffness, movement restriction, and chronic-progressive pain of the knee joint. Osteoarthritis management aims to slow down disease progression and relieve pain and joint stiffness. Its management includes non-pharmacological, pharmacological, and operative treatment. One therapeutic modality for osteoarthritis is intra-articular platelet-rich plasma (PRP) injection with an ultrasonography (USG) guide. In this case, PRP was made from the patient's blood by centrifugation to obtain a highly concentrated sample1 of platelets. Platelets play a role in the healing process of osteoarthritis because they contain broad-spectrum growth factors. This scientific narrative report aims to prove the effectiveness of PRP management in patients with grade III knee-osteoarthritis. A 56 years old woman was diagnosed with 3rd-grade bilateral genu osteoarthritis. The patient underwent intra-articular PRP injection guided by Ultrasonography (USG). The procedure was performed on the right knee. A total of 2 procedures in 3 weeks. The patient came back 3 months later because of a relapse but with a lower pain score (VAS 4-5). The same procedure was carried out and evaluated a month later. The patient explained there were no pain experiences after the procedure even though no medicines were consumed during this period.

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KEY WORDS: Osteoarthritis, knee; Platelet-rich plasma; Ultrasonography, interventional.

Osteoarthritis (OA) is a degenerative joint disease with multiple risk factors. This disease is classified into primary and secondary OA.[1] Primary OA is caused by genetic factors which affect collagen abnormalities, while secondary OA is caused by endocrine disorders, inflammation, metabolic syndrome, micro or macro trauma, and prolonged immobility.[2] The abnormalities found in OA are cartilage damage and the formation of joint effusion. The disorder may be accompanied by subchondral bone thickening, ligament damage, osteophyte growth, and synovial inflammation.[3] OA causes pain and disability, which interfere with daily activities. Patients, their families, and their environment are economically, psychologically, and socially impacted by this disease.

OA is the second leading cause of physical disturbances in walking and climbing stairs.[4] Ten to fifteen percent of adults aged 60 years have OA. Approximately 1.3-1.75 million people in the United Kingdom complain of OA symptoms, and 1 in 7 Americans suffers from OA.[5] OA is one of the most common inflammatory joint diseases in Indonesia. The World Health Organization (WHO) states that OA in Indonesia is 65% in those aged over 60 years, 30% at the age of 40-60 years, and 5% in the population aged less than 40 years. Based on its location, knee OA has the highest prevalence, in males by 15.5% and femalesby 12.7%.[6]

OA predilection areas are generally in the supporting joints of the body, such as the knee joint, carpometacarpal joints I, metatarsophalangeal joints I, and apophyseal joints of the spine. The diagnosis is made from the his-

tory, physical examination, and investigations.[1] Knee-OA patients often feel stiffness in the morning, movement restriction, and complaints of chronic and progressive pain in the knee joints.[7] Physical examination of the joint revealed crepitus, joint swelling, bone tenderness, and warm skin on palpation.[1] Knee examination to confirm the diagnosis of OA includes McMurray, Anterior-Posterior Drawer Test, Lachman Test &, Apley Compression-Distraction Test.[8] Radiological examination of OA showed narrowed joint space, increased subchondral bone density, osteophytes, bone cysts, and changes in anatomical structures. Kellgren and Lawrence classified the radiological changes of the knee and hip OA into five degrees.[9]

OA management includes pharmacological, non-pharmacological, and operative treatment. Pharmacological treatment is the first choice for OA patients, but the side effects limit its use as long-term OA therapy.[10] There is no definitive treatment in preventing cartilage degenera- tion from holding OA progression yet. Platelet-rich plasma (PRP) is currently the target of researchers to determine its effectiveness in OA patients. PRP was believed to pre-vent OA cartilage degeneration. PRP is a high content of platelets as the result of plasma centrifugation. It contains growth factors such as vascular endothelial growth factor, transforming growth factor-b, platelet-derived growth factor, and type I insulin-like growth factor, which plays a role in bone and tissue regeneration.[11] This case report aims to demonstrate the effectiveness of intra-articular PRP injection on grade 3 knee-OA patient.

Case report

A 56 years old woman came to Jember Klinik Hospital outpatient service in November 2020, suffering from pain in both knees since 9 months ago. The pain was getting worse with right knee swelling two days before the hospital. The pain was throbbing and stabbing. She experienced knee stiffness for approximately 20 minutes after awake. The knee stiffness sometimes appears for a few minutes after getting out of the chair during the day. She has walking difficulty, unable to kneel, squat, or descend stairs due to pain (Visual Analog Score: 8). Pain is reduced when the patient rest or lies down (Visual Analog Score: 4). These symptoms worsen in humid or cold weather. The patient's maximum knee flexion is less than 120°. There is pain and patellofemoral crepitus on joint palpation. She has a history of hypertension, and her sibling has had bilateral Total Knee Replacement (TKR) surgery due to knee OA. She works as staff in the research institute with an office on the 3rd floor without an elevator, which requires her to go up and down the stairs daily. The patient is worried about her illness, whether it will get worse, un-curable, or hinder his daily work.

The patient's general condition appeared to be seriously ill, GCS 465, blood pressure 130/80 mmHg, pulse 72 x/minute regular, respiratory rate 20 x/minute, temperature 36.5°C, weight 78 kg, height 160 cm, BMI 30.4 (1st-degree obesity). Physical examination of the head revealed anemic conjunctiva (-), icteric sclera (-), isocor round-pupil with 3 mm diameter, light reflex (+), the trachea was found in the middle of the neck and no lymph node enlargement, symmetrical thorax without retractions, heart murmur (-) and wheezing/rhonchi (-), flat abdomen, normal (+) bowel sounds, not palpable liver/spleen, warm superior extremities and CRT<2 seconds. On examination of the right knee joint, we found redness, swelling, undulation, warmth, tenderness on palpation, and pain when moved. On the other hand, crepitus was felt on both knee joints. Lower extremities sensibilities were normal, the lower muscle strength and tones were normal. There were no abnormalities on the anterior drawer test, posterior drawer test, McMurray test, Apley grinding test, and Apley distraction test. X-ray examination of both knees at anteroposterior/lateral view shows the osteophytes, narrowed joint spaces, and subchondral sclerosis without fracture or dislocation, which impressed bilateral genu OA (Figure 1).

The patient was diagnosed with 3rd-grade bilateral genu osteoarthritis. The Lachman test showed negative results.

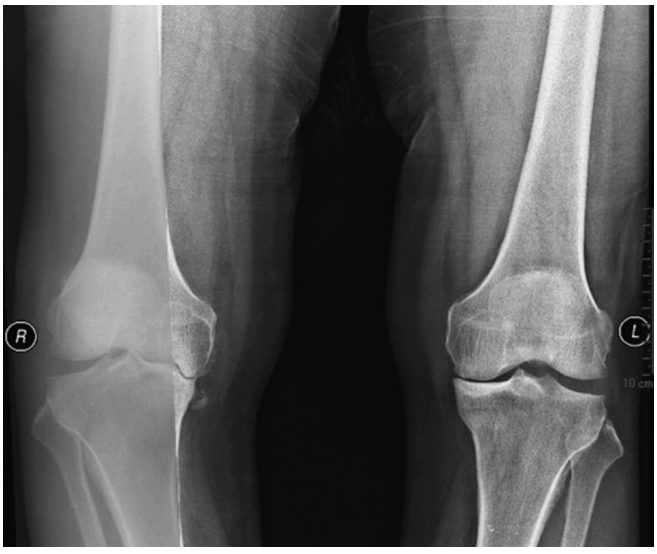

Figure 1.—Genu X-ray.

The patient's pelvis and back were also examined to rule out sources of pain outside the knee, including a full lumbosacral range of motion (ROM), all motion free of pain, ultrasound examination revealed effusion in the right knee joint.

Management

The patient underwent intra-articular PRP injection guided by Ultrasonography (USG) eZono 4000, using a 3–12 MHz linear probe (transducer) and a 25 G spinal needle.

Preparation

We drained 30 mL of the patient's blood from a cubital vein, then processed it into PRP in the laboratory of the Jember Clinic Hospital into 10 mL of PRP (with the hope that the platelet level is three times above the baseline). We prepared 4 mL of lidocaine 1%, a 25 G spinal needle, Linear USG-probe coated with sterile wrap, jelly, gauze, and antiseptic drug (povidone-iodine and 70% alcohol).

PRP production

PRP was made by inserting 1.5 mL of Anticoagulant Citrate Dextrose Solution A (ACD-A) into a syringe and extracting the blood into the same syringe to mix with ACD-A. The sample then underwent two-phase centrifugation, called plasmapheresis. The first phase with a speed of 3850 RPM for 7 minutes. The second with a speed of 3850 RPM for 8 minutes. We separated plasma containing platelets and a buffy layer (rich in leukocytes). If the buffy layer and platelets are removed, it becomes L-PRP, whereas it will become P-PRP if only platelets are removed. For this patient, we took the Pure PRP (P-PRP) or Leukocyte-Poor PRP and injected it into the patient's joint. It is a type of PRP without leukocytes and a low-density fibrin network.

PRP injection procedure

The patient was lying down in a supine position, with the knee flexed about 30°, supported by a pillow on the posterior side of the knee. The operator was on the ipsilateral side of the patient, with the ultrasound in an ergonomic position facing the operator. Scans were performed on both knees, with the longitudinal probe positioned on the superior midline pole of the patella. We visualize the femur, pre-femoral fat pad, and the quadriceps tendon that inserts into the patella from deep to superficial structures. Then the probe was rotated 90° to the axial (transverse) to visualize the femur, prefemoral fat pad, suprapatellar and parapatellar joint cavities, suprapatellar fat pad, and quadriceps tendon (Figure 2). The probe is moved medially and laterally to assess fluid in the parapatellar recess. Bilateral suprapatellar joint effusions were found.

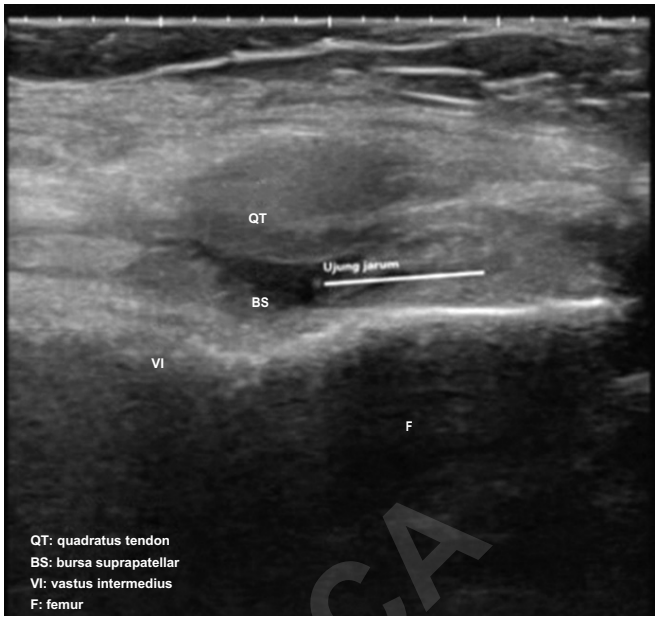

Figure 2.—Ultrasonography visualization of knee joint.

Aseptic procedures were performed with povidone-iodine and 70% alcohol, then with ultrasound guidace, the 30 mL of effusion was aspirated. The intra-articular injection was performed using a 25 G spinal needle from lateral to medial position with an ultrasound guide in the plane section. The medication injected into the joint was consisted of 4 mL of 1% lidocaine and 5 mL of PRP.

The procedure was performed on the right knee. A total of 2 procedures in 3 weeks. The patient came back on 2nd February 2021 because he had a relapse but with a lower pain score than the start of the procedure (Visual Analog Scale: 4-5). The same procedure was carried out and evaluated on 31st March 2021. The patient explained there were no pain experiences after the procedure even though no medicines were consumed during this period.

Discussion

OA diagnosis was established according to the guideline criteria determined by the ACR (American College of Rheumatology). Some OA manifestations include pain, crepitus, and joint stiffness. Pain gets worse with activity and improves with rest. The OA patient often visited the doctor several times because of the chronic progres-

sive pain. The patient, in this case, experienced all these symptoms. The patient came with right and left knee pain for the previous 9 months, getting worse and swelling in the right knee 2 days before the hospital. The pain worsens with movement and subsides when sitting, resting, and lying down. Some OA patients also complain of joint stiffness and moving difficulty due to pain. Joint stiffness in OA lasts less than 30 minutes.[12] The patient also feels his knee joint stiffen for about 20 minutes when he wakes up in the morning and a few minutes after getting up from a chair during the day. The patient could not kneel, squat, descend the stairs, and had walking difficulty due to the pain (Visual Analog Scale: 8).

OA patients, in general, are usually found to have a high BMI, which leads to crepitus on local palpation. Theright knee joint inspection revealed swelling, erythema, and slight deformity. The pain was felt when the patient moved.[13] In this case, we felt the crepitus warm on palpation of the right knee joint. The right knee also looks edema and erythema. The patient had difficulty in flexing the right and left knees. The result was 0°-110°, which normally is 0°-135°.[14]

The radiologic features of OA are normal in the early stages and become more apparent as the disease progresses. Joint space narrowing, osteophytes, sclerosis, and cysts.[1]The degree of OA can be seen from the radiological picture based on the Kellgren and Lawrence criteria which divides OA into 5 degrees (degrees 0-4).[15] In this case, there were osteophytes on the left and right genu, narrowed joint space, and subchondral sclerosis with the impression of third-degree bilateral genu osteoarthritis.

The patient, in this case, has risk factors that can trigger the onset of OA. Age over 50 years increases the incidence of OA. The patient is 56 years old. In addition, occupational factors also affect the development of OA. The patient works as a staff member of the research institute with an office on the 3rd floor and goes up and down the stairs almost daily. The stiffness is worsened by the patient's 1st degree of obesity, increasing the burden on the knee joint.[16] The presence of risk factors and clinical symptoms supported by radiological features make the patient diagnosed with 3rd grade OA.

OA management includes pharmacological, non-pharmacological, and operative treatment. Oral OA medication mostly uses NSAIDs, while injection therapy uses corticosteroids or hyaluronic acid. Several studies have shown better results by using prolotherapy as an OA treatment.[17] The treatment goals are to relieve pain, reduce disability, improve the function of the affected joint, and inhibit the disease progression. This patient underwent injection of intra-articular PRP. The procedure used ultrasound eZono 4000, a 3-12 MHz linear probe (transducer) as a guide, and a 25 G spinal needle. This concentrated plasma contains high platelets (2 times more than blood). The procedure helps control tissue homeostasis and inflammation. High platelets also prevent apoptosis of chondrocytes, inflammation, help collagen formation, and bone also blood vessel remodeling.[18]

The mechanism of action of PRP has benefits for OA healing. The growth factor activates platelets rapidly. During the first 10 minutes, seventy percent of the growth factor is secreted in granules, stimulating chondrocyte proliferation and SIM chondrogenicity. This process triggers the secretion of the cartilage chondrocyte matrix and inhibits the catabolic effect of pro-inflammatory cytokines. PRP contains the main growth factors, namely vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), tissue growth factor-β (TGF-β), insulin-like growth factor 1 (IGF). -1), bone morphogenetic proteins (BMP), fibroblast growth factor (FGF), and hepatocyte growth factor (HGF). These growth factors play an important role in regenerating joint cartilage, which is involved in healing OA.[19]

Conclusions

PRP has shown benefits in the treatment of knee OA. Clinical use shows that PRP therapy is safe and gives good results. Clinicians used PRP to consider the patient's pathological condition and treatment goals. In addition, patients must know that after PRP injection, they must continue to pay attention and monitor the disease improvement, even though the results obtained are quite good and have minimal complications. PRP intervention does not guarantee absolute successful results for all cases of knee osteoarthritis.

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