# THE CARPAL TUNNEL SYNDROME AND AMYLOIDOSIS. A CLINICAL AND HISTOLOGICAL STUDY

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SUMMARY

Twenty-six non-randomized patients with carpal tunnel syndrome are presented. It is documented that three out of four patients may be diagnosed pre-operatively by five or more clinical parameters. All patients were screened for amyloidosis in biopsies from the carpal tunnel. One patient presented amyloid deposits in the transversal carpal ligament. The importance of macro- and microscopic findings in the carpal tunnel inclusive local amyloidosis for the pathogenesis of the carpal tunnel is discussed. It is concluded that provided systemic amyloidosis is not suspected, screening for amyloidosis may have diagnostic interest, however without therapeutic consequences and therefore unnecessary.

Key words: carpal tunnel syndrome, amyloidosis

## INTRODUCTION

The carpal tunnel syndrome (CTS) with symptoms of complex sensory, trophic and motor nature is a result of impaired function of the median nerve. The CTS may appear secondary to welldefined diseases,[1] but a large number of patients are referred to as idiopatic.[2] Idiopatic and secondary CTS both follow conditions with reduced volume or increased content of the carpal tunnel, which results in compression of the median nerve and its surroundings.[3] The CTS is indicated by various clinical tests and by electromyography (EMG). The diagnosis is often confirmed by surgery.

The diagnosis of amyloid deposits can be verified by demonstrating the intercellular material in biopsies using specific histochemical tests. Amyloidosis occurs in local or systemic forms, the latter being idiopatic or secondary to various chronic diseases e.g. rheumatoid arthritis, myelomatosis, infections. Depending on the expansion of the amyloid deposits the symptoms vary, resulting in differential dysfunctions of the organ affected. Medical treatment is preferred usually. Amyloidosis has a grave prognosis in the majority of systemic cases.[4]

It has been emphasized that amyloid could cause compression of the median nerve in the carpal tunnel.[5] However, in previous examinations of tissue from the carpal tunnel in CTS, only two reports included the specific histochemical tests able to unveil the amyloid.[2,3,6-8] In a retrospect study of eighty-seven patients two males with local amyloidosis were found.[7] Lambird and Hartmann[2] did not demonstrate amyloid in specimens of thirty-one patients. In both reports it was recommended to check upon amyloidosis in cases of CTS, especially of male patients.

The aim of our investigation was to decide,

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| number | parameter | N positive | % | 95% exact confidence limits |
|---|---|---|---|---|
| 1 | pain in the median nerve area | 26 | 100 | 87-100 |
| 2 | sensoric symptoms in the median nerve area | 23 | 88 | 65- 96 |
| 3 | atrophy of muscles innervated by the affected median nerve | 19 | 73 | 52- 88 |
| 4 | Tinel's sign | 21 | 81 | 61- 93 |
| 5 | Phalen's test | 17 | 65 | 44- 83 |
| 6 | Anti-Phalen's test, $N_{total} = 18$ | 7 | 39 | 17- 64 |
| 7 | tourniquet test, $N_{total} = 11$ | 4 | 36 | 11- 69 |
| 8 | electromyography, $N_{total} = 16$ | 16 | 100 | 79-100 |
| 9 | macroscopic pathological appearance of transversal carpal ligament | 13 | 50 | 30- 70 |
| 10 | macroscopic pathological appearance of flexor tendons | 4 | 15 | 4- 35 |
| 11 | cases of secondary CTS | 9 | 35 | 17- 56 |

$N_{total} = 26$ if nothing else is indicated.

Table 1.
Symptoms and sign, including electrophysiological findings, pathology and conditions associated with carpal tunnel syndrome in present study.

based on clinical and histological study, whether screening for amyloid had any diagnostic or therapeutic consequences.

## MATERIAL AND METHODS

The series comprised a total of twenty-six non-randomized patients, admitted during a period often months to the neurosurgical departments of the University Hospitals of Odense and Copenhagen and to the department of hand-surgery, University Hospital of Copenhagen. Female/male ratio was 20:6. The inclusion criterium was a certain CTS. Both idiopatic and secondary CTS were accepted. The median age for the total material was 53 years (range: 23 to 82 years; interquartile range: 39 to 66 years). Median age specified for females was 53 years (range: 23 to 82 years; interquartile range: 40 to 65 years). Median age specified for males was 50 years (range: 34 to 80 years; interquartile range: 38 to 68 years). Each patient contributed only once to the series. All patients were treated operatively by cleaving the transversal carpal ligament and decompression of the median nerve.[3] Nine patients presented a bilateral syndrome. In these patients a decompression of the contralateral median nerve had already been performed or was scheduled. Nine patients had secondary CTS: myxoedema, arthrosis in carpal joints, diabetes mellitus, polyneuropathy, rheumatoid arthritis. Symptoms, clinical findings, EMG, associated conditions and operative findings are listed and statistically expressed in Table 1. The tourniquet test was performed by inflating a pneumatic cuff around the arm, above the elbow, at a value above the systolic blood pressure. Aggrevation of symptoms within sixty seconds indicated CTS.[13] The Phalen's test (wrist-flexion test) and the anti-Phalen's test (sustained extension of the wrist) was carried out as described by Phalen.[3]

| number of positive symptoms and signs including EMG | no. patients | % | 95% exact confidence limits |
|---|---|---|---|
| 8, 7 or 6 | 9 | 35 | 17-56 |
| 5 | 11 | 42 | 23-63 |
| 4 | 4 | 15 | 4-35 |
| 3 | 2 | 8 | 1-25 |
| 0-2 | 0 | 0 | 0-13 |
| 5-8 | 20 | 77 | 56-91 |

Table 2.
Summarized symptoms and signs including EMG.
Extracted from parameters numbers 1 to 8 in Table 1.

EMG was termed positive, indicating CTS when the conduction time for the motor fibers was significintly reduced and/or the sensory conduction velocity was prolonged through the carpal tunnel from either finger number one or finger number three. Simultaneously, normal motor and sensory conduction velocities were present at more proximal segments of the median nerve, and findings regarding the ulnar nerve were normal at the wrist. In Table 2 symptoms and clinical findings, including the EMG, are summarized, describing the diagnostic basis in statistic terms.

At each of the twenty-six operations two biopsies were taken, one of the carpal ligament and one of the peritendinous tissue or synovialis. All specimens were at once formalin fixed. Ail fifty-two biopsies were embedded in paraffin and stained with hematoxylin-eosine. van Gieson, orceine and alcaiic Congo red. The same pathologist examined all biopsies without knowledge of the symptomatology.

## RESULTS

The signs and symptoms in the 26 patients are summarized in Table 1. It proved that in 20 patients the diagnosis CTS was supported by five or more positive signs, symptoms or electromyographic findings (Table 2). This is in 77% of the patients with 95% confidence (limits 56-91). On operation the carpal ligament was found to be macroscopically thickened or fibrous in 13 patients (50%), while the flexor tendons were found to be thickened in four other cases. In one case an additional synovitis was found. In all other cases the structures appeared macroscopically normal.

No haemangiomas or ganglion cysts were encountered.

The median nerve was often cyanotic and showed compression neuroma. These findings were confirmed by different surgeons involved in the study.

In twenty-four patients no abnormalities were found on histological examination. In only one case (a female patient) in which the peritendinous tissue appeared to be normal, histochemical test including fluorescence microscopy showed deposits of amyloid in the carpal ligament. No abnormalities were found in the vessels of the connective tissue. In another female patient with minor signs of rheumatoid arthritis, the connective tissue contained moderate, non-specific inflammotory changes primarily located around the vessels.

## CASE HISTORY

An eighty-year-old woman, with no previous serious illness, developed seven months before admission, in connection with knitting, pain in the three radial fingers on the left side. She noticed herself to be butter-fingered and the left arm felt heavy. Nocturnal pain in the median nerve area was relieved by massage.

At objective examination she presented with reduced force of the handshake, normal sensibility, a positive Tinel's sign and positive Phalen's test. The tourniquet test did not aggrevate the pain. EMG indicated a carpal tunnel syndrome. Operative decompression was performed with good result. In the biopsy taken from the transversal carpal ligament amyloid deposits were demonstrated. She was admitted to the medical ward for further examination for amyloidosis.

She had no cardiopulmonal, gastrointestinal or urologic complaints. A slight cardiac decompensation was treated with diuretics. An X-ray of the chest showed slight arteriosclerosis of the aorta.

The following laboratory findings were normal: hemoglobin, sedimentation rate, reticulocyte count, WBC and differential count, liver tests, serum-urat, -creatinin, -immunoglobulins. Sheep cell agglutination test, rheumatoid arthritis test, Wassermann reaction, DNA — antibody titer, anti-nuclear antibody titer, direct Coomb's test and urin examinations for hemoglobin, albumine and glucosis were all negative or normal.

Based on these findings the amyloid changes in the transversal carpal ligament were interpreted as local (age-depended), neither idiopatic nor secondary systemic amyloidosis were found.

## DISCUSSION

The diagnosis of CTS may be verified in three out of four patients using anamnestic infor-

mation, simple bedside tests combined with EMG (Table 2). However, in most cases the pathogenesis of CTS remains obscure. It is generally accepted that the flexor retinaculis is ah important factor in the pathogenesis, producing venous stasis, ischaemia or mechanical pressure on the median nerve and its surroundings.[3,8,11-14] Clinically an indication of ischaemic mechanism may be achieved in cases where the tourniquet test aggrevates the symptoms. The operative findings in our investigation support the assumption that the transversal carpal ligament is involved, but the importance of fibrosis, rheumatic or non-specific, age-dependent manifestations in the flexcr synovialis for the pathogenesis are not clarified.[2]

The origin of amyloidosis is unknown. Previous proteincomplex thesis has been challenged by Teilum's biphasic cellular theory.[4,15] In most cases it is quite unexplainable why amyloid is found in tissue of the carpal tunnel. No predisposing conditions were present in the two (male) patients reported by Bastian,[7] or in our (female) patient.

Bastian[7] reported amyloid in both the synovialis and in the transversal carpal ligament in the two patients. Thus the deposits were more distinct than in our patient. In all three cases it was concluded, based on the remaining tests, that the patients did not suffer from systemic amyloidosis.

The local amyloid deposits reported in the flexor retinaculum in the three patients may be responsible for the CTS. Systemic amyloidosis with CTS may present similar pathological findings without evidence of intrinsic nerve involvement.[16] Alternatively, amyloid may infiltrate the vessels and lead to vascular obliteration, producing ischaemia.[16,17] This was not suspected clinically nor verified histologically in our patient. Using routine operative procedure, the therapeutic results for patients with local amyloidosis in the carpal tunnel in cases of CTS are compatible with other patients with CTS,[7,16,17] and the present case history.

In total, Bastian's. Lambird's and Hartmann's and our own series represent 144 patients with CTS screened by histological tests able to demonstrate amyloid in specimens from the carpal tunnel. Three patients (2%) were found to have non-systemic amyloidosis.

We conclude that histologic tests may have diagnostic interest, however without additional therapeutic consequences. Provided systemic amyloidosis is not suspected, searching for deposits therefore does not seem requisite.

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