BRIEF REPORT

IMMEDIATE "STEROID FLARE" FROM INTRAARTICULAR TRIAMCINOLONE HEXACETONIDE INJECTION: CASE REPORT AND REVIEW OF THE LITERATURE

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We describe a patient who had an immediate, intense, localized synovitis due to intraarticular triamcinolone hexacetonide injection. The reaction was secondary to rapid intracellular ingestion of the steroid microcrystals as demonstrated by compensated polarized microscopy. We report the unique nature of this patient's response, and we review previous literature regarding "steroid flare" after intraarticular injection.

The efficacy and safety of intraarticular corticosteroid injection in the treatment of rheumatic disease is well established (1). The major complication of this therapy is thought to be a localized inflammatory "flare" in the injected joint. This response usually occurs 4–24 hours after injection and is supposedly less common with the use of long-acting steroid esters than with hydrocortisone acetate. This phenomenon has been demonstrated experimentally in normal volunteers, but few reports detail its occurrence and pathogenesis in clinical practice. We describe a patient who developed an intense, localized inflammatory reaction to intraarticular triamcinolone hexacetonide within 90 minutes after injection. Results of synovial fluid analyses before and after injection, polarized microscopy findings, and a review of the literature are presented.

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Case report. The patient, a 32-year-old white man with no past rheumatic disease or drug allergies, developed pain and swelling of the right knee without preceding trauma. No systemic symptoms were present, and no other joints were symptomatic. A skin rash involving the nails and hands, consistent with dyshidrotic eczema, had been present for a few years and treated topically. A physical examination performed 3 days after the onset of symptoms revealed a large right knee effusion with mild warmth, stable collateral and cruciate ligaments, and a negative McMurray sign. A chronic eczematous rash was present on the hands in association with onycholysis. The patient was afebrile. Arthrocentesis yielded 20 ml of clear, straw-colored fluid with moderate viscosity. The total nucleated cell count was 1,000/mm^3, and no birefringent crystals were seen with compensated polarized microscopy.

An intraarticular injection of 40 mg of triamcinolone hexacetonide was administered for symptomatic treatment of mild synovitis, which was presumed to be secondary to acute internal derangement of cartilage or cruciate. The patient returned to work, but returned to the clinic 90 minutes later; he was unable to walk, and he had intense knee pain and inflammation, a temperature of 38°C, and a tense, hot, right knee joint, with no pain-free range of motion. A repeat arthrocentesis yielded cloudy fluid with poor viscosity and a total nucleated cell count of 30,000/mm^3, which consisted predominantly of polymorphonuclear leukocytes. Compensated polarized microscopy revealed numerous negatively birefringent intracellular and extracellular rod-shaped crystals, consistent with the injection of triamcinolone ester (Figure 1). The patient was treated aggressively with the instillation of 20 cc

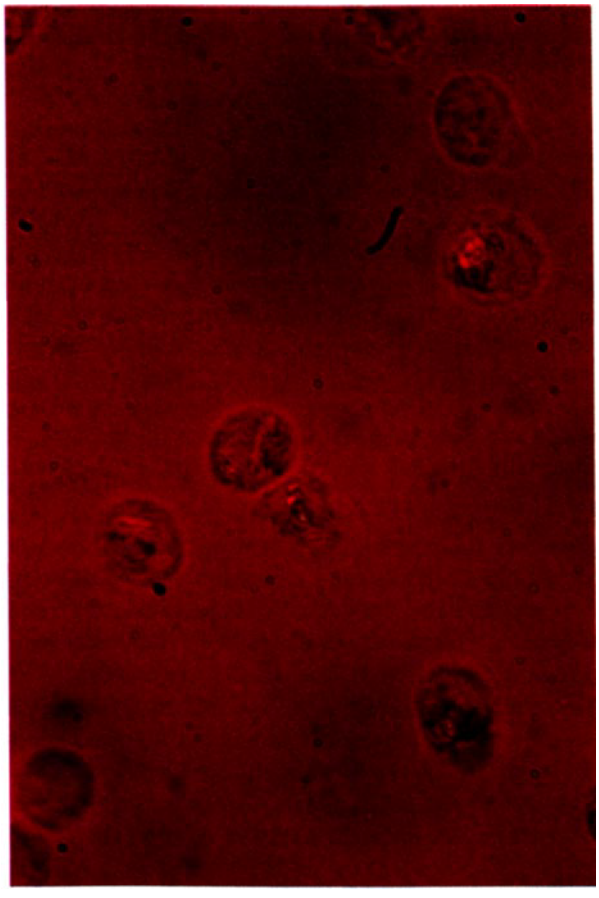

Figure 1. Polarized microscopy of synovial fluid obtained from the patient's knee 90 minutes after the intraarticular injection of 40 mg of triamcinolone hexacetonide, showing intracellular negatively birefringent triamcinolone crystals.

of bupivacaine hydrochloride into the joint, which was ineffective in eliminating his pain or inflammation after 1 hour. He was then treated with naproxen and bed rest, which resulted in resolution of the symptoms over a 24-hour period. One week later, only a small, cool effusion on the knee was present.

Discussion. The effectiveness of intraarticular hydrocortisone acetate in relieving symptoms of arthritis was first reported by Hollander et al in 1951 (1). Prompt resolution of inflammatory articular symptoms was observed, particularly in patients with rheumatoid arthritis. The technique was also employed with success in patients with osteoarthritis, though a double-blind study in 1958 showed that at 6 weeks, there was no difference in pain, range of motion, or patient satisfaction between knees injected with hydrocortisone acetate, saline, lidocaine, or sham injection (2).

As the technique of intraarticular injection became widespread, anecdotal reports of a postinjection "steroid flare" of inflammatory symptoms in the injected joint prompted McCarty and Hogan to study this phenomenon in more detail in 1964 (3). Of 25 normal volunteers who had their knees injected with corticosteroid preparations, only 1 developed clinical postinjection synovitis. All those receiving hydrocortisone acetate had increased synovial white blood cell (WBC) counts and intracellular ingestion of the acetate crystals 6 hours after injection. Arthrocentesis produced no synovial fluid after injection in volunteers who received triamcinolone hexacetonide, and the authors suggested that this preparation should be used instead of hydrocortisone acetate because of the unlikelihood of its producing a "steroid flare."

In 1970, Hollander reinforced this concept by reporting his almost 20-year experience with intraarticular steroid injection, noting a postinjection inflammatory flare in approximately 1–2% of patients, which was more common with use of the earlier steroid preparations (4). The development of the long-acting, microcrystalline, branched chained steroid esters such as triamcinolone hexacetonide and prednisolone tebutate resulted in their widespread use for intraarticular injection. Though these preparations have not previously been reported to cause an inflammatory flare, increased synovial fluid WBC counts similar to that seen with hydrocortisone acetate have been observed after injection (5). Steroid crystals have also been demonstrated, by polarized and electron microscopy, to be present intracellularly 24 hours after intraarticular injection of these agents in patients with osteoarthritis of the knee (6).

Our patient had the first reported case of an immediate (<2 hours) inflammatory reaction to triamcinolone hexacetonide. The phlogistic property of these steroid crystals in this patient was confirmed by the dramatic clinical signs of inflammation, the rapid increase in synovial fluid WBC count, and the presence of the steroid crystals intracellularly. The ineffectiveness of the large dose of local bupivacaine in alleviating the patient's pain was surprising; his symptoms were improved only with a systemic antiinflammatory agent and with the passage of time. Many rheumatologists (including us) use a local anesthetic agent, either lidocaine or bupivacaine, mixed with a microcrystalline steroid ester for intraarticular injec-

tion. This practice is not supported by the literature and deserves randomized, blinded study.

In conclusion, a severe, immediate, local inflammatory reaction may occur in some patients after intraarticular injection of triamcinolone hexacetonide. This reaction is caused by rapid intracellular ingestion of the microcrystalline steroid ester, and it appears to be different in its time of onset and severity than previously reported reactions noted in volunteers injected under controlled conditions.

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