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RESEARCH

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Inflammatory and degenerative changes in the extensor pollicis longus muscle and tendon following ruptures caused by distal radius fractures

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Abstract

Background Rupture of extensor pollicis longus tendon (EPL) is a known complication following a distal radius fracture (DRF). Although the precise mechanisms behind these ruptures remain unclear, vascular impairment is thought to play a significant role. Additionally, the impact of an EPL rupture on microstructure of the tendon and muscle is not well understood, but such information could be important in guiding treatment strategies. This study aims to explore the histopathological changes in the EPL tendon and muscle in patients who have experienced an EPL rupture following a DRF.

Methods Consecutive patients with an EPL rupture following a DRF were included and treated with an Extensor Indicis Proprius to EPL tendon transfer. Samples were taken from the distal part of EPL muscle and the proximal tendon from the musculotendinous junction to the rupture site as well as from the tendon distal to the rupture. The tendon specimens were analysed by standard histopathological techniques including immunohistochemistry. In cases of sufficient amount of muscle, fresh frozen specimens were analysed by enzyme- and immuno-histochemistry on cryostat sections.

Results Thirteen patients (12 females, 1 male; median age 61, range 18–72 years) were included in the study. The EPL muscle in all participants showed extensive inflammatory changes, muscle fiber necrosis and regeneration, structural changes in the muscle fibers and slight interstitial fibrosis. The EPL tendon showed profound degenerative changes mainly in the central part of the tendon whereas there were regenerative changes in the periphery of the tendon. The pathological changes were present in all samples regardless of time between the DRF and the EPL rupture or the time between the diagnosis of the rupture and surgery.

Conclusions The extensive inflammatory changes in the EPL muscle indicate that immune mediated mechanisms are involved in muscle degeneration following tendon rupture. The EPL tendon showed characteristic degenerative changes at the myotendinous junction, as well as proximally and distally to the rupture site. The reversibility and the clinical significance of the severe pathological changes seen in the EPL muscle alongside the healing potential of the tendon need further investigation.

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Keywords Extensor Pollicis Longus (EPL) tendon rupture, Distal Radius Fracture (DRF), Histopathology, Muscle Pathology, Tendon Pathology

Background

Fracture of the distal radius is the most common fracture in the body [1]. A known complication to a distal radius fracture (DRF) is a rupture of the Extensor Pollicis Longus (EPL) tendon with a reported incidence between 3 and 5% [2, 3]. The exact cause of EPL tendon rupture, which typically occurs 4–8 weeks after a DRF, is still unclear. Engkvist and Lundborg's [4] microangiographic study on cadaveric EPL tendons identified poor vascularization near Lister's tubercle, a common site of rupture. They suggested that DRFs, especially non or minimally displaced ones cause a hematoma in the EPL tendon sheath, further compromising its already vulnerable blood supply and leading to tendon weakening and eventual rupture. Additionally, severely displaced or comminuted DRFs might cause the tendon to repeatedly glide over sharp bone fragments, progressively weakening and tearing it [5–7].

Treatment options for EPL rupture include direct suture, free tendon interposition grafting, or tendon transfer [8]. Direct suture involves removing the tendon parts, closest to the rupture, and suturing the remaining tendon, sometimes relocating the tendon subcutaneously to prevent tightness [9]. Alternatively, a more extensive resection of the ruptured tendon is performed to secure viability of the remaining tendon parts, with the gap bridged using a tendon graft, like the palmaris longus. A third treatment option is an Extensor Indicis Proprius (EIP) to EPL tendon transfer where the EIP is detached at the level of second metacarpophalangeal joint, rerouted, and attached to the EPL's distal part. As opposed to the two prior mentioned techniques, this technique does not depend on function in the EPL tendon and muscle, instead thumb extension is controlled by the EIP muscle [8, 10].

Direct suture and grafting aim to restore normal anatomy, relying on the viability and contractility of residual EPL tendon and muscle, which are assessed subjectively due to the absence of objective measures. EIP to EPL transfer sacrifices EIP function in the index finger and requires cerebral adaptations such as plasticity, to learn to control the new thumb extension mechanics. Prior case studies show good results after both interposition grafting and EIP to EPL transfer [11, 12], but there are no randomized studies comparing the outcome after tendon interposition graft and EIP-EPL tendon transfer.

Previous studies indicate that tendons, including the EPL, and their associated muscles require stretching and loading to maintain their elasticity and responsiveness [13]. In situations of degenerative rupture, such as an EPL rupture, the tendon segments near the rupture site typically are nonviable. Current research does not address the rate at which hand and forearm tendons and muscles become stiff and lose their contractility following a rupture. Animal studies indicate that larger muscles can undergo fat tissue replacement within 4–6 weeks following tendon rupture [14, 15]. Additionally, the capacity for tendon and muscle to remodel after suture or grafting remains unclear. Thus, a better understanding of histological changes in the EPL tendon and muscle following a rupture could crucially guide surgical treatment decisions. In cases of severe EPL muscle degeneration, an EIP to EPL tendon graft might be preferable whereas an interposition graft may be more optimal in a patient with a functioning EPL muscle.

The aim of this study was to evaluate the histopathology of the EPL tendon and muscle in patients who have experienced an EPL rupture after a DRF.

Methods

Between April 2022 and October 2023 patients planned for surgical treatment of a clinically diagnosed rupture of the EPL tendon following a DRF were prospectively included in the study. Inclusion criteria were: a clinically diagnosed EPL rupture following a DRF, age between 18 and 85. Exclusion criteria were: rheumatic diseases, inability to read and understand Swedish. Mental illness leading to inability to understand the study procedure and rehabilitation protocol or ongoing drug abuse. Following oral and written information about the study participants gave written consent to participate.

Epidemiology/participants

The participants were assessed for sex, age, medication, prior treatment with steroid injections in the hand and wrist and prior surgical procedures to the hand and wrist. Time point of the rupture was defined as the first time the patient experienced lack of function in the thumb. Fractures were classified according to the AO/OTA classification by one reviewer (CS) according to the Fracture and Dislocation compendium of 2018 [16].

Surgical procedure and harvesting of tissue samples

In order to allow for histopathological investigation of the EPL muscle and tendons all participants were operated with an EIP to EPL tendon transfer. By pulling the proximal EPL tendon the muscle was exposed making it possible to harvest a sample from the muscle together with the whole tendon proximal to the rupture without extending the skin incision proximally. In addition, an approximately 5-10 mm long sample of the tendon distal to the rupture was obtained to avoid compromising the tendon anastomosis, ensuring the full width of the tendon was included.

Histopathology

All specimens were examined by an expert in muscle pathology (AO). The specimens were fixed in formalin and embedded in paraffin. In addition, in those cases where a sufficient amount of muscle was available, a muscle specimen was fresh frozen in isopentane in dry ice. Histochemical analyses were conducted on eight-µm-thick cryostat tissue sections of the fresh frozen muscle biopsies following standard protocols [17]. They included hematoxylin and eosin (H&E), Gomori trichrome, NADH-tetrazolium reductase (NADH-TR), cytochrome c oxidase (COX), succinate dehydrogenase (SDH), periodic acid and Schiff reagent (PAS) and Sudan black (SD). Muscle fiber typing was performed by quadruple immunofluorescence analysis of myosin heavy chain (MyHC) isoforms as described [18]. For other immunostainings brightfield microscopy was applied and tissue sections were processed in a Dako Autostainer using the EnVision FLEX DAB + Substrate Chromogen System kit and incubated with the following primary antibodies for one hour: anti-embryonic MyHC (F1.652, DSHB, 1:20) and anti-fetal MyHC (MHn, Leica, 1:20), major histocompatibility complex class I (MHC-I; M0736, Dako 1:1000), lysosomal associated membrane protein 2 (LAMP2; H4B4,Abcam, 1:200), T lymphocytes, (CD3; M7254, Dako, 1:200) B lymphocytes, (CD20; L26, Dako, 1:200) and macrophages (CD68; IR609, Dako, 1:100). The paraffin embedded muscle specimens were analysed by H&E and Van Gieson-elastin in addition to staining of inflammatory cell markers CD3, CD20 and CD68. The paraffin embedded tendon specimens from the proximal region, the middle rupture region and the distal region were analysed by H&E and Van Gieson-elastin staining. Selected specimens were also immuno-stained with inflammatory cell markers (CD3, CD20 and CD68) as described above and the endothelial marker CD31 (Dako, M0823;1:600).

Results

Thirteen patients (12 females, 1 male; median age 61, range 18–72 years) participated in the study (Table 1). All eligible patients identified in our department were enrolled in our study. The time span between rupture diagnosis and surgery ranged from 1 to 81 days, as many patients were treated as elective cases, resulting in prolonged waiting times for surgery. Patient 4, with a history of ulcerative colitis, had received oral cortisone treatment for 8 weeks a year before the rupture. Patient 5 had a cortisone injection for thumb base arthritis and underwent excision arthroplasty a year before the rupture. Patient

Table 1 Patient demographics

Patient no	Sex	Age† at the time of DRF	Days from DRF to EPL rupture	Days from osteosynthesis to EPL rupture	Days from rupture to surgery	Fracture treatment method	Classification of DRF according to AO/OTA
1	Female	64	18	8	21	ORIF[a]	2R3A3
2	Female	66	19	NA[b]	9	Cast	2R3A2[5a]
3	Female	61	21	NA[b]	54	Cast	2R3A2[5a]
4	Female	46	133	130	24	ORIF[a]	2R3A3
5	Female	64	20	3	7	ORIF[a]	2R3A2[5a]
6	Male	56	89	NA[b]	11	NT[c]	2R3A2 [1]
7	Female	19	97	NA[b]	45	NT[c]	2R3A2[5b]
8	Female	17	9	-2	14	ORIF[a]	2R3A3
9	Female	54	4	NA[b, d]	5	ORIF[a]	2R3C1
10	Female	70	100	96	58	ORIF[a]	2R3A2[5b]
11	Female	63	15	NA[b]	13	Cast	2R3A2[5a]
12	Female	53	1332	1185	1	Cast	2R3A2[5a]
13	Female	72	218	210	81	CRPP[e]	2R3A2[5a]

[a] *ORIF* Open reduction, internal fixation, [b]*NA* Not applicable, [c]*NT* No treatment, [d]Concurrent ORIF and tendon transfer, [e]*CRPP* Closed reduction, percutaneous pinning.
†We report ages in exact years, without rounding up

8 was 17 years old when she sustained the fracture and 18 years old when the rupture occurred, at which point she was enrolled in the study.

Seven patients had received surgical treatment for their distal radius fractures (DRFs): six underwent volar plating and one had closed reduction with percutaneous pinning. Four patients were treated conservatively with casting, and two did not initially seek medical care. Prior to undergoing osteosynthesis, patient 8 exhibited prodromal symptoms, and the rupture occurred two days following the open reduction and internal fixation (ORIF). Patient 9 experienced the rupture four days after the fracture while awaiting ORIF and underwent surgery with volar plating and an EIP to EPL tendon transfer concurrently. Patient 6 fell, experiencing wrist pain, but did not have immediate radiographs taken. The patient later presented with a spontaneous EPL rupture 89 days after the injury. A subsequent CT scan revealed minor bone defects near Lister's tubercle, suggesting a non-displaced distal radius fracture from the fall. Patient 12 underwent a corrective osteotomy with volar plate fixation, three months after the fracture. This patient later presented with an EPL rupture 1185 days after the osteotomy. For patients who had volar plating prior to the rupture, patients 4, 8, and 10 underwent CT scans to exclude any protruding dorsal osteosynthesis material as the cause of the rupture.

The EPL muscle samples from patients 1, 2, 10, 11 and 13 were sufficient for analysis both fresh frozen in isopentan and in formalin.

Histological results of the distal EPL muscle

We quantified all histopathological findings as absent (-), low (+), moderate (++) and extensive (+++). The results are presented in Tables 2 and 3. Inflammation, characterized by inflammatory cell infiltration, was observed in all muscle specimens, predominantly in the perivascular areas but also in the endomysium (Fig. 1).

Table 3 Complimentary histological results of EPL muscle in specimen preserved fresh frozen

Patient	MHC-I	Structural changes	Fibers type 1	Fibers type 2A	Glycogen depletion
1	+++	++	50%	50%	-
2	+++	++	50%	50%	+
10	+	+++	80%	20%	++
11	+++	+	50%	50%	+++
13	+	+++	60%	40%	+++

absent (-), low (+), moderate (++) and extensive (+++)

The inflammatory cells consisted mainly of CD3+T-cells and CD68+macrophages. CD 20+B-cells were less abundant. Necrotic muscle fibers were seen in all cases (Fig. 1D and I). A slight or moderate endomysial fibrosis was present in all cases but there was no fat tissue replacement. In the five cases with fresh frozen muscle tissue a more extensive histochemical investigation of the muscle tissue was performed. Mitochondria in all five investigated cases showed normal enzyme histochemical activity. MHC class I was strongly upregulated in all these cases in agreement with an ongoing inflammation in the muscle. Disruption of the normal intermyofibrillar network of muscle fibers were seen in all cases and was extensive in some of them (Fig. 1E). Some muscle fibers showed depletion of glycogen (Fig. 1F) but there was no abnormal lipid storage. In addition to inflammation, a key morphological feature observed was the presence of numerous regenerating muscle fibers following necrosis (as shown in Fig. 1G and H). Fiber typing revealed the presence of type 2A and type 1 fibers, but no type 2B

Table 2 Histological results of distal EPL muscle (in normal muscle none of the following is present)

Patient	Inflammation	Necrosis	Fibrosis	CD3 T-Cells	CD20 B-Cells	CD68 Macrophages
1	+	++	++	+	+	++
2	+++	++	+	+++	+	+++
3	+	++	+	++	-	++
4	+++	++	+	+++	++	+++
5	++	+	+	++	+	++
7	+++	+	+	+++	++	++
8	++	+	-	++	+	++
9	++	+	++	++	-	++
10	+++	+	+	+++	+++	+++
11	+++	+	+	+++	++	+++
13	+	++	+	+	+	++

absent (-), low (+), moderate (++) and extensive (+++)

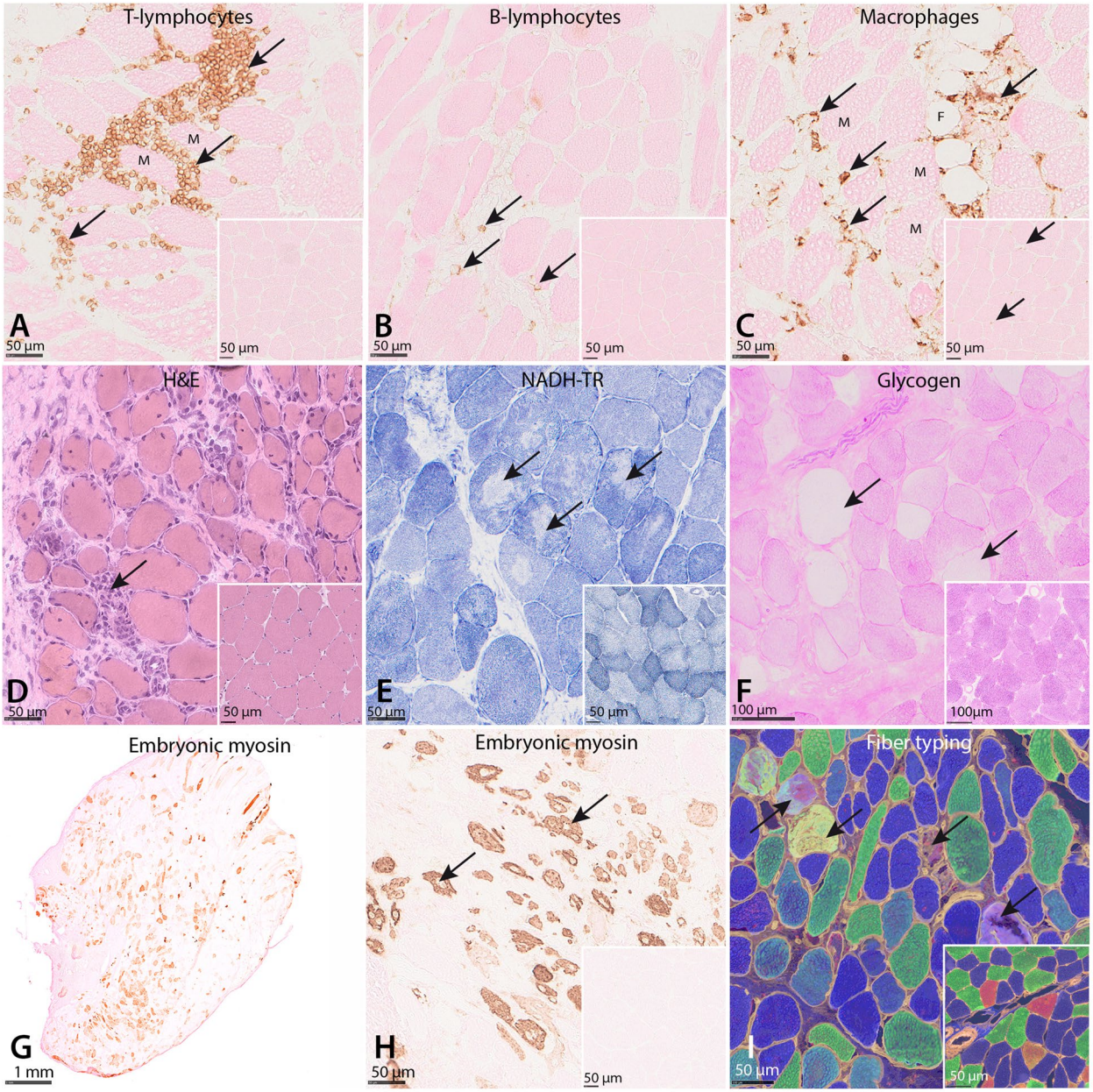

Fig. 1 Histopathological changes in distal EPL muscle after tendon rupture. Representative images. **A** Endomysial infiltration of numerous T-cells (arrows, grade + + +) surrounding the transversely cut muscle fibers (M). The muscle fibers appear with a light red colour by eosin staining. Inset shows normal muscle without any T-cells. Immunostaining CD3. **B** Sparse endomysial and perivascular B-cells (arrows, grade +). Inset shows normal muscle without any B-cells. Immunostaining CD20. **C** Numerous and large endomysial macrophages (arrows, grade + + +) between muscle fibers (M). Fat cells (F) in an epimysial region with connective tissue is a normal finding but the number and size of macrophages is increased also in the epimysial tissue. Inset shows normal muscle with sparse and small endomysial macrophages. Immunostaining CD68. **D** Transverse section of EPL muscle showing numerous necrotic muscle fibers (arrows), with ongoing phagocytosis, infiltration of inflammatory cells in the endomysium and increased interstitial connective tissue between the muscle fibers (fibrosis). The myotendinal junction is seen in the left part of the panel. Inset: Normal muscle. H&E staining. **E** Abundant muscle fibers with severe disorganization of the intermyofibrillar network (arrows), indicating myofibrillar disorganization. Inset: Normal muscle. NADH-TR staining. **F** Glycogen depletion in several fibers (arrows) indicated by absent staining with PAS. Inset: Normal muscle. **G** and **H** Massive ongoing muscle fiber regeneration in the entire cross section of the muscle as indicated by expression of embryonic myosin heavy chain, which is developmentally regulated and re-expressed only in regenerating muscle fibers. Inset (H): Normal muscle without expression of embryonic myosin. **I** Muscle fiber typing showing type 1 fibers (blue) and type 2A fibers (green) as well as several hybrid fibers. Scattered necrotic fibers are present (arrows). Inset: Normal muscle with three fiber types (type 2B fibers in red)

fibers were detected. Necrosis affected both type 1 and type 2A fibers (Fig. 1I).

Histological results of EPL tendon near the myotendinous junction

Inspection of transverse cross-section specimens in the majority of cases revealed a characteristic pattern of disorganization in the tendon structure, confined to the inner two-thirds of the proximal tendon and extending from the muscle insertion distally to the level of the rupture (Fig. 2A). The collagen was, in these parts of the tendon, arranged in whorled and disrupted bundles (Fig. 2B). There was depletion of tenocytes and vessels but mild inflammation with invasion of macrophages. In the outer rim of the tendon the structure showed regular arrangement of the collagen fibrils and marked tenocyte proliferation (Fig. 2C). The tenocytes, characterized by large nuclei and frequently including a distinct nucleolus, were surrounded by collagen fibrils, indicating ongoing regeneration.

At the border between the central degeneration and the outer rim of regeneration there was distinct capillary proliferation (Fig. 2D) and inflammation with lymphocytes (Fig. 2E) and macrophages (Fig. 2F). In four cases (patients 2, 6, 8 and 11) the central degeneration was even more pronounced with apparent necrosis where the collagen was replaced by fibrinous excudate and granulation tissue (Fig. 2G and H). In two cases there was a

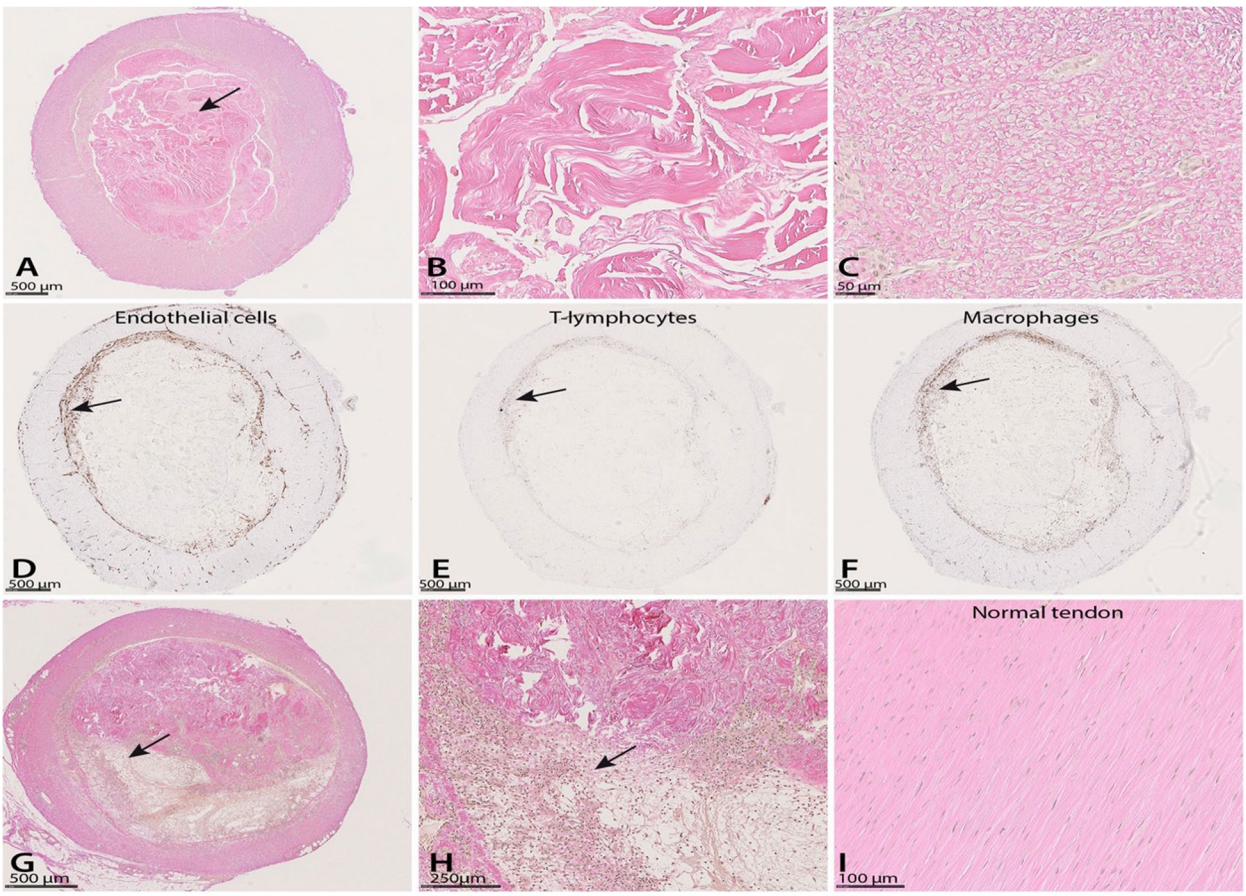

Fig. 2 Representative illustration of EPL tendon after tendon rupture close to the musculotendinous junction. Serial sections stained with different methods. **A** and **B** Van Gieson-elastin staining showing collagen in red illustrating profound disorganization of the central part of the tendon (arrow). **C** In the peripheral and more organized part of the tendon there are numerous large tenocytes between collagen fibrils, Van Gieson-elastin staining. **D** Capillary proliferation in the outer border of the central degenerated part of the tendon (arrow) visualized by immunostaining with antibody to endothelial cells (CD31). **E** and **F** Immunostaining of T-cells (CD3) and macrophages (CD68) showing inflammation mainly in the outer border of the central degenerated tendon. **G** and **H** Van Gieson-elastin staining with collagen in red showing profound disorganization of the central part of the tendon and a large degenerated region (arrow) with replacement of the collagen by fibrin, inflammatory cells and capillary proliferation, indicating necrosis in the region. **I** Normal tendon (longitudinal) stained with van Gieson-elastin for comparison. The collagen bundles are arranged in an ordered fashion and there are scattered small, elongated tenocytes

granulomatous reaction with multinuclear giant cells at the site of degeneration.

Histological results of EPL tendon just proximal to the rupture

Histopathological examination of the ruptured tendon parts revealed high variability, with many samples lacking visible tendon and composed instead of fibrous and fatty tissues with moderate inflammation. Some samples contained thin, often longitudinally ruptured tendon fragments, accompanied by capillary proliferation. Specifically, case no. 7 exhibited signs of prior haemorrhage, evidenced by macrophages containing hemosiderin.

Histological results of EPL tendon distal to the rupture

The tendon distal to the rupture showed in most cases a similar pattern as the proximal tendon with disorganisation but in general somewhat less extensive (Fig. 3). Only cases 7 and 10 showed more collagen fiber disorganisation in the distal specimens compared to the proximal ones.

Discussion

This study demonstrates that EPL rupture after a DRF was consistently associated with degenerative and inflammatory changes in both the EPL muscle and its proximal tendon. Degeneration and inflammatory changes were present to a lesser extend also in EPL tendon distally to the rupture. The degeneration and inflammation were present in all samples regardless of time between the DRF and the EPL rupture or the time between the diagnosis of the rupture and surgery. EPL rupture was more commonly seen after displaced fractures, and we found no histopathological differences between patients who underwent surgery and those who received non-operative treatment for DRF.

The presence of inflammatory changes in all muscle specimens and, in some of the cases, intense inflammatory cell infiltration was a remarkable finding showing many similarities with autoimmune inflammatory myopathies [17, 19, 20]. These changes included perivascular and endomysial inflammatory cell infiltration with predominance of T cells and macrophages, MHC-I upregulation, muscle fiber necrosis and muscle fiber regeneration. The presence of large numbers of regenerating muscle fibers, comparable to what is seen in immune mediated necrotizing myopathy (IMNM) or rhabdomyolysis, was striking. However, in these conditions there is neither massive inflammatory cell infiltration nor strong MHC-I upregulation [19]. IMNM is usually seen associated with statin treatment and show anti-HMGCR auto-antibodies in serum. The inflammatory cell infiltration in dermatomyositis and anti-synthetase syndrome is mainly seen in the perimysium and frequently perivascular [17], which to some extent is similar to what was seen in our specimens. However, in the EPL muscle specimens there was also endomysial cell infiltration. In the group of autoimmune inflammatory myopathies this pattern is mainly associated with inclusion body myositis (IBM). In IBM there are several other features not seen in the EPL muscles in this study. Thus, the inflammatory changes in the EPL muscle were not identical to any of the autoimmune inflammatory myopathies. In some autoimmune diseases, so-called overlap syndromes, an unspecific inflammation in muscle can sometimes be observed [19, 20]. All these autoimmune inflammatory myopathies are generalized whereas the EPL muscle inflammation after tendon rupture can be anticipated to be focal. There is a condition known as focal myositis that may appear as a

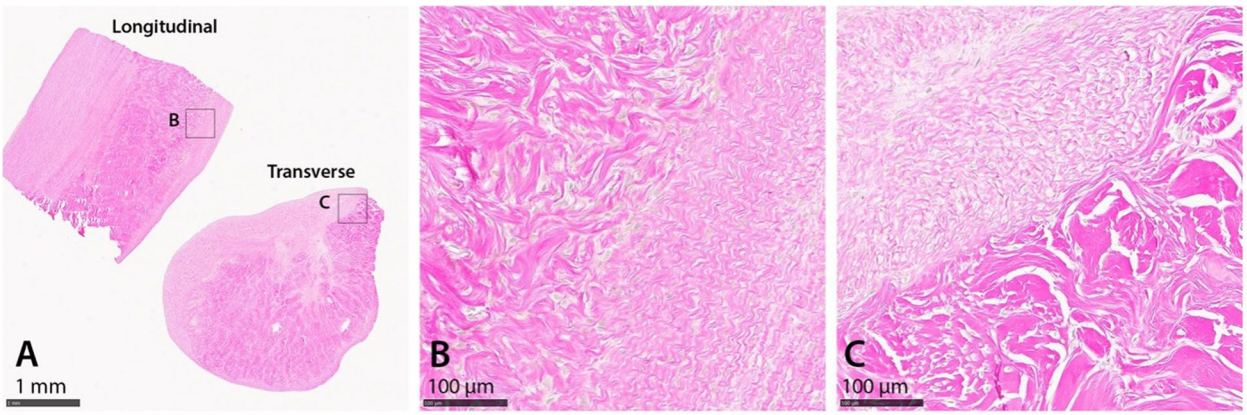

Fig. 3 Representative illustration of EPL tendon distal to the rupture. **A** Disorganization of the collagen bundles in a large part of the tendon. Both longitudinal (upper left) and transverse (lower) sections are shown. **B** and **C** Border between disorganized and nearly normal tendon in longitudinal (**B**) and transverse (**C**) sections. Van Gieson-elastin staining

pseudo tumor. Its pathogenesis is not established but may be seen as an epiphenomenon to denervation [21]. In our patients with inflammatory changes in the EPL muscle, secondary to distal EPL tendon rupture, the inflammation was much more intense than in the adjacent tendon. Although trauma may induce inflammation at the site of the injury there was no trauma related to the EPL muscle in our cases and the inflammation was probably secondary to the distal tendon rupture and retraction of tendon and muscle. Furthermore, muscle ischemia results in infiltration of macrophages in necrotic fibers rather than the T-cell infiltration seen in our cases. The direct pathogenesis of the histopathological findings remains enigmatic, i.e. what triggers the inflammation and muscle degeneration. The widespread muscle fiber necrosis is probably not causing the lymphocytic cell infiltration since inflammation is usually not seen in muscular dystrophies or rhabdomyolysis, which are diseases characterized by muscle fiber necrosis and regeneration from satellite cells.

Other important questions that remain to be investigated is whether the entire EPL muscle is affected or only the distal part and the final outcome of the inflammatory and degenerative changes that we observed a few weeks after the tendon rupture. It is well known from autoimmune inflammatory myopathies that if they are left untreated or in cases where no treatment is available they will end up in loss of muscle tissue, fibrosis, fat tissue replacement and ultimately loss of function [22]. This may also be the case in the EPL muscle with inflammatory and degenerative changes induced by the tendon rupture but remains to be investigated. In the present study, fibrosis was observed only to a limited extent, which could be explained by the short duration from tendon rupture to muscle biopsy. We can only speculate that if the EPL muscle is left without stimulation for a longer period, fibrosis will progress over time rendering the muscle non-functional. On the other hand, it is possible that if the EPL muscle is loaded again, following an interposition tendon grafting, it will regenerate and recover adequate force to drive the thumb extension. Future studies should focus on time dynamics in muscle cell response to tendon rupture and also response to tendon reconstruction.

To our knowledge, this is the first study to report histopathological findings in an extrinsic hand muscle following tendon rupture. In clinical practice, it is widely recognized that early surgical intervention for flexor and extensor tendon lacerations in the hand leads to improved functional outcomes. Delayed surgery increases the likelihood of requiring tendon reconstruction [23]. However, there is no definitive time frame beyond which reconstruction and muscle function are no longer viable. Notably, successful hand transplants have been performed years after amputation, yielding functional outcomes that suggest reversibility of the muscle stiffness to some degree with appropriate stimulation and loading [24]. It remains to explore whether the changes observed in our study are consistent across all hand tendon ruptures and can serve as histopathological model of the muscle degeneration after a tendon rupture.

All tendon specimens, both proximal and distal from the rupture site, as well as at the myotendinous junction exhibited disorganized collagen fibers primarily and signs of haemorrhage and necrosis. Previous research indicates the tendon's main blood supply near the tubercle of Lister is via the tendon sheath [4, 25]. Impaired blood flow in the tendon sheath could explain the core-focused degeneration and support ischemia as the rupture cause. In contrast, mechanical factors would typically affect the outer parts of the tendon, a finding that was absent in our specimen, even in patients who sustained a rupture close to the fracture date and underwent prompt surgery. Therefore, we speculate that the cause of tendon rupture might be ischemia. In a previous study, Owers et al. [26] used high-resolution ultrasound to demonstrate that both the extensor retinaculum and EPL tendon sheath appear to have increased thickness 6 weeks after a distal radius fracture. This corroborates Engkvist [4] and Kondo et al. [27] who suggested that a bleeding around the EPL-tendon in the third extensor compartment impale the vulnerable vascularity in this area. This is also supported by a study in patients with prodromal symptoms and clinical signs of impending EPL rupture who were treated successfully with decompression of the third extensor compartment [28].

The histopathological findings of the EPL tendon share similarities with other degenerative tendon ruptures, such as those of the Achilles tendon, quadriceps tendon, and rotator cuff. Previous studies on rupture of these tendons have described increased waviness and disruption of collagen bundles [29–33]. However, the central degeneration observed in this study appears unique to EPL tendon ruptures. Notably, the EPL tendon has a significantly smaller diameter compared to the Achilles tendon, quadriceps tendon, and rotator cuff tendons. In our study, analysis of the EPL cross-sectional samples represented nearly the entire cross-sectional area of the tendon. In contrast, previous studies on the histopathology of Achilles tendon, rotator cuff, and quadriceps tendon ruptures [29–33] utilized smaller samples that represented only a portion of the tendon's cross-section. Additionally, we included patients treated with tendon transfer, which allowed analysis of the tendon's cross-sectional area at different levels. These differences in sampling techniques may have contributed to the identification of this

distinctive central degeneration pattern. Vessel proliferation is a common feature of degenerative tendon ruptures [29–33] and was present in our samples as well. Tallon et al. [29] reported in their study on Achilles tendons that specimens from ruptured tendons demonstrated more pronounced neovascularization compared to samples from tendons with tendinopathy without rupture. Similarly, studies of rotator cuff vascularity suggest that smaller ruptures, which exhibit greater healing potential, display more prominent vascularity than larger, more extensive ruptures [33]. Fibroblast activity and inflammation are also typical features of degenerative tendon ruptures with healing potential [29–33]. Tenocytes with large, rounded nuclei, are observed in such cases [29–33]. In contrast, massive rotator cuff tears with limited healing capacity exhibit reduced fibroblast cellularity and increased chondroid metaplasia [33]. Interestingly, prior studies link higher fibroblastic activity to greater abundance of inflammatory cells [29–33]. In our cases, tenocytes and inflammatory cells were concentrated in the outer third of the tendon specimen, while the central portion exhibited collagen bundle disruption, tenocyte and vessel depletion, and mild inflammation. Based on known patterns of fibroblast activity and inflammation in Achilles and rotator cuff tendon ruptures, the histopathological findings in EPL tendons suggest limited healing capacity in the central two-thirds of the tendon, with some healing potential present in the outer third.

Regarding the inflammation findings at the tendon level, a previous study has shown differences in cell infiltration based on the chronicity of the rupture [34]. Klatte-Schulz et al. compared the histological findings in acute versus chronic Achilles tendon ruptures reported a higher infiltration of CD68 + macrophages in acute ruptures. In our cases, CD68 + macrophage infiltration showed no significant differences among specimens relative to the time between the DRF and rupture or the time from rupture to sampling. However, our methods were not focused on quantification of inflammatory cells rather on description of the histopathological findings. Thus, the results of the two studies are not directly comparable. Moreover, macrophages are known to be present in both the early and late stages of tendon healing and remodelling [30]; therefore, their presence alone cannot provide a solid answer to the temporal dynamics of inflammation in our study. It is important to highlight that the degenerative changes described at the myotendinous junction, far from the rupture site, cannot be certainly attributed to the cause of rupture. An alternative explanation could be that tendon retraction following the rupture leads to insufficient nutrition and subsequent degeneration, ultimately resulting in this specific histological pattern.

The inflammation pattern in the EPL muscle showed some similarities to an experimental model of supraspinatus rupture in mice. Stengaard et al. [35] reported that inflammation peaked at 5–7 days post-rupture and then declined. CD3 + T cell counts remained stable over time, while macrophage levels peaked at 7 days. In our case series, patients with early muscle sampling post-rupture (earliest was 1-day post-rupture) showed inflammation. Variable intensity of T-cell infiltration was observed up until 58 days post-rupture, whereas the patient with the longest time interval between symptoms of EPL rupture and sampling (81 days), showed only mild inflammation despite ongoing muscle fiber necrosis. From our results it may be concluded that degenerative muscle changes continue at least 2–3 months after rupture if left untreated. Future research should focus on how the histological changes observed in the EPL muscle progress over time, both in cases where the muscle remains unloaded and when it is reloaded, as in the case of patients undergoing surgery with an interposition graft. In addition, histopathological analysis of the EPL muscle with sampling later than 3 months after the rupture would provide valuable insights into the progression of the degenerative process.

The findings of this study do not offer definitive guidance for clinical treatment. However, the study revealed inflammation, necrosis, regeneration, disorganized myofibrils, and fibrosis in the EPL muscle following EPL tendon rupture. The presence of abundant T-cells excludes ischemia as the sole cause of the histopathological changes in the EPL muscle, suggesting an immune mediated pathogenesis. Future research should focus on how the histological changes observed in the EPL muscle progress over time, both in cases where the muscle remains unloaded and when it is reloaded. Additionally, an intriguing observation was the similarity between the histological appearance of the EPL muscle in this study and that seen in patients with autoimmune myopathies. This raises the question of whether pharmacological immunosuppressive treatments used for autoimmune myopathies could help improve EPL function following rupture, warranting further investigation.

Limitations

This study was limited by a small sample size and considerable variation in the time between rupture and sampling among cases, which constrained the scope of statistical analysis. Additionally, not all patients with volar plating underwent CT scans to check for protruding screws in the third extensor compartment. However, we observed no macroscopic evidence of damage on the ruptured tendons from the osteosynthesis material. Furthermore, our cohort included patients who had received

both surgical and non-surgical treatments for their DRF, but all surgically treated patients underwent procedures via a volar approach, which likely does not disturb vascularity on the dorsal side of radius and around the EPL. It is noteworthy that half of our patients underwent surgery, challenging the common belief that EPL ruptures predominantly occur in patients with non-displaced DRFs. Future studies with larger cohorts could explore whether specific fracture patterns are linked to EPL rupture.

Conclusions

EPL rupture following a DRF result in profound degenerative changes in the tendon at the myotendinous junction and EPL muscle in addition to degenerative changes in the tendon at the rupture site. These degenerative changes in the central part of the EPL tendon raise questions about its healing potential. Following such a rupture, the EPL muscle is rapidly affected by inflammation, muscle fiber necrosis, and regeneration. The pathology of the muscle is remarkably similar to autoimmune inflammatory myopathies. Further research is necessary to determine whether the changes in the EPL muscle are permanent or if the muscle can regenerate with appropriate loading, and if there is a time limit from rupture until development of irreversible damage of the muscle.

Abbreviations

EPL	Extensor pollicis longus
DRF	Distal radius fracture
EIP	Extensor indicis proprius
H&E	Hematoxylin and eosin
NADH-TR	NADH-tetrazolium reductase
COX	Cytochrome c oxidase
SDH	Succinate dehydrogenase
PAS	Periodic acid and Schiff reagent
SD	Sudan black
MyHC	Myosin heavy chain
ORIF	Open reduction and internal fixation
NA	Not applicable
CRPP	Closed reduction, percutaneous pinning

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Authors' contributions

CS contributed to data collection, analysis, and was a major contributor to writing the manuscript. MU contributed to the conception and planning of the project, data collection, and manuscript revision. IA assisted with patient identification, inclusion, and text revision. AO conducted the histopathological analysis of all samples, interpreted the findings, and contributed to writing and revising the manuscript. AB contributed to the project planning, interpreted the findings from a hand surgeon's perspective, and revised the manuscript. All authors read and approved the final manuscript.

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Data availability

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request. Data are in controlled access data storage at Sahlgrenska University Hospital.

Declarations

Ethics approval and consent to participate

The study was approved by the Swedish Ethical Review Authority. Diary number: 2022–06845-01. All patients received oral and written information about the study and gave written consent to participate.
The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Publisher's Note

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