A pilot study of IL-1 inhibition in acute calcific periarthritis of the shoulder

Acute calcific periarthritis is a known cause of a painful shoulder. The calcium deposits are composed of different crystalline forms, including hydroxyapatite. Usually, these acute episodes are self-limiting. Current treatment approaches include non-steroid anti-inflammatory drug (NSAID) and steroids. Microcrystals are capable of triggering interleukin (IL)-1 mediated inflammation. Therapeutic inhibition of IL-1 signalling has been shown to be effective in gout, and may have a place in the treatment of other crystal-induced inflammatory conditions. We have therefore investigated the effects of IL-1RA (anakinra) in acute calcific periarthritis in a pilot study.

Five consecutive patients (mean age of 60 years) were treated. They all had acute shoulder pain for <7 days and had not responded to 48 h of high dose NSAIDs. The clinical evaluation consisted of evaluation of total, at rest and day pain by visual analogue scale (VAS) at days 0, 1, 3, 15 and 42; shoulder mobility at days 0, 3 and 15; and erythrocytes sedimentation rate (ESR) and C reactive protein (CRP) at days 0 and 3. x-Rays were performed at days 0 and 15 and an ultrasound (US) at days 0, 3 and 15. Anakinra 100 mg was administered subcutaneously for three consecutive days after the evaluation at day 0. Rescue analgesics were allowed and recorded.

Following treatment, pain improved rapidly. Rest pain (VAS) declined from 9.6±0.5 to 0.5±0.5 by day 1. No patients required rescue analgesia at day 3. The effect on day pain was also positive but less spectacular (figure 1). Shoulder mobility improved, and near complete recovery was observed at day 15. CRP and ESR normalised in all patients. At day 42, four of the patients were totally asymptomatic. One patient developed a new flare 3 days after the last anakinra injection and responded to corticosteroids. No systemic or local adverse effect was reported. On x-rays and US, periarticular calcifications shrank: mean diameter was 21 mm at entry and 12 mm at day 15. There was a rapid reduction of Doppler activity around the calcifications by day 3 (figure 2).

This is the first study showing that administration of an IL-1 inhibitor reduced the signs and symptoms of acute calcific tendinitis. The effect on rest pain was prominent with near total disappearance of pain within a few hours that lasted for up to 6 weeks in four patients. We also observed a rapid fall in CRP that paralleled the clinical improvement and reduction of Doppler signal on US. The absence of total dissolution of the calcification is not surprising, as the follow-up time was too short. The very rapid effect on pain before the reduction in the

Figure 1  Evolution of VAS before and after the treatment in the five patients.

Figure 2  Patient 4: regression of Doppler activity around the calcification from day 0 to day 3.
size of the calcification suggests that as in gout\(^4\) or in traumatic knee injury\(^6\) it is the drastic reduction of inflammation that is the main mechanism of action. Although this is an open-label study with a small patient numbers, it adds proof to the concept that IL-1 inhibition effectively suppresses clinical inflammation in various microcrystal-induced inflammatory states. In patients who are intolerant or have contraindications to NSAIDs or corticosteroids, IL-1 inhibition can be an interesting therapeutic alternative. A controlled study is needed to validate the effectiveness and safety in the short and longer term.

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