

TREATMENT OF AVASCULAR NECROSIS WITH HYALURONIC ACID IN THE CANCER POPULATION: A CASE SERIES

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Background: Intra-articular hyaluronic acid (HA) injections in non-cancer patient populations have shown some positive outcomes in treating avascular necrosis, however outcomes in the oncology population are scarce. This pilot study describes 7 oncology patients who received ultrasound-guided HA injections and their associated outcomes.

Case Report: This study included 4 female and 3 male patients with radiographic evidence of avascular necrosis. Six of the patients had avascular necrosis of the hip, while one patient had avascular necrosis of the shoulder. All patients underwent single or multiple ultrasound-guided injection(s) of hyaluronic acid to the affected joint. Outcomes were tracked using a combination of subjective pain and functional improvement and/or numeric pain scale. Five patients had improvement in their symptoms, while 2 patients did not.

Conclusion: Intra-articular HA may be a viable alternative to the treatment of avascular necrosis in oncology patients.

Key words: Avascular necrosis, cancer pain, case series, hyaluronic acid, joint pain

BACKGROUND

Avascular necrosis (AVN) is a condition characterized by bone cell death secondary to inadequate blood supply, often induced when bone tissue is directly damaged, or due to a lack of oxygen and/or nutrients. There are many causes and risk factors for AVN which have been well documented in the literature; some of these include trauma, medical conditions (such as diabetes, sickle cell anemia, HIV/AIDS, among others), excessive alcohol use, and a multitude of iatrogenic causes (e.g., bisphosphonate use) (1). Oncology patients are 3.4 times more likely to develop AVN compared to the non-cancer population, and AVN is a substantiated complication of frequently used cancer therapies,

including numerous chemotherapeutic agents, radiation therapy (RT), and corticosteroid use (2). Though used for curative and/or palliative means in cancer patients, these treatments can initiate death of bone tissue, affect blood supply to bone, or obstruct bone healing, leading to AVN (2,3).

Avascular necrosis often results in pain, decreased function, and disability. Treatment for AVN is often a progressive approach with varying degrees of pain relief. Conservative treatments can involve anti-inflammatories, oral pain medication, physical therapy, integrative and complementary medicine approaches, and alteration of chemotherapy and radiation protocols (4). Common surgical options for AVN include core decompression,

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osteotomy, and hip arthroplasty (1). Intra-articular steroid injections have shown temporary relief of pain but may further promote AVN even after a single injection (12). Intra-articular hyaluronic acid (HA) injections in non-cancer patient populations have shown some positive outcomes in treating avascular necrosis (5-7). However, in oncology patients there is a scarcity of literature on HA use for treating AVN. This pilot study describes 7 oncology patients who received ultrasound-guided HA injections and their associated outcomes.

METHODS

This retrospective review was approved via waiver for informed consent by Memorial Sloan Kettering Cancer Center's (MSKCC) Internal Review Board and supported by MKSCC Support Grant (PP30 Core Grant) and the Department of Anesthesiology and Critical Care. A chart review of 7 patients with avascular necrosis of major joints (femoroacetabular or glenohumeral) and a history of oncologic diseases was performed. We reviewed the patients' pain symptomology, relevant medical history, and pre- and postprocedure pain levels and subjective improvement.

In preparation for the femoroacetabular intraarticular hyaluronic acid injections, the patient's affected groin and thigh were prepped with sterile solution. The femoral shaft was located under ultrasound guidance; then under longitudinal view, the femoral neck, head, and acetabulum were viewed. Then after giving 1 mL of 1% lidocaine for skin anesthesia, a 25-gauge 3.5-inch spinal needle was directed to the femoral neck under ultrasound guidance. After negative aspiration, Orthovisc or Hymovis was given. The needle was removed, the patient's leg was cleaned, and dressings were applied. There were no complications.

In preparation for the glenohumeral intraarticular hyaluronic acid injections, the patient's affected shoulder was prepped with sterile solution. The posterior shoulder was visualized with ultrasound guidance. Once the glenohumeral joint was located, a 25-gauge needle was inserted in an out-of-plane approach. Using ultrasound guidance for placement, the needle was directed beneath the glenoid. After negative aspiration, Hymovis was injected. The needle was removed and there were no immediate complications. The patient's shoulder was cleaned, and dressings were applied. There were no complications.

Patients were followed post procedure per standard practice at MSKCC.

CASES

Case 1

A 79-year-old woman with stage IIIC endometrial cancer status post total abdominal hysterectomy and 6 cycles of carboplatin presented with severe right hip pain that had progressively worsened over 8 years. X-ray showed severe arthrosis of the right hip, subchondral sclerosis, and deformity of the femoral head, suggestive of AVN. The patient received a right hip intraarticular Orthovisc-plus-steroid injection with partial pain relief and increased mobility. After the pain returned, she elected for a second right hip intra-articular Orthovisc-plus-steroid injection with her pain score improving to 3 of 10 within a few days.

Case 2

A 31-year-old woman with a history of T-cell lymphoblastic lymphoma that was treated with chemotherapy (vincristine, cytarabine, methotrexate, daunorubicin, cyclophosphamide) and surgical resection of abdominal lymph nodes presented with 2 years of chronic multifocal pain and corresponding AVN of the bilateral shoulders, bilateral humerus, and hips (hips being her primary source of pain). She described "aching" 6 to 9 of 10 pain with movement, especially of her right hip. She was taking morphine sulfate 30 mg twice a day and oxycodone 30/30/45 mg each day with mild relief. The patient received a right hip Orthovisc injection with one day of relief. She continued to have pain and was referred to orthopedics for consideration of a right hip replacement.

Case 3

A 48-year-old man with T-cell lymphoblastic leukemia/lymphoma, treated with chemotherapy (vincristine, Erwinia, cytarabine), presented to the pain clinic with bilateral shoulder pain, right greater than left. The patient reported 6 of 10 pain on average and took no pain medications. Physical exam showed his right shoulder with decreased range of motion in all planes when compared with his left shoulder. X-ray revealed AVN of the right humeral head. The patient received 3 mL of Hymovisc with 1 mL of 1% lidocaine under ultrasound guidance without complications. The patient endorsed improvement in pain but no change in range of motion on follow-up. He continued to manage his symptoms with acetaminophen as needed.

Case 4

A 52-year-old man with a history of prostate adeno-

carcinoma was treated with hormone (leuprolide) and radiation therapy. Post-therapy complications included radiation proctitis, rectal pain, low back pain, and right hip pain (with radiographic evidence of right hip avascular necrosis). Pain was reported as constant and severe, "10 of 10". A series of 3 hyaluronic acid injections were performed under ultrasound guidance with a total of 3 to 5 mL of injectate at each encounter. Two weeks following initial injection, the patient reported partial improvement in pain and received a repeat injection. At the third encounter nearly 5 months later, the patient reported complete pain relief for "several days" after the second injection, with a slow return of right hip pain, now 6 of 10 on the pain scale. With multiple locations of pain and incomplete right hip relief, the patient ultimately decided on spinal cord stimulation for wide-spread coverage of pain, reporting 60% pain relief one month after the procedure.

Case 5

A 24-year-old man with a history of testicular cancer status post orchiectomy and chemotherapy (etoposide and cisplatin) reported bilateral hip pain following treatment and was found to have AVN with subsequent bilateral hip core decompression. He presented to the pain clinic with worsening left hip pain over several months with a "dull" pain exacerbated with movement. Additionally, he reported stiffness and frequent "giving out" of his right hip with ambulation. He reported that his right hip had minimal discomfort. The patient elected for a series of 3 ultrasound-guided hyaluronic acid injections. At the initial presentation he reported 6 of 10 left hip pain. He was taking acetaminophen as needed for pain. At one month's follow-up he reported significant improvement in pain and function since the first HA injection, and he declined a second injection at that time. At 2 months' follow-up the patient's reported pain had returned, now rating it as 6 of 10. A second ultrasound-guided HA injection was performed at that time. Three weeks later the patient returned with 5 of 10 pain and received a third HA injection. Subsequently during a telehealth follow-up encounter, the patient reported "great relief."

Case 6

A 72-year-old woman with metastatic adenocarcinoma of the lung status post L4-S1 percutaneous instrumented stabilization with cement augmentation, L5 kyphoplasty, and left L5 facetectomy/hemilami-

notomy/pedicle excision presented to the pain clinic for persistent low back pain. The pain was previously managed with sacroiliac joint injection, but the patient presented now with right hip pain secondary to stage IV AVN. She underwent a right intraarticular 3 mL of hyaluronic acid injection with 10 mg of triamcinolone with 1.5 mL of 0.25% bupivacaine. It was unclear if she had any benefit, as she underwent right total hip arthroplasty shortly after.

Case 7

A 63-year-old woman with a history of B-cell lymphoma requiring long-standing steroid therapy presented with bilateral hip pain with magnetic resonance imaging demonstrating bilateral AVN. Bilateral hip injection with 3 mL of Hymovis and 2 mL of lidocaine was provided without significant improvement. The patient subsequently had bilateral femoral nerve component injection without any benefit and ultimately underwent bilateral hip replacement.

Discussion

This case series demonstrates the potential efficacy of HA injections to joints with AVN to help decrease pain and improve function.

Synovial fluid, which is composed primarily of hyaluronic acid and chondroitin sulfates, is essential for joint lubrication and nutrition of articular cartilage. HA consists of repeating D-glucuronic acid and N-acetylglucosamine units that function as a shock absorber and lubricant for the joints (8). It naturally occurs in various human tissues like the skin, thoracic lymphoma, umbilical cord, and synovial fluid. With osteoarthritis and AVN, there is not only a loss of synoviocytes, resulting in decreased production of synovial fluid, but often, also corresponding inflammatory and synovial content changes when compared to a normal, healthy joint.

HA use in treatment of osteoarthritis, which can be associated with both erosive and inflammatory processes within the intra-articular space, has been well-documented in the literature (9). Likewise, studies also suggest that AVN can alter the synovial environment and increase intraarticular inflammation, as evidenced by decreased levels of glucose and elevated levels of lactate, T-cells, and macrophages within the joint, which can lead to further destruction of articular tissue and increased pain (10,11). Thus, it is reasonable to postulate potential benefits of HA injections for patients with AVN as explored in this case series.

With increased risk of AVN in the oncologic population due to their cancer treatments, we were able to identify 7 patients at MSKCC who have undergone HA injections for joint pain in the setting of AVN. Six of the patients had HA injections to the hips, while one had HA injection to the shoulder. There was a range in magnitude of relief, from no relief as demonstrated in case 7, to complete relief in case 4. Differentials in duration of relief are also significant, ranging from 0 days to 6 months as seen in case 4. Case 1 demonstrates that even with bone-on-bone apposition, HA injection can still provide substantial relief. Case 2 suggests that a patient with diffuse long-standing pain may not benefit as much from a localized injection of HA. Case 3 shows that although pain symptoms may improve, range of motion might not change for the joint. Cases 4 and 5 illustrate that a series of 3 HA injections may offer more symptomatic relief than a single injection. Lastly, cases 6 and 7 indicate that end-stage AVN HA injections may not be helpful, and a practitioner can potentially just have the patient progress to joint replacement.

In reviewing the cases, there are 2 notable issues that are prudent to discuss. First, in cases 2 and 7, the lack of benefit may suggest that the inflammatory synovial contents exceeded any possible therapeutic effect of HA treatment. While intraarticular steroids may have provided short-term benefit, the risk of steroids would also increase the long-term risk of fracture (and possible subsequent joint replacement). Secondly, we would like to note that in cases one and 6, steroids were also used

as intra-articular injectate and thus we are unable to adequately comment on intra-articular HA versus the steroid as being responsible for the end effect.

CONCLUSION

This case series demonstrates potential therapeutic benefit for HA injections in the oncologic population with AVN pain at the shoulder and hips. Future studies are needed in order to fully elucidate the magnitude and duration of relief that HA injections can provide.

Contributions

AG and NR: They are the guarantors. They developed the idea for the study, designed data collection tools, method of analysis, monitored data collection for the whole study, cleaned and analyzed the data, and assisted in drafting and revising the manuscript prior to submission.

JC: This author assisted in creating data collection tools, performed data collection, analyzed the data, assisted in drafting the manuscript, and approved the final version to be published.

PJ: This author assisted in creating data collection tools, performed data collection, analyzed the data, assisted in drafting the manuscript, and approved the final version to be published.

AP: This author assisted in creating data collection tools, performed data collection, analyzed the data, assisted in drafting the manuscript, and approved the final version to be published.

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