Rotator cuff degeneration and lateral epicondylitis: a comparative histological study

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Abstract

Objectives—Rotator cuff tendinitis and lateral epicondylitis are common in clinical practice but the underlying pathology is poorly understood. The study examined both normal and biopsy tendon specimens histologically, to determine the mechanisms involved in tendon degeneration.

Methods—Rotator cuff tendons from 83 cadavers aged 11–94 and tendon biopsy specimens from 20 patients with lateral epicondylitis aged 27–56 years were examined histologically.

Results—The microscopic changes found in the tendon biopsies from the elbow were similar to those found in the cadaveric rotator cuff tendons. Abnormalities ranged from minor blood vessel wall changes and loss of tenocytes to calcification. The most frequent abnormality was glycosaminoglycan infiltration and fibrocartilaginous transformation. There appeared to be some sequence in the changes observed which were milder in younger patients. Only 17% of cadaver tendons, below the age of 39 were abnormal but abnormalities increase in later life to around 40–50%.

Conclusions—There was an increasing incidence of degenerative changes in tendons with age. The changes observed in biopsy samples of common extensor tendons were the same as those seen in aged supraspinatus tendons, but these changes were not seen in control common extensor tendons.


Rotator cuff tendinitis and lateral epicondylitis (tennis elbow) are the principal soft tissue lesions affecting the upper limb and are commonly seen in rheumatological and orthopaedic practice. Together they give rise to considerable disability within the adult population, yet the underlying pathology remains unclear. Like many soft tissue lesions, biopsy is not necessary for diagnosis and surgery is not often indicated. Therefore material for pathological study is rarely available.

Age-related or degenerative changes in tendon would appear to predispose to lesions, as rotator cuff tendinitis and tennis elbow are infrequently seen before middle age. In addition, rotator cuff rupture is a frequent finding in elderly cadavers, although the relationship of age-related change to symptoms has been thought to be poor. In the absence of operative material, a study of changes in the rotator cuff with age would at least give insight into changes that occur which might predispose individuals to symptomatic lesions.

Studies on cadavers have described changes within the rotator cuff and also at their insertion. It is probable that changes within the tendon itself are of most relevance to clinical symptoms. Rupture of the cuff and calcification is usually seen within the substance of the tendon, 1–2 cm from the insertion. As this area is the ‘watershed zone’ of blood supply from muscle and bone it is relatively avascular making it prone to ischaemic stress and has been called the critical zone. However, a recent qualitative study on the number and size of blood vessels in this region suggests that there is little difference between the supraspinatus and infraspinatus tendons. As most problems occur in the supraspinatus tendon, other factors in addition to blood supply most predispose this tendon to degenerate.

Rotator cuff degeneration has had limited study. An early investigation by Lindblom in 1939 was followed by an extensive study on 125 cases by Wilson and Duff in 1943 who attempted to grade the severity of changes and looked at the effects of age. A later paper by Brewer on just three tendons included some electron microscopy studies and most recently an investigation by Clark emphasised the interdependence of the individual components of the rotator cuff. These studies are descriptive and it is often unclear how frequently changes were found and at what age.

The region of the tenoperiosteal junction is believed to be the usual site of the lesion in lateral epicondylitis, although only minor age-related changes have been documented. A variety of abnormalities have been documented in operative specimens. Tendon rupture is uncommon and the relationship to previous local steroid injections is uncertain. Microfractures, cystic and fibrinoid degeneration and round cell infiltrations (often considered to be inflammatory granulation tissue) and attempts at repair have been described in some specimens. Macnab reported that some degenerate cadaver rotator cuff tendons show changes that might be interpreted as granulation tissue.

We proposed that there might be similarities in the pathological changes that occur with age in the rotator cuff, and which probably predispose to symptomatic lesions, and those seen in the condition of lateral epicondylitis. In this study we investigated the changes with respect to age that occur in rotator cuff tendons and compare them with those seen in tendons removed from patients with lateral epicondylitis.
Methods

The rotator cuffs were obtained from cadavers at necropsy within 48 hours of death. For local ethical considerations the rotator cuff was removed without removal of the shoulder joint itself. A longitudinal incision was made extending over the lateral aspect of the shoulder to below the deltoit insertion. The deltoit was reflected back and the shoulder positioned to reveal the rotator cuff. The conjoined tendons of supraspinatus and infraspinatus (plus a variable amount of subscapularis) were removed by incision at the bony insertion and muscle origin. The bony insertion could therefore not be examined microscopically and the area of interest for this study was the ‘critical area’ approximately 1” from the point of insertion.\(^{15,16}\) Specimens were then trimmed to remove all muscle tissue, fat and as far as possible, all remains of the subacromial bursa and shoulder joint lining, without disrupting the tendon which forms the bonding between the two. No cadaver had a known history of shoulder pain as assessed from medical records. Cadavers who had a large rupture of the rotator cuff were excluded.

All specimens from the shoulder and elbow were preserved in formal saline until processed. Histological examination including staining with Haematoxylin and Eosin, Weigert’s Resorcin Fuchsin, Ponceau S (showing elastic fibres black and collagen red) and Alcian Blue at Acid pH (to show glycosaminoglycan). Specimens were batch processed and microscopic examination was performed by the same investigator (GAG) and was undertaken without knowledge of specimen details to ensure blind conditions.

SPECIMENS

Eighty three rotator cuff tendons were examined with an age range of 11 to 94 years. There were 48 men, 21 specimens were from the left and 27 were from the right shoulder. Thirty five women were studied, 16 were from the left shoulder and 19 from the right. Rotator cuffs were removed from both shoulders in 3 patients (2 men and 1 woman).

Common extensor tendon biopsy specimens from patients with lateral epicondylitis were taken from 20 patients (9 male, 11 female) with an age range of 27 to 56 years (mean 44 years) at the time of a lateral release procedure around the site of insertion. Nine control biopsies were taken from cadavers of similar age with no recorded history of elbow pain.

Results

ROTATOR CUFF SPECIMENS

At the time of removal, 10 rotator cuff specimens had macroscopic evidence of a partial rupture, with either marked irregularity and thinning, or a small perforation (8 right and 2 left). There were also 7 which had areas of thickening in the tendon, with calcification in 4 cases.

Twenty eight rotator cuff tendons had histological abnormalities and these changes are listed in Table 1. The mild changes included thickening of the blood vessel walls with the formation of collagen in association with them (fig 1A). Cell ‘fall-out’ (that is, a reduction in the number of tenocytes) was the next visible abnormality. Fifteen specimens, showed the most frequent change, an increase in glycosaminoglycans. This was laid down between the tendon fibrils. It was more diffuse in those with the most marked changes (fig 1B). In 9 of the 15 cases where glycosaminoglycan infiltration of the tendon was found, there was also patches of fibrocartilaginous change. In 7 specimens, however, fibrocartilaginous change was found alone, without glycosaminoglycan infiltration. These occurred either in plaques or as more diffuse change.

Rounded cells with the appearance of chondrocytes, sometimes arranged in rows between the collagen fibrils, were found (fig 1C). These changes were sometimes accompanied by areas of fibrocartilage within the tendon substance associated with glycosaminoglycan production (fig 1B), but in some cases no increase in glycosaminoglycan was seen (fig 1C). This could be due to difficulties with reliably staining the glycosaminoglycans in the sections. This section (fig 1C) illustrates the classic ‘glassy’ appearance observed in some tendon biopsy specimens. In its most severe form the fibrocartilage was undergoing calcification producing poorly formed bone. The most florid cases were seen in association with synovial chondromatosis. Some tendons (fig 1D) showed the deposition of calcium in regions that also stained positively with Alcian blue. These calcium deposits did not always stain well with von Kossa stain. This may indicate that hydroxy-sapite may not be the predominant form of calcium deposited.

The numbers of the rotator cuff tendons in each decade and the relative percentage found to be abnormal are listed in table 2. Abnormalities increase in middle life to remain fairly constant at around 40% and then increase to 57% for those of 90 years and over. Perhaps unexpectedly no abnormal specimens were found in the age range of 40 to 49, although around a quarter were abnormal in the preceding decade. Changes were found approximately twice as frequently in those over 90 compared with those under 40. Several very

<table>
<thead>
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<th>GAG type</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycosaminoglycan infiltration</td>
<td>9</td>
</tr>
<tr>
<td>Fibrocartilaginous change</td>
<td>7</td>
</tr>
<tr>
<td>Blood vessel wall thickening</td>
<td>6</td>
</tr>
<tr>
<td>/or tenocyte loss alone</td>
<td>6</td>
</tr>
<tr>
<td>Glycosaminoglycan infiltration alone</td>
<td>1</td>
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</table>
elderly subjects had complete massive ruptures which could not be assessed in this study and so the true level of tendon abnormality in this group is really higher than that recorded.

The changes observed did not correlate with sex, body weight, manual occupation or side of body affected, although macroscopic changes included more partial ruptures in the right shoulder.

COMMON EXTENSOR TENDON SPECIMENS

The microscopic changes found in the common extensor tendon biopsies showed similar changes to those found in the cadaveric rotator cuff tendons and are detailed in table 3. In 13 specimens there was a moderate or marked increase in glycosaminoglycan within the tendon close to the insertion. Six specimens showed evidence of new bone formation at the site of tendon insertion (distinct from the normal transitional area of tendon insertion into bone) (fig 2) with or without increase in glycosaminoglycan. In a further 2 cases, fibrocartilage was forming within the tendon, calcifying in one (fig 3), while in 4 there was noticeable fibrofatty change, 2 with increased elastin. There were 4 specimens that showed changes suggesting partial rupture, with tendon insertion disorganisation in 3, and cartilage dehiscence in another one. One specimen showed changes at the tendon attachment suggesting myxoid fibrillar proliferation.

In 1 case a mild lymphocyte infiltration was found and in another, giant cells were observed. These changes were not observed in nine specimens taken from cadavers of similar age.

In the control biopsies there was some patchy glycosaminoglycan between tendon fibres but of a very mild nature in 2 cases. Two specimens had patchy irregular calcification at the junction of tendon insertion into bone and 1 showed some evidence of arterial thickening of blood vessels in the tendon.

**Table 2.** Number of patients in decades with number and percentage of abnormal specimens in rotator cuffs

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of patients</th>
<th>Number of abnormal</th>
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<tr>
<td>10-19</td>
<td>5</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>20-29</td>
<td>2</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>30-39</td>
<td>11</td>
<td>3</td>
<td>27%</td>
</tr>
<tr>
<td>40-49</td>
<td>7</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>50-59</td>
<td>10</td>
<td>4</td>
<td>40%</td>
</tr>
<tr>
<td>60-69</td>
<td>10</td>
<td>4</td>
<td>40%</td>
</tr>
<tr>
<td>70-79</td>
<td>19</td>
<td>8</td>
<td>42%</td>
</tr>
<tr>
<td>80-89</td>
<td>12</td>
<td>5</td>
<td>42%</td>
</tr>
<tr>
<td>90-99</td>
<td>7</td>
<td>4</td>
<td>57%</td>
</tr>
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**Discussion**

Although the association between the changes in the rotator cuffs of cadavers and clinical disease is uncertain, it might be expected that those subjects with an abnormality would have a predisposition to tendinitis. None of the subjects in this study had any hospital record of shoulder symptoms, but it is unknown...
vessels in human supraspinatus and infraspinatus tendons. They concluded that other factors were important in the development of tendon lesions in addition to vascular supply, that predisposed the supraspinatus to rupture.

The type of changes found in the cadaveric rotator cuff specimens were similar to those found in biopsies from tennis elbow lesions but not in control tendon biopsies from a similar area. The similarity of the changes with age in the rotator cuff and tennis elbow in disease suggests a similar mechanism producing fibrocartilaginous change.

Apart from one case showing minor lymphocyte infiltration, inflammation would appear not to be a histological feature of tennis elbow, at least in our patients coming to surgery after extensive medical treatment. How such changes relate to more acute lesions remains unclear. If there is no inflammation then there must be an explanation why the patients had a chronic painful tennis elbow. A chronic traction phenomenon may occur as has been previously suggested as a cause of tennis elbow. Apart from ischaemia new bone formation would tend to be stimulated at the insertion as was found in six cases and there were four patients who had changes suggesting partial tendon rupture. Both areas are likely to be generously innervated by pain fibres and give rise to symptoms with continued traction.

Some of the changes observed in the tendon were similar to that described by previous authors, especially Wilson and Duff. These authors noted a loss in the intensity of H & E staining, and a hyaline appearance with the loss of the wavy lines of collagen fibres. Similar changes were noted in the present study. Kannus et al examined histological changes in 891 patients with spontaneously ruptured tendons and 445 age and sex matched controls who had died accidentally. Although neither the supraspinatus nor the tendon from lateral epicondylitis were studied, similar changes were noted. These included hypoxic degenerative changes, mucoid degenerative changes, tendolipomatosis, calcifying tendinitis, and vascular changes. The changes observed in control tissues were significantly less frequent. All the ruptured tendon samples had observed abnormalities of which 97% were degenerative whilst 34% of the control tendons had similar degenerative changes.

There appeared to be some sequence in the changes observed, suggesting an increasing severity of the process. Blood vessel and fibroblast abnormalities, mainly cell fall-out, were early changes. Areas of glycosaminoglycan infiltration replacing collagen fibres might indicate that the stressed tendon fibroblasts could no longer maintain their normal function of maintenance and turnover of the tendon collagen. With these changes a rounding up of the cells occurred, proceeding to a transformation of the fibroblasts to chondrocyte-like cells, with subsequent cartilage formation which then proceeded to calcify to produce bone. It would therefore appear that with increasing severity of the process the tendon fibroblasts undergo a fibrocartilaginous change as though

whether presentation to a general practitioner had previously occurred. The absence of any true rotator cuff tendon abnormality below the age of 30 is consistent with the clinical rarity of rotator cuff tendinitis before that age. No subject in the fifth decade had an abnormality. This was unexpected and it is not thought that this is likely to be representative of this age group as a whole. Only 7 samples were examined in this group and future studies will be needed to confirm this finding.

Relative ischaemia of the rotator cuff is strongly believed to be an important factor in the 'degenerative' changes that occur. The subjects in each age group with an abnormal rotator cuff may be those with poorer vessels in the tendon as a consequence of congenital changes and/or atherosclerosis. Mechanical factors, with impingement, may have a role as has been suggested but is likely to be a secondary aggravating factor. However, a recent study by Brooks et al investigating the vascularity of different tendons showed no difference in the size and number of blood vessels in human supraspinatus and infraspinatus tendons. They concluded that other factors were important in the development of tendon lesions in addition to vascular supply, that predisposed the supraspinatus to rupture.

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their response to the ischaemia is to ultimately try to convert areas of tendon to bone.

Only basic routine histological stains were used in this study and further work needs to be carried out using more specific staining techniques. These might be used to investigate the type of glycosaminoglycan present, lipid content, collagen type, cell density and relationship to fibrillar elements and interstitial material. In addition, electron microscopy could be used to assess collagen fibril size, the localisation of collagen types and blood vessel distribution. The findings of microscopic tendon changes in symptomatic chronic tennis elbow of the same nature as that found in a subgroup of rotator cuffs from normal ageing individuals, strengthens the belief that such changes may predispose them to symptomatic shoulder disease. With improvements in surgical techniques, patients with chronic rotator cuff lesions are coming to operation earlier, which will provide biopsies for histological assessment and comparison with those changes described above. Both the techniques used in this study and the more detailed approaches including immunolocalisation of collagen types need to be used in the assessment. Such studies are at present underway in our departments.