Session A – 11:01 – 11:08 am

Apoptosis – the Cause of Non-insertional Achilles Tendinopathy?

Presenting:

Christopher Jon Pearce, FRCS, MFSEM
Richmond, Surrey, UK

Additional Author:
James David Calder, MD, FRCS, FFSEM

Summary:

We found significantly raised levels of apoptosis as well as Nitric Oxide Synthase isoforms in tendinopathic Achilles tendons compared to controls taken from normal areas of tendon in the same subjects. Apoptosis clearly plays a role in the development of non-insertional Achilles tendinopathy and appears to be related to the presence of raised eNOS and iNOS levels.

Introduction

The pathogenesis of chronic tendinopathy is unclear. The role of the increased apoptosis of tenocytes has been suggested. The upregulation of nitric oxide synthase in the Achilles tendon in non-insertional Achilles tendinopathy was reported in a previous study. The purpose of this study was to investigate whether apoptotic cells were present in tendinopathic Achilles tendon tissue with raised endothelial (eNOS) and inducible (iNOS) nitric oxide synthase levels.

Methods

Ethical approval was granted by the research ethics committee and all patients gave informed consent. Samples were obtained from the Achilles Tendons of 14 patients with non-insertional Achilles tendinopathy who had failed conservative treatment for at least 6 months and were undergoing a surgical procedure. Several biopsies were taken of the visibly abnormal tendon tissue. Control samples were taken from macroscopically normal tendon. Both sample sites were chosen in correlation with the pre-operative MRI scan. Standard immunohistochemical techniques were used to identify the expression of eNOS and iNOS. Apoptotic cells were identified using terminal deoxynucleotidyl transferase-mediated dUTP neck end labelling (TUNEL reaction) and the demonstration of Caspase-3 activation.

Results

Significant differences were found between the diseased tendon and the controls for all of the parameters measured. The mean Caspase-3 cell count for diseased tendon was 51.9 compared to 28.3 for the controls ($p=0.000001$). The mean TUNEL cell count for diseased tendon was 24.1 compared to 14.8 ($p=0.00014$). iNOS densitometry revealed a mean of 26.1 for the diseased tissue verses 15.0 for the controls ($p=0.000009$) and the values for eNOS were 48.3 and 23.7 respectively ($p=0.015$).

Conclusions

The new finding of apoptosis in Achilles tendinopathy may help to explain why previous studies have demonstrated a lack of significant inflammatory response in tendinopathic tissue. It appears that this is nitric oxide mediated and raises the possibility of modulating disease progression by inhibiting key elements in the pathway. With a better understanding of the pathophysiology of the condition, it is hoped that this may lead to the development of treatment strategies for early Achilles tendinopathy.