Case Report

A Patient with Fatal Necrotizing Fasciitis following the Use of Intra-Articular Sodium Hyaluronate Injections: A Case Report

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1. Introduction

Osteoarthritis (OA), a degenerative joint disease, is a key cause of disability around the world and a large, ever-growing public health concern. Both obesity and the aging population are expected to increase the prevalence of OA [1, 2]. Sixty-seven million Americans, about 25% of the adult population, are projected to have OA by 2030 [2]. OA is characterized by progressive cartilage damage and loss of the synovial fluid's lubricating and viscoelastic properties [3]. Intra-articular hyaluronic acid viscosupplementation was first approved by the Food and Drug Administration (FDA) in 1997 and is used as a conservative option for OA knee pain relief [1–3]. Synovial fluid and articular cartilage contain hyaluronan, a natural compound that reduces the coefficient of friction, thereby giving ease in joint movement [3]. An osteoarthritic knee has up to 50% less hyaluronan and the molecule itself is degraded, reducing its molecular weight. This causes increase in coefficient of friction and difficulty with joint movement [4]. Hyalgan (Fidia, S.p.A., Abano Terme, Italy) is a sodium hyaluronate intra-articular injectable medication, derived from rooster combs, having identical viscoelastic properties as human hyaluronic acid [5].

Viscosupplementation, with intra-articular sodium hyaluronate, is now a widely used method for treatment of knee OA. In general, the literature has shown an excellent safety profile for this treatment modality, with the most common adverse events being mild injection site pain and swelling [1, 4, 6–11]. In this report, we describe a case of a woman who had received multiple sodium hyaluronate injections and developed severe necrotizing fasciitis near the injection site.

2. Case Presentation

Our patient is a 63-year-old female with osteoarthritis in the lumbar spine and bilateral knees. Knee X-rays showed bilateral mild osteoarthritic changes. MRI of left knee showed grade II–III patellar chondromalacia and mild osteoarthritic...
changes. Her left knee pain was uncontrolled with conserva-
tive measures including NSAIDs and narcotics. Steroid injec-
tions were provided once with no pain relief. Subsequently,
over a period of five years, she received multiple courses
of sodium hyaluronate injections to the left knee without
complications, waiting at least six months between each series
of five injections. The skin was thoroughly examined prior
to each injection and was noted to be in a good condition,
with no breaks, rashes, or bruises evident. She had great pain
relief from the Hyalgan injections and repeatedly requested
them. Clean technique was employed prior to each of these
injections, including use of betadine, alcohol, and gloves.

Pertinent past medical history included treatment for
invasive ductal left breast cancer with lumpectomy and
radiation five years prior to this hospital presentation. She had
been in remission until four months prior to hospitalization,
when she was diagnosed with recurrent left breast ductal car-
cinoma. She then underwent mastectomy with axillary lymph
node dissection and received one round of chemotherapy
treatment, with Taxotere, Carboplatin, and Herceptin, 11 days
prior to hospital admission. The surgery and chemotherapy
proceeded without complications.

Five days after the last sodium hyaluronate injection to
the left knee, she presented to the hospital with complaint of
left leg pain that woke her from sleep. She initially noticed
a small area of erythema in the left popliteal fossa. Over the
next few hours, she developed rapidly progressive swelling,
expansion of the erythema, and formation of multiple large
bullae extending from the thigh to proximal leg. By the
time she arrived at the hospital, the bullae and erythema
had expanded to the gluteal fold and inguinal region. CT of
left lower extremity showed free gas through the adductor
musculature and posterior and superior to ischial tuberosity.
Given the aggressive symptoms, the patient was emergently
taken to operating room for extensive debridement and
amputation at the lesser trochanter. She was then admit-
ted to intensive care unit on broad spectrum antibiotics
for septic shock secondary to necrotizing fasciitis of the
left lower extremity, involving both posterior and anterior
compartments. She deteriorated and required vasopressors,
intubation and multiple debridements. Over the next 3 days,
she suffered multiorgan failure and required hemodialysis.
Given her wishes and poor prognosis, life support was
withdrawn. She died 20 days after last chemo, 13 days after
the most recent Hyalgan injection, and 7 days after the onset
of necrotizing fasciitis.

3. Discussion

Necrotizing fasciitis is a rare, but potentially fatal, rapidly
progressive soft tissue infection involving subcutaneous fat
and fascia [12, 13]. Early diagnosis, use of antibiotics, and
debridement are essential [12, 13]. The causative bacteria
could be aerobic, anaerobic, or mixed flora [12]. The most
common pathogens are streptococci and S. aureus [12]. Risk
factors include immunosuppression, diabetes, trauma, and
operative infections [12]. There are case reports of necro-
tizing fasciitis occurring after intra-articular corticosteroid
injections and diclofenac injections [14–19]. However, there
are no previously described cases of necrotizing fasciitis fol-
lowing viscosupplementation. As mentioned earlier, sodium
hyaluronate injections have proven to be quite safe and have
a low incidence of serious side effects [1, 4, 6–11]. The overall
incidence of side effects is approximately 1–3% per injection
[20]. The most common side effects include injection site
pain, GI complaints, local skin reaction, and pruritis; rare
serious adverse outcomes are septic arthritis and gout [6, 20–
23].

Apart from the issue of adverse outcomes, the efficacy of
viscosupplementation has recently been called into question
[24–26]. In 2012, Rutjes et al. did a systematic review of
89 large trials, involving 12,667 patients, and showed that
there was only a small, clinically irrelevant benefit in terms
of pain, with no positive effect on function [24]. Jørgensen
et al. did a multicenter, randomized, and double blinded
study of 337 patients and found no improvement in pain or
function compared to placebo. The American Association of
Orthopedic Surgeons recommends neither for nor against the
use of viscosupplementation for the nonarthroplasty treatment
of OA of the knee based on their systematic review of the
published studies [24, 25, 27].

Typically, patients who develop necrotizing fasciitis have
a preexisting condition making them more susceptible to
infection [12, 13]. Our patient was recently treated for invasive
ductal carcinoma of the left breast, with chemotherapy 11 days
prior to hospitalization. She was likely immunosuppressed
secondary to malignancy and recent use of chemotherapeutic
agents. Necrotizing fasciitis most frequently occurs following
local trauma which compromises skin integrity [12, 28]. Our
patient's rapidly spreading, fatal necrotizing fasciitis started
near the site of her multiple injections. Sodium hyaluronate
injections are contraindicated if infection or skin disease
is present at the injection site, in order to reduce risk of
septic arthritis [5]. However, there is no mention of avoiding
viscosupplementation in immunosuppressed patients, such
as diabetics or patients with underlying malignancy. Our
patient was examined by physician prior to each injection and
was noted to have no local skin condition near the injection
site.

Though our patient had no skin compromise at the
injection site, this possibly was the source of bacterial inoc-
ulation. The American College of Rheumatology guidelines
state that sterile gloves should be worn for intra-articular
steroid injections [29]. However, Charalambous et al., in
their survey, noted that 53.4% of responders did not follow
aseptic techniques prior to these injections [21]. It should
further be noted that there are no proper guidelines regarding
implementation of clean or aseptic technique with Hylgan
injections.

4. Conclusion

Despite the rarity of adverse events, intra-articular sodium
hyaluronate injections can cause life-threatening infections.
Furthermore, the long-term effectiveness of these injections
is still a matter of debate [24, 25, 30, 31]. We recommend
clear guidelines for clean technique be put in place for use with sodium hyaluronate injections. In immunosuppressed patients, it may be necessary to observe full sterile technique, given the increased likelihood of infection. Further studies should be done examining the incidence of adverse events following such injections in immunosuppressed patients. The practical implications of such studies could be crucial, as many patients receiving these injections may be on concomitant immunosuppressive agents such as disease modifying antirheumatic drugs (DMARDs) or chemotherapeutic agents.

Conflict of Interests

The authors declare that they have no competing interests.

Authors’ Contribution

Shanti Virupannavar collected patient information and wrote the paper. Carla Guggenheim helped edit the paper and collect additional information.

References


