Inflammation and fibrosis of transverse carpal ligament and flexor tenosynovium in severe idiopathic carpal tunnel syndrome

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Abstract

**Background:** We approached a histopathologic study of idiopathic carpal tunnel syndrome (CTS) to identify its probable causative factors. The purpose of this study was to assess the prevalence of inflammation and fibrosis in the transverse carpal ligament (TCL) and flexor tenosynovium (FT) in severe idiopathic carpal tunnel syndrome.

**Methods:** Thirty nine patients with severe idiopathic CTS undergoing open carpal tunnel release between 2008 and 2010 were selected. The TCL and FT biopsy specimens were analyzed to assess the prevalence of inflammation and fibrosis.

**Results:** The mean age of cases was 49 years (16 to 81). Ten (25.64%) were male and 29 (74.36%) female. Fibrous thickening was observed in 11 hands (28%); TCL fibrous thickening in 9 (21.95%), FT fibrous thickening in 1 (2.43%) and in one hand (2.43%) fibrous thickening was present in both of TCL and FT. Inflammatory changes were observed in four (10%) specimens; one (2.43%) in TCL, two (4.87%) in FT and one (2.43%) in both TCL and FT.

**Conclusion:** Histopathologic study of TCL and FT in idiopathic CTS showed inflammation and fibrosis in some cases.

**Keywords:** Carpal tunnel syndrome, Fibrosis, Inflammation, Tenosynovium, Transvers carpal ligament.

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Introduction

Carpal tunnel syndrome (CTS), or compression neuropathy of the median nerve at the wrist, is the most common peripheral mononeuropathy which causes pain, paresthesia and numbness in hand and digits (1). This syndrome occurs most commonly in adults older than 30 years (range of 30-60 years), is more prevalent in females (female to male ratio is 3:1) and bilateral in 59% of patients when first seen (2).

The cause of CTS is median nerve entrapment or compression at the wrist in carpal tunnel. The CTS can be produced by a variety of factors including fractures, malunions, trauma, endocrinopathy, connective tissue disorders, and anomalies in the anatomy of wrist structures, abnormal muscle insertion and anomalous artery accompanying the nerve (3).

The condition of cases with unclear etiology of CTS, is referred as idiopathic.

There are numerous studies conducted to elucidate the role of anatomy, ultrastructures, histology of transverse carpal ligament (TCL) and flexor tenosynovium (FT) in idiopathic CTS with different and sometimes contradictory results (2-7).
This study has been performed to describe the histology of TCL and FT in severe idiopathic CTS with especial attention to fibrosis and inflammation.

**Methods**

The study was approved by our institutional review board. This prospective study was performed on 39 patients with severe idiopathic CTS undergoing open carpal tunnel release between 2008 and 2010 in Shafa Orthopedic Hospital, Tehran, Iran.

The inclusion criteria in this study included:

1. Idiopathic and severe CTS that needed to be released by surgery.
2. Agreement of patient by informed written consent.

The exclusion criteria were:

1. Any history of acute or chronic inflammatory and rheumatologic disease in medical history.
2. Underlying diseases such as arthritis and endocrine disease.
3. Special conditions such as renal dialysis and pregnancy.
4. Previous wrist, arm and hand surgery or trauma.
5. Non-surgical treatment including physiotherapy and steroid injection in carpal tunnel.
6. Any abnormal results in routine laboratory tests like erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and rheumatoid factor (RF).

The diagnosis of CTS was based on positive classical history of pain and paresthesia in median nerve territory, a positive physical examination of common provocative tests such as Phalen’s test, flexion compression test and/or a positive Tinel’s sign. Reduced two-point discrimination in the median nerve distribution or weakness/wasting of abductor pollicis brevis were also considered. The electrodiagnostic tests were used to support the clinical diagnosis.

During open carpal tunnel release surgery, a small sample was obtained from the TCL and FT in the carpal tunnel. The samples were stained with haematoxylin and eosin and analyzed by an expert histopathologist to ascertain the presence of inflammation and/or fibrosis in TCL and FT.

**Results**

In this study, 10 (25.64%) patients were male and 29 (74.36%) were female and female to male ratio was approximately 3:1. In 10 (25.64%) patients CTS was in right side and in 27 (69.23%) in the left. In 2 patients (5.21%) severe CTS was present in both sides (Table 1).

| Table 1. The involved side in patients with severe idiopathic carpal tunnel syndrome. |
|------------------------------------------|-------------|-------------|-------------|
|                                          | Right       | Left        | Bilateral   |
| Male                                     | 6 (15.4%)   | 4 (10.2%)   | 0           |
| Female                                   | 21 (53.8%)  | 6 (15.4%)   | 2 (5.1%)    |

| Table 2. Age distribution in patients with idiopathic carpal tunnel syndrome. |
|------------------------------------------|-------------|-------------|
|                                          | Male        | Female      |
| Age                                      | Number of patients |
| 10 – 19                                  | 0           | 1 (2.56%)   |
| 20-29                                    | 1(2.56%)    | 1(2.56%)    |
| 30-39                                    | 1(2.56%)    | 6(15.38%)   |
| 40-49                                    | 3(7.69%)    | 5(12.82%)   |
| 50-59                                    | 2(5.12%)    | 13(33.33%)  |
| 60-69                                    | 2(5.12%)    | 3(7.69%)    |
| 70-79                                    | ---         | ---         |
| 80-89                                    | 1(2.56%)    | 0           |
| Total                                    | 29(74.35%)  | 10(25.64%)  |
The mean patients’ age was 49 years (16 to 81). This syndrome most commonly involved patients aged 50-59 (Table 2).

None of our participants had heavy manual activity or vibration tool usage in their past history. In this study none of cases involved in professional sport activities.

According to the pathological analysis of TCL and tenosynovium (Table 3):

1. Fibrous thickening was observed in 11 hands (28%); TCL fibrous thickening in 9 (21.95%), FT fibrous thickening in 1 (2.43%), and in 1 hand (2.43%) fibrous thickening was present in both TCL and FT.

2. Inflammatory changes were observed in 4 (10%) specimens; 1 (2.43%) in TCL, 2 (4.87%) in FT and 1 (2.43%) had inflammation in both TCL and FT.

3. Twenty eight hands (71%) were free of TCL and tenosynovial inflammation and thickening (Table 3).

**Discussion**

Symptoms in CTS are attributed to the elevated pressure in carpal tunnel and mechanical pressure and local ischemia which cause median nerve damage (8-10).

Endocrine disease, inflammatory and collagen vascular diseases, trauma, malunions, edema and similar etiologies can decrease the carpal tunnel volume or increase the volume of its contents and in turn result in symptoms which is known as CTS (3).

In idiopathic CTS none of the mentioned factors are present and it is unclear the exact pathophysiology of the syndrome. There have been several studies with different results attempted to find out the exact mechanism and etiologic factors in idiopathic CTS (3-5). Neal et al (3) studied the pathology of the flexor tendon sheath in the idiopathic CTS in 45 consecutive patients aged 18 to 82 years in surgical tunnel release. Their study was limited to the FT and did not investigated the histopathology of TCL (3). According to their results there was only one fibrosis and one inflammation in studied cases. Their results were close to ours.

Schuind et al (11) studied flexor tendon synovium of 21 patients with idiopathic CTS and reported typical connective tissue undergoing degeneration under repeated mechanical stresses.

In contrast, Gross et al (12) studied 44 patients with CTS and performed histological examinations of tenosynovium taken at the time of carpal tunnel release. They did not find any significance in the histologic changes in patients with CTS.

Fuchs et al (13) investigated the relationship between idiopathic CTS and tenosynovial histology, especially inflammation. They studied tenosynovial biopsy removed from 177 wrists of patients during carpal tunnel release. Inflammation was present in only 10% of specimens.

Fibrosis was reported in 3% and synovial hyperplasia in 1% of their cases. They concluded that tenosynovitis is uncommon in patients undergoing surgery for treatment of idiopathic CTS (13). Findings of this study were similar in parts to the results of our study. In our study the inflammation was present in 7% of cases compared to 3% of their patients. Fibrosis was evaluated in only 3% of Fuchs et al series which was the same as ours. Fuchs et al did not addressed the TCL histology in their study (13).

Up to our inspection, the majority of published studies have addressed the histopathology of the FT, and ignored the focus on...
the histologic changes of the TCL in idiopathic CTS. In the present study inflammation and fibrosis in TCL have been reported in 2.43% and 21.95% cases, respectively.

Several limitations in the study were recognized as follows:
1. Small number of patients.
2. The study was a descriptive research and did not compare the results with normal subjects without CTS.
3. We did not addressed other characters of the TCL and FT like pathologic findings in regard to vessels, collagen fibers structures, hyaline change, amyloid deposits and mucoid degeneration.

Therefore, we suggest some studies with larger number of cases and comparing the findings with normal subjects.

Conclusion
Histopathologic study of TCL and FT in idiopathic CTS showed the presence of inflammation and fibrosis in some cases. Further studies are recommended to clarify the role of inflammation and fibrosis in the pathophysiology of idiopathic CTS.

References