CARPAL TUNNEL SYNDROME
IN LONG-TERM HEMODIALYZED
PATIENTS

ABSTRACT

The etiopathology, clinical features, and treatment of carpal tunnel syndrome (CTS) in long-term hemodialyzed patients, are discussed in the light of new clinical findings. Conclusions summarizing the specific characteristics of CTS in hemodialyzed patients include the following. 1) There is a relatively equal sex ratio of patients. 2) The pathogenesis is complex and includes a) the presence of hemodynamic alterations related to the AV fistula; b) the presence of beta 2 M amyloid deposits related to biocompatibility of the dialysis membranes; and c) a correlation between CTS and the duration of hemodialysis related to years and hours/week. 3) A dramatic increase of CTS incidence occurs after five years of dialysis treatment.

Prevention as a realistic goal in dialysis CTS is discussed, and specific recommendations are offered by the authors.

Hand pain and numbness are frequent in patients undergoing hemodialysis. For many years, these symptoms have been related to the location of the AV fistula or to an uremic arthropathy of the finger joints. Only in the last ten years, many reports1–9 have begun to connect symptoms to the carpal tunnel syndrome (CTS). The etiology is debated and not yet clarified. Hemodynamic alterations related to the AV fistula, as well as amyloid deposits, have been reported as the sole or concurrent causes of dialysis CTS.

Clinical Material

Between 1982 and 1987, 34 CTSs were operated on in 21 patients, 11 percent of a population of 187 patients (109 males and 78 females) actually undergoing hemodialysis at the Renal Unit of the University of Parma. All patients were treated with Cuprophan dialyzers employing a distal AV fistula. Between 1966 and 1971, the dialysis schedule had been 24 hr/week; since 1971, patients have been dialyzed 12 hr/week.

In 13 patients, CTS was bilateral (61.9 percent), and the mean age at the time of surgery was 55.9 years (range 37 to 73 years) with 11 male and 10 female patients. The fistula side was involved in 19 CTS (55.8 percent) and, in two patients only, the contralateral side alone was affected (Table 1). The duration of hemodialysis before surgery ranged from six to 17 years, with an average of 12 years and six months. Figure 1 shows the frequency of CTS related to number of years on hemodialysis. CTS increased from 0.76 percent in the first seven years of treatment, to 41.66 percent after 14 to 21 years of hemodialysis (Table 2). Among the causes of nephropathy, chronic glomerulonephritis was predominant both in patients without CTS and in the 21 patients with CTS (42.85 percent). Parathyroidectomy was performed in 10 patients (47.61 percent).

Clinical Features

There were no significant differences between the symptoms of dialysis CTS and idiopathic CTS. The first symptoms were paresthesiae and nocturnal pain irradiating along the median nerve territory and alleviated by shaking the arm. Often, these symptoms appeared during the dialysis session, usually after the first hour of dialysis.
Table 1. Characteristics of 21 Hemodialyzed Patients with CTS

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age &amp; Sex</th>
<th>Dialysis (years)</th>
<th>Causes of Nephropathy</th>
<th>Carpal Tunnel Syndrome</th>
<th>Amyloid</th>
<th>Parathyroidectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.A.</td>
<td>52 M</td>
<td>15</td>
<td>Glomerulonephritis</td>
<td>F/C</td>
<td>/</td>
<td>+</td>
</tr>
<tr>
<td>R.C.</td>
<td>40 M</td>
<td>16</td>
<td>Alport's Syndrome</td>
<td>F/C</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>G.C.</td>
<td>62 M</td>
<td>10</td>
<td>Hypertension</td>
<td>F/C</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>A.D.R.</td>
<td>64 F</td>
<td>14</td>
<td>Polycystic</td>
<td>F/C</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>G.F.</td>
<td>62 M</td>
<td>14</td>
<td>Glomerulonephritis</td>
<td>F</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>R.F.</td>
<td>55 M</td>
<td>12</td>
<td>Glomerulonephritis</td>
<td>F/C</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>F.G.</td>
<td>37 M</td>
<td>12</td>
<td>Unknown etiology</td>
<td>F/C</td>
<td>/</td>
<td>+</td>
</tr>
<tr>
<td>E.G.</td>
<td>64 M</td>
<td>10</td>
<td>Polycystic</td>
<td>C</td>
<td>/</td>
<td>-</td>
</tr>
<tr>
<td>A.M.</td>
<td>53 F</td>
<td>16</td>
<td>Unknown etiology</td>
<td>F</td>
<td>/</td>
<td>+</td>
</tr>
<tr>
<td>L.M.</td>
<td>65 F</td>
<td>12</td>
<td>Polycystic</td>
<td>F</td>
<td>/</td>
<td>+</td>
</tr>
<tr>
<td>E.P.</td>
<td>73 M</td>
<td>9</td>
<td>Diabetes</td>
<td>F/C</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>G.P.</td>
<td>55 F</td>
<td>12</td>
<td>Unknown etiology</td>
<td>F/C</td>
<td>/</td>
<td>-</td>
</tr>
<tr>
<td>L.R.</td>
<td>59 F</td>
<td>14</td>
<td>Unknown etiology</td>
<td>F</td>
<td>/</td>
<td>-</td>
</tr>
<tr>
<td>I.R.</td>
<td>71 F</td>
<td>12</td>
<td>Glomerulonephritis</td>
<td>F</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>C.S.</td>
<td>48 F</td>
<td>17</td>
<td>Glomerulonephritis</td>
<td>F/C</td>
<td>/</td>
<td>+</td>
</tr>
<tr>
<td>A.S.</td>
<td>44 M</td>
<td>15</td>
<td>Glomerulonephritis</td>
<td>F/C</td>
<td>/</td>
<td>+</td>
</tr>
<tr>
<td>M.T.</td>
<td>49 F</td>
<td>15</td>
<td>Glomerulonephritis</td>
<td>F/C</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>A.T.</td>
<td>54 M</td>
<td>16</td>
<td>Glomerulonephritis</td>
<td>F</td>
<td>/</td>
<td>-</td>
</tr>
<tr>
<td>M.C.*</td>
<td>43 F</td>
<td>9</td>
<td>Interstitial</td>
<td>C</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>E.P.*</td>
<td>64 M</td>
<td>10</td>
<td>Glomerulonephritis</td>
<td>F/C</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>G.V.*</td>
<td>61 F</td>
<td>6</td>
<td>Hypertension</td>
<td>F/C</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

F = fistula side; C = contralateral side; (*) = deceased. Amyloid (/) = not examined.

of treatment. The reason seems to be related to the prolonged immobilization of the arm in a forced position and to the hemodynamic problems caused by the AV fistula.9

A particular symptom was a feeling of swelling of the hand in the morning, with finger stiffness due to chronic tenosynovitis of the flexor tendons or an arthropathy. These concurrent pathologies complicate the clinical features, so that the CTS may sometimes be unrecognized.10 According to Naito,11 weakness with flattened and atrophic thenar muscles are present in patients where the duration of symptoms before surgery have lasted for more than two years.

Electromyographic (EMG) Study

EMG studies were done in all patients preoperatively. The EMG investigation included the evaluation of motor conduction velocity (MCV), distal motor la-
tency (DML), and the amplitude of the muscular action potential (MAP) of the median and often of the ulnar nerves of both hands. EMG studies were carried out by examining muscles, using concentric needle electrodes.

We also examined the shape and amplitude of sensory action potential (SAP) in the "finger-to-wrist" tract. The relative frequency of a sensory polyneuropathy in hemodialyzed patients makes the EMG diagnosis of CTS more difficult. For this reason, we consider the study of the sensory fibers of the median nerve in the "finger-to-wrist" tract as a basic test and, when indicated, in the "wrist-to-elbow" tract also.

The normal values (X ± 2SD) used in our laboratory were: SCV: >40 m/S; SAP amplitude: >10 μV; DML: <4.5 mS; MCV: >49 m/S; MAP amplitude: >5 mV.

Surgical Treatment and Findings

On the fistula side, all operative procedures were performed under axillary block anesthesia without pneumatic tourniquet\textsuperscript{12,13} to avoid the risk of damaging the AV fistula, especially in those patients with a long dialysis history (Fig. 2).

On the contralateral side, regional anesthesia with a pneumatic tourniquet was used. According to Tubiana,\textsuperscript{14} the surgical procedure was carried out with a longitudinal skin incision starting in the palm to the superficial arterial arch. It was diverted to the ulnar side of the palmar flexor creases of the wrist, and prolonged proximally on the median side (Fig. 3). This type of surgical approach permits the avoidance of the sensitive branches of the median and ulnar nerves and, at the same time, allows achieving the proximal flexor synovium. The transverse carpal ligament (TCL) was completely released on the ulnar side, checking for anomalies of the motor branches of the median nerve. A subsequent neurolysis with epineurotomy and a wide tenosynovectomy completed the procedure.

Macroscopic evidence in the surgical field showed a TCL that was very thick, tight, and hard to cut. The median nerve was always flattened under the TCL and sometimes was surrounded by a cuff of connective tissue adherent to the TCL (Fig. 4). The flexor tendons basically presented a hyperplastic synovitis, with proliferative adherent nodules and the appearance of grey deposits of amyloid (Fig. 5). According to Allieu,\textsuperscript{9} these deposits are localized mainly on the ulnar or radial side of the carpal tunnel.

Histologic Findings

Biopsies of the transverse carpal ligament, the flexor synovium, and the epineurium were taken in 19 hands. Histologic examination was performed with Congo red staining under polarized light microscopy. The amyloid deposits were present in 14 hands (73.6 percent). In 81.9 percent of these specimens, amyloid substance was found only in the flexor synovium show-
ing, under polarized light, a positive birefringence (Fig. 6).

RESULTS

We examined 18 patients with 29 CTS (11 bilateral); three patients died during the year following surgery (Table 1). The follow-up ranged from six months to five years. Pain and paresthesiae disappeared after surgery in all patients. In 14 cases (77.7 percent), we had improvement of hand sensibility. Static two-point discrimination ranged pre-operatively from 8 to 0 mm, while in the postoperative control, it ranged from 2 to 8 mm except for four patients tested with only protective sensation. Pre-operative muscle atrophy was present in nine cases; six of these cases had a significant improvement.

Figure 3. Surgical approach of dialysis CTS; drawing of the skin incision according to Tubiana.

Figure 4. Intraoperative view of the median nerve. A. Pronounced constriction of the nerve under the proximal part of the transverse carpal ligament, resulting in a flattened appearance. B. Connective tissue wraps around the nerve, modifying its aspect.
EMG Findings

A postoperative EMG examination was performed in 11 patients (18 hands). In this control group, four cases were unilateral (Table 3). The DML was significantly reduced after surgery in 13 hands out of 18 (72.2 percent). In two hands (11.1 percent), it remained unaltered, while in the remaining three hands (16.6 percent), it increased. The SCV or SAP amplitude increased in 12 hands (66.6 percent) out of 18. Five hands (27.7 percent) with a marked sensory impairment remained unchanged, while the SCV decreased in one hand (5.5 percent).

It is interesting to note that in five hands that presented unexcitability of the sensory fibers before surgery, an SAP became evident at postoperative control, suggesting a neuropraxis conduction block.

DISCUSSION

The etiopathology of CTS in hemodialyzed patients differs from that of idiopathic CTS, and its incidence is not related to age, sex, or hand dominance. The first report published in 1975 by Warren and Otieno suggested that the CTS in hemodialyzed patients was caused by edema in the hand due to increased venous pressure during the dialysis session produced by the AV fistula. Many other authors...
phased the same theory: that increased volume related to a vascular compromise caused by the AV fistula is responsible for the hemodynamic difficulties that would play a basic role in the development of CTS with a mechanism of fluid compression.

On the other hand, ischemia\textsuperscript{5,6} would be the main factor for nerve damage induced by a vascular steal mechanism. The blood flow bypasses the digital arteries, with resultant digital vascular insufficiency and ischemic hand pain. Nevertheless, other causes were added to CTS pathomechanics by some authors\textsuperscript{7-9} who reported the presence of CTS also in the hand without fistula, and evidence of amyloid deposits in the flexor synovium of the wrist. These deposits have nothing to do with systemic amyloidosis.

More recently, Gejyo et al.\textsuperscript{10} analyzed amyloid fibrils, discovering a substance identical to $\beta$ 2 microglobulin (M). The mechanism of production and accumulation of $\beta$ 2 M starts with the interaction between the blood flow and Cuprophane membranes. This contact causes complement activation (alternate way) and interleukin-1 production, increasing $\beta$ 2 M release from lung cells. Consequently, serum $\beta$ 2 M level increases during hemodialysis using Cuprophane dialyzer, because of the absence of any significant removal of $\beta$ 2 M across the membrane. The high affinity of $\beta$ 2 M for articular surfaces (synovium and tendons) would explain the amyloid deposits in the wrist and shoulder. According to this immunologic mechanism, our data suggest that CTS in hemodialyzed patients is closely
related not only to the dialysis age of patients, but also to the duration of dialysis sessions.13,17,18

The recent analysis of amyloid fibrils and our clinical findings both suggest changing Cuprophane membranes to newer high-efficiency membranes such as Polysulphone and AN 69 Polyacrylonitrile. These newer membranes allow the removal of 8 M yloid by two different mechanisms—high-sieving coefficient plus adsorption.19,20

**SUMMARY**

Conclusions of the specific characteristics of CTS in hemodialyzed patients include: 1) the relatively equal sex ratio of patients; 2) the complex pathogenesis which entails the presence of hemodynamic alterations related to the AV fistula, the presence of 8 M amyloid deposits related to biocompatibility of the dialysis membranes, and a correlation between CTS and the duration of hemodialysis related to years and hr/week; and 3) a dramatic increase of CTS incidence after five years of dialysis treatment.

Because of all these considerations and possibilities, prevention seems to be a realistic goal in dialysis CTS. It would include the following. 1) The use of new membranes such as Polysulphone or AN 69 Polyacrylonitrile that, because of their high biocompatibility, allow removal of high quantities of 8 M microglobulin, without increasing synthesis. 2) A shorter dialysis schedule is necessary (12 hr/week or less). 3) EMG screening of all dialyzed patients in treatment for more than five years is strongly urged.

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