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Case Report

Steroid Flare Reaction; a Complication of Intraarticular Steroid Injection

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Abstract

A 63 year old man with bilateral knee osteoarthritis underwent an intraarticular steroid injection. After two days the patient developed severe pain and marked effusion in the left knee joint. Cultures were negative. He subsequently underwent bilateral knee replacement. The synovial biopsy of the left knee revealed marked granulation tissue and peculiar neutrophilic response against degenerated cartilage and osseous tissue.

Keywords: Osteoarthritis, Intraarticular steroid injection, Steroid flare reaction

Case Report

A 63 years old man, known case of Grade 4 bilateral osteoarthritis since last 8 years presented to the emergency department on July 1th 2014 with complains of severe pain in left knee for 2 days. 4 days back he had received bilateral intra-articular steroid injections (20mg Beclomethasone with 5mg Lidocaine) in home setting after pyodine scrub. His pain in both knees significantly reduced and he had better mobility. He overexerted and completely flexed both knees multiple times that day. On 3rd day the patient lifted a water container containing about 19 Liters of water momentarily. After 2 hours, to the patient's dismay he could not stand up due to swelling and pain in the left knee. The pain was sudden in onset, non-radiating exacerbated with joint movements and not relieved with analgesics. There was neither fever nor redness of joint. The right knee was "better than ever" in his words. On inquiry, the patient had been advised bilateral knee replacement many a times before this episode. Due to his profession as a professor at a college, he sought for a quick solution for his disabling osteoarthritis and opted for bilateral steroid injections.

On examination, the patient had a swelling in left knee measuring almost 10 X 8cm. No redness or oozing pus was noted at the site of injection. No other skin changes were observed. The involved knee joint was tender and slightly warm on palpation crepitus was noted. Emergency drainage was carried out in the E.R department, and 15cc of bright yellow viscous fluid was aspirated. The specimen was sent to the laboratory. The results showed a white cell count of 1,29000/mm3, out of which 95% were Neutrophils. Culture were negative after 72hrs of aspiration. Microscopically no atypical or crystals were noted. Urgent X-ray of the left knee showed grade 4 osteoarthritis. (Figures 1&2)

Figure 1 & 2 X-Rays of Left Knee showing advanced osteoarthritis

The patient was discharged later that evening, with a prescription of OTC painkillers and a 5 day course of levoflox-

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acin. Minimal activity and assisted movement was advised. On the follow up, two days later, the patient complained of gradually increasing pain and swelling in the same joint. C reactive protein (CRP) came out to be 67 and total blood count was normal. Emergency day care arthroscopic wash-out was done the next day, to prevent a highly possible risk of septic arthritis. The sample collected was again sent for culture and sensitivity. No growth was noted again after 72 hrs. The patient was advised physiotherapy and prescribed a course of ciprofloxacin. No appreciable improvement in symptoms was noted over the course of the following week. Second opinion was sought by another orthopedic surgeon, who aspirated 10cc of red viscous fluid and advised total rest to the involved joint and minimal flexion. The left leg was bandaged with a wooden back slab till mid thigh. Again no improvement was noted by the patient, rather he complained of upper thigh and hip ache. The bandage was taken off at home due to severe pain at night and worry of risking deep vein thrombosis. Cold fomentation relieved pain significantly. The patient gradually felt much better with cold fomentation and mild physiotherapy. Still, the left leg could not bear weight.

On third opinion, the surgeon injected an intra-articular steroid formulation consisting of 80mg Depomedrol with 7.5mg Abociane, which dramatically lessened the severity of pain over the next couple of days. The swelling was reduced to almost null, and has not been complained of since then. He tried physiotherapy with inferential and ultrasonic treatment for a week, which were of no gain and increased the pain. The patient started walking with a cane, gaining some pace but still complained of mild pain in the left leg.

Finally he decided to have bilateral knee replacement. The orthopedic surgeon found quite hypertrophic synovial membrane in left knee and sent samples for histopathological examination. The sections showed several small fragments of broken and degenerated cartilage and some osseous tissue surrounded by intense acute inflammatory cells. At one place the broken cartilage gave an impression of Actinomyces! (Figures 3-5). However there was lack of thin filamentous bacteria at the edges and there was no definite Splenodre-Hoeppli phenomenon! As tissue for culture was not sent Intravenous ampicillin was immediately started in order to not to take any chance. It was considered wise to complete a course of oral Ampicillin for 6 weeks. His both knees are now completely free of pain, stiffness, tenderness, swelling and any other previous complaints. He had complaints of post-operative urinary tract infection (due to indwelling catheter for a prolonged period of 3 days), which were treated with oral Levofloxacin. His both knees have a flexion of 120 degrees and are independently mobile.

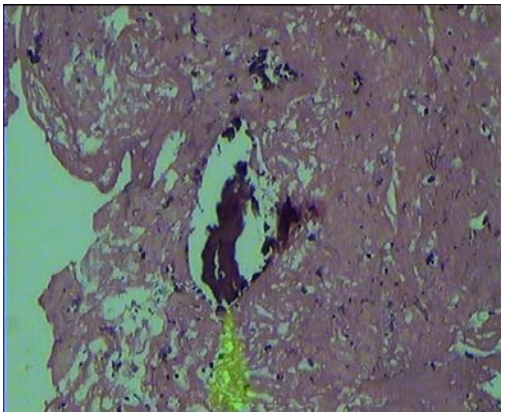

Figure 3: Degenerated fragment of degenerated osseous tissue (H&E X 100)

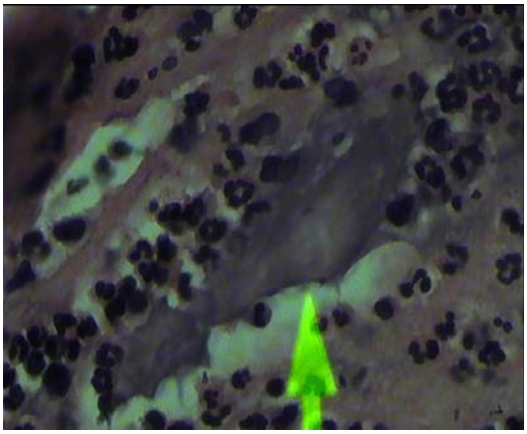

Figure 4: Fragment of osseous tissue surrounded by neutrophils (H&E X 400)

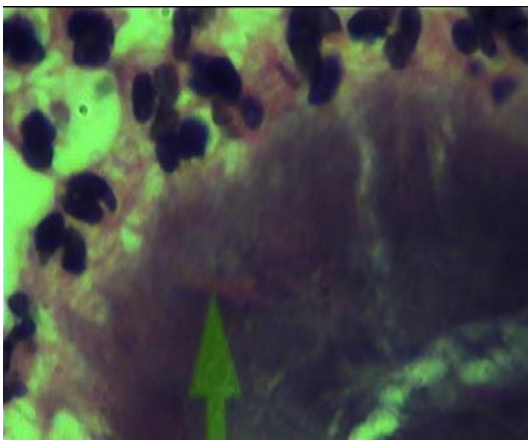

Figure 5: Fragment of degenerated cartilage surrounded by neutrophils. Note lack of filamentous bacteria at the edges& Splendor- Hoeppli phenomenon. (Figure X 1000)

Discussion

Osteoarthritis is the most common degenerative arthritis involving almost 250 million people worldwide.[1] Its one of the five leading causes of disability amongst non institutionalized adults.[2] It results from degenerative disorder arising from biochemical breakdown of articular cartilage. It commonly involves the weight bearing joints, i.e. most commonly hip and knee joints. Diagnosis is made by detailed history and clinical examination. Radiological tests including X-rays, CT scan and MRI may confirm the diagnosis. Changes seen on the radiological film include most commonly: joint space narrowing, subchondral sclerosis and cysts, and osteophytes. According to Center for Disease Control (CDC), osteoarthritis of the knee is Knee and hip arthritis are ranked as 11th highest contributor to global disability as well as being 38th highest in terms of Disability adjusted life years (DALY).[3]

Various treatment modalities for managing pain and improvement of functional status include both pharmacological and non pharmacological modalities as follows.[4] Pharmacological therapies include: Acetaminophen, oral NSAIDS, topical NSAIDS, viscosupplementations, dietary supplementations and intra-articular corticosteroid injections. Non pharmacological interventions include patient education, lifestyle modification, heat and cold fomentation, weight loss, exercise, physical therapy and occupational therapy. Surgical therapies include arthroscopy, cartilage grafting, synovectomy, osteotomy and arthroplasty.

Intra-articular (IA) steroid injections are one of the many techniques used by physicians to manage disabling osteoarthritis. Due to the ease of procedure and quick results, it has attracted a lot of attention of both the physicians and concerned patients. Steroids being anti inflammatory drugs reduce the inflammatory mediators, particularly interleukin-1, and thus alleviate pain. Due to intra-articular administration, the systemic side effects of corticosteroids are by-passed, such as systemic infections, poor wound healing, weight gain, hypertension, and diabetes mellitus.[5] Though there are studies that indicate that long term IA steroid injections can cause joint destruction and tissue atrophy, there is also evidence that long term IA steroid may prevent or at least delay such destruction. The procedure involves skin preparation using alcohol or povodine-iodine swabs, aspirating any joint fluid and then injecting a mixture of steroid of choice and a local anesthetic at a suitable anatomical landmark i.e. parallel to inferior border of patella in knee joint. Important precautions which were missed in our patient and should be kept in mind are as follows:

1) Injections should always be administered in utmost sterile hospital settings.
2) Let the povodine-iodine swab dry on the skin to have its full anti-bacterial activity.
3) The mixture should be shaken before injecting.
4) Different needles should be used to aspirate the mixture from the vials and to inject in the joint space.
5) Following the injection, the area should be iced.
6) The patient should be informed that joint will be painless for the first two hours after injection due to the effect of local anesthetic.
7) Increased pain, even worse than before, is experienced and it lasts for two days. It should be treated with ice and minimal activity. Complete bed rest for minimum of two days should be strongly advised.

As mentioned before, our patient was injected at home settings and in contrast to minimal activity, he over-exerted his joints afterwards. No cold fomentation was applied. This led to increased inflammation and pain. Hyper secretion of synovial fluid led to the tense swelling. Another explanation of this can be the lifting of a water container (19 liters) that led to torn necrotic piece of cartilage initiating the inflammatory cascade. The laboratory tests of the fluid aspirated in the emergency showed a very high white cell count, indicating a possible iatrogenic septic arthritis.

The possible differential of septic arthritis was doubtful due to no growth on culture media. Even the sample obtained from the emergency arthroscopic washout procedure showed no bacterial growth in spite of high white cell count. The only possible explanation of this acute unilateral episode seems to be a post-injection steroid flare reaction. Post-injection steroid flare reaction is an adverse effect that occurs in 2-6% of the patients receiving intra-articular injections. It is caused be either needle puncture or crystallization of injected cortisone. The pain caused by it is very severe, most often worst than the pain of osteoarthritis itself. In some cases as ours, this flare reaction had lead to post injection synovitis, severe enough to require repeated aspirations. Retrospectively, the emergency arthroscopic procedure carried out on our patient with high synovial fluid WBC count but negative culture, was unnecessary and grossly increased morbidity.

Synovial fluid is one of the most chemo attractant materials in our body. In chronic arthritis, increased amount of stem cell factor (SCF) and transforming growth factor-B (TGF-B)

leads to increased white cell count, especially mast cells in rheumatoid arthritis. Thus, labeling and managing a swollen joint with no history of fever or local redness, with high WBC count can be misleading and as in our patient can severely increase morbidity and hence delay the actual treatment. On personal communication, one busy highly experienced microbiologist told that she quite frequently examines synovial fluid and find rather quite a high number of Neutrophils, which turn out negative on culture and bacterial strains. Thus it strongly suggests high chemotactic characteristics of synovial fluid and some modified contents of knee joint such as fragments of damaged cartilage and bone.

In our case, the inflammation was neither self-limiting nor did it subside by complete rest and washout of the joint. One of the physicians advised another formulation of intra articular steroid to our patient. It miraculously lessened the pain and swelling. No fluid has accumulated and no disabling pain has been complained of by the patient since that second steroid shot.

It should be kept in mind that CRP is not a test for septic conditions; rather it is a non specific marker for inflammatory conditions and often indicates aseptic inflammation, e.g infarction, ischemia, chronic arthritis, atherosclerosis etc. High CRP should be accompanied with positive culture and sensitivity to label it as a septic condition. High count of neutrophils should always raise a suspicion of septic condition, but the site of sample obtained should be correlated with the clinical findings. It is always better to send the operative samples for both culture and sensitivity and for histology. In this patient, the samples were sent in formalin which made culture and sensitivity impossible and hence the diagnosis of actinomycetes remained doubtful. A multidisciplinary team (MDT) of specialized doctors should work hand in hand to limit patient morbidity and to come to the actual diagnosis in lesser time. The fragmented pieces of cartilage and osseous may give a false impression of actinomycetes colonies. It is recommended that any suspicious synovial membrane should be submitted both for culture and histopathological examination.

Conclusion

Acute steroid flare reaction is rare very painful complication of intraarticular steroid injections that may mimic acute and/or suppurative arthritis. Fragments of broken cartilage and osseous tissue surrounded by neutrophils may give a false impression of actinomycetes. Steroid flare reaction must be necessary procedures and superfluous treatments must be avoided.

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