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## Subcutaneous Injection of Anakinra in Patients with Shoulder Pain Due to Rotator Cuff Tendonitis and Subacromial Bursitis

The pathology involving the rotator cuff is a spectrum ranging from simple inflammation, as in rotator cuff tendonitis, subacromial bursitis, and impingement syndrome, to rotator cuff tears [1,2]. The management of rotator cuff pathology depends on various factors including the extent of the tear and failure to improve after 6 months of conservative treatment. Initially, patients are treated conservatively with the use of nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and rest. The second line of treatment is injection of corticosteroids into the subacromial bursa. For unresponsive cases and for larger tears of the rotator cuff, surgical intervention becomes the preferred treatment option [3]. We have treated numerous patients with rotator cuff pathologies using anakinra. Here, we provide a case report of one patient who presented with pain in his right shoulder after a fall. On examination, there was severe tenderness in his rotator cuff. There were no signs of joint dislocation or fractures. A magnetic resonance imaging (MRI) scan of his right shoulder was ordered, and findings were compatible with a complete tear involving the anterior aspect of the supraspinatus tendon adjacent to the intertuberous sulcus. He was subsequently given anakinra (Kineret®; Amgen Inc., Thousand Oaks, CA) at a dose of 100 mg subcutaneously. On re-evaluation 1 week later, he gave the information that his pain had dropped from a score of 9/10 to 3/10 within 5 minutes of receiving the injection. He received six more subcutaneous doses of anakinra over a period of 5 months. The first three doses were given once weekly; thereafter, he got the injections at an average frequency of once a month. The range of motion in his right shoulder joint improved dramatically. Five months after initiating treatment, his range of motion had been fully restored from an initial value of 40° of abduction. A subsequent MRI scan of the patient's right shoulder showed no sign of the rotator cuff tear. However, that MRI was done at a different facility and read by a different radiologist.

The origins of pain are the biochemical mediators of inflammation and the inflammatory response. To treat pain, we must block these mediators and block the signals they send up through

the nerve cells. A variety of mediators are generated by tissue injury and inflammation. These include substances produced by damaged tissue, substances of vascular origin, as well as substances released by nerve fibers and various immune cells [4]. In one study of patients with rotator cuff diseases, the level of the cytokine interleukin (IL)-1 $\beta$ was significantly correlated with the degree of pain [5]. In another study, levels of IL-1 $\beta$  were significantly higher in the shoulder joints in patients with anterior instability and chronic inflammation of the joint [6]. Immunohistological staining has demonstrated the expression of IL-1 $\beta$ , tumor necrosis factor alpha, transforming growth factor beta, and basic fibroblast growth factor in subacromial bursa derived from patients with rotator cuff tears [7]. Anakinra is a form of human IL-1 receptor antagonist, produced by recombinant DNA technology. In this study and in other patients that we have treated, we obtained complete pain resolution for significant periods of time with a subcutaneous injection of anakinra. These patients were able to avoid surgery and achieve full ranges of motion in their shoulders. Subcutaneous anakinra could obviate the need to administer intra-articular steroid injections for subacromial bursitis or rotator cuff tendonitis. The risks of a subcutaneous injection of anakinra are much less than those of an intra-articular steroid injection. Steroid injections are associated with a myriad of local and systemic side effects, while subcutaneous injection of anakinra is associated with a decreased immune response and increased risk of infection when the injection is administered daily, as in rheumatoid arthritis patients. In patients with rotator cuff tendonitis and subacromial bursitis, we have only had to administer a single subcutaneous injection once every week for up to 6 months. Subcutaneous injection of anakinra is an exciting new option in the treatment of inflammatory pain syndromes such as rotator cuff tendonitis and subacromial bursitis.

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