Are The Symptoms Of Calcific Tendonitis Due To Neoinnervation And/or Neovascularisation?

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Introduction: Calcific tendonitis is a very painful condition that affects the range of movement and function of the shoulder. Pain is often aggravated by elevation of the arm above shoulder height or by lying on the affected shoulder. The cause of calcific tendonitis is not yet understood, many studies have been published on its symptoms and aetiology. Previous papers have suggested that calcific tendonitis may be attributed to ischemia, metabolic disturbances and fibro-cartilaginous transformations of the tendon tissue. To our knowledge there has been no previous studies regarding neo-vascularisation, neo-innervation and increased pain with patients presenting with calcific tendonitis, therefore the aim of this study was to determine the relationship between pain, increases vessels and increased nerve growth in patients presenting with calcific tendonitis.

Methods: This was a prospective case control study. After regional anaesthesia, ultrasound was used to identify calcium within the tendon and a breast biopsy localisation needle was placed in the calcific region in patients with calcific supraspinatus tendonitis. At arthroscopy the needle was utilized to identify and subsequently remove the calcium from the supraspinatus tendon. Small 2mm samples were taken from the supraspinatus tendon adjacent to the calcific lesion (calcific tendonitis, n = 7), torn supraspinatus tendon of patients undergoing rotator cuff repair (RCT, n = 6 ) and the subscapularis of patients undergoing stabilisation surgery (control, n = 6 ). Samples were paraffin embedded, sectioned and stained with hematoxylin and eosin. The following antibodies were used for immunohistochemical evaluation; macrophages (CD68), M2 macrophages (CD202), mast cells (mast cell tryptase), T cells (CD3), vascular endothelium (CD34) and general nerve marker (PGP9.5) utilising the appropriate isotype controls

Results: There were no significant differences in T-cell count between the calcific tendonitis group and the RCT group; however both the calcific tendonitis and RCT group had 5-6 fold higher T-cell counts compared to the control group (p < 0.001; p < 0.004). There was a 3-8 fold increase of nerve markers, neovascularisation, macrophages, M2 macrophages, and mast cells in the calcific tendonitis group compared to the RCT group (p < 0.0002) and control group (p < 0.0001). There were approximately three times more of each markers in tendon from patients with calcific tendonitis compared to tendon from patients with rotator cuff tears.Increased blood vessels positively correlated with more frequent pain during sleep (spearman correlation, r = 0.6, p < 0.01) and extreme pain (r = 0.6, p < 0.01). Increase blood vessels also positively correlated with increased CD68 macrophages (r = 0.5, p < 0.02), M2 macrophages (r = 0.6, p < 0.01), mast cells (r = 0.6, p < 0.005) and T-cells (r = 0.7, p<0.001). Increase nerve counts positively correlated with more frequent extreme pain (r = 0.6, p < 0.01), with increase neovascularisation (r = 0.7, p < 0.01), counts of CD68 macrophages (r = 0.6, p < 0.04), M2 macrophages (r = 0.6, p < 0.01), mast cells (r = 0.8, p < 0.0001), and T-cells (r = 0.6, p < 0.01).
**Discussion:** To our knowledge this is the first time markers for nerves and blood vessels have been evaluated in tendon from patients with calcific tendonitis. This study shows a very significant concomitant eight (8) fold increase in mast cells, macrophages, and neo-neurovascular infiltration in the tendons of patients with calcific tendonitis. These increases in neo-neurovascular infiltration were strongly associated with shoulder pain. The data is consistent with the hypothesis that deposition of calcific material is associated with a foreign body immune reaction, new blood vessels and nerves, and the very severe pain often noted in patients with calcific tendonitis.

**Significance:** Results from this study showed calcific material is associated with a foreign body immune reaction, new blood vessels, new nerve growth and very serve pain with patients presenting with calcific tendonitis. There was also an eight fold increase of nerve markers, new blood vessels in patients with calcific tendonitis compared to patient with or without rotator cuff tear.

![Neovascularisation](image)

![Vessel count (per mm2)](image)

**Study groups**

* *** p<0.001
* **** p<0.0001
Nerves

Study Groups

Control
Rotator cuff tear
Calcific Tendonitis

Nerve counts

****p<0.0001

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