Diagnostic and therapeutic value due to suspected diagnosis, long-term complications, and indication for sural nerve biopsy

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Abstract

In order to elicit the usefulness of sural nerve biopsy we retrospectively evaluated the courses of disease of every patient, who underwent this procedure in our department between January 1995 and March 2000. Sixty seven patients with the suspected diagnosis of peripheral neuropathy could be included. From these chart reviews and patient questionings were done.

Inflammatory-demyelinating neuropathies were suspected in 14 patients (20.9%), specific histological findings confirmed diagnosis in 50% of these patients and resulted in therapy. In cases of polyneuropathy of unknown etiology (46 patients, 68.6%) diagnosis was made in 11 patients (23.9%), and lead to therapy in 9 patients (19.6%), merely. In all, diagnostic consequences arouse in 32.8%, therapeutic consequences in 26.9%. The follow-up of 47 patients (mean 24.4 months) found chronic pain in the distribution of the sural nerve in 14 patients (29.8%), dysesthesia in 22 patients (46.8%), and persistent sensory loss in 34 patients (72.3%). Only 24 patients (51.1%) would submit to biopsy again.

Because of high complication rates and poor results we conclude that sural nerve biopsy should be done only in carefully selected cases after thorough clinical work-up, and should be limited to cases of suspected inflammatory neuropathies, collagenoses and immunologic neuropathies, and hereditary neuropathies.

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Keywords: Sural nerve biopsy; Diagnostic value; Therapeutic value; Complications; Indication

1. Introduction

Despite choosing the sural nerve for biopsy—largely a sensory nerve easily accessible under local anaesthesia because of its constant and superficial location [1]—several long-term complications are described [2–4]. In addition the indications for performing sural nerve biopsy vary widely and most biopsies yield only non-specific pathological changes [5,6]. From the literature point of view it is not clear, whether sural nerve biopsies give further diagnostic conclusions in different suspected diagnosis. The purpose of our study was to investigate the therapeutic and diagnostic consequences of sural nerve biopsies in different pathologies.

2. Materials and methods

We retrospectively evaluated the courses of disease of every patient, who underwent sural nerve biopsy in our department between January 1995 and March 2000. In the majority of cases patients were given in-patient treatment in the Department of Neurology, including therapy and after-treatment, documented in the charts. In all cases the sural nerve biopsied was clinically affected. Sural nerve biopsies were performed in the Department of Neurosurgery. After local anaesthesia (lidocaine 1%) at ankle level, skin incision was made in a vertical direction midway between the lateral malleolus and the Achilles tendon, extending 5–6 cm above the ankle. After dissection from adjacent tissue with a minimum of traction the whole nerve was sharply transected proximally and then distally, thus receiving 3–4 cm of sural nerve. The biopsy specimen was divided into three
posts. One part was cryogenic frozen, cut in 3–5 μm thick serial longitudinal and transverse sections, and examined after hematoxylin and eosin staining. The second part was fixed in 10% formaldehyde, paraffin-embedded, and after cutting in 3–5 μm thick sections examined with following staining techniques: hematoxylin and eosin, trichrome Masson-Goldner, and periodic-acid-Schiff. Depending on formulation of the question further stainings were done, such as Congo red. The third part was processed for semi-thin sections and used for electron microscopic examination. The results and therapeutic consequences could be seen from the charts; to gain information about postoperative complaints questionnaires were sent to the patients, 2–60 months after biopsy (mean follow-up 24.4 months). Thus data from patient charts concerning wound infections, delayed wound healing, pain in the scar area or in the distribution of the sural nerve, dysesthesia, and persistent sensory loss, could be completed.

3. Results

A total of 67 patients (39 male, 28 female) with a mean age of 60.5 years (27–90 years) underwent sural nerve biopsy during the study period.

On the basis of detailed history, neurological examination and electrophysiologic studies patients were divided into four suspected diagnosis groups. Histologic findings, diagnostic and therapeutic value are shown in Table 1. Inflammatory-demyelinating neuropathies were suspected in 14 patients (20.9%). This category includes collagenoses, sarcoidosis, vasculitis, and idiopathic polyradiculoneuritis (Guillain-Barré-Syndrome). Specific histological findings confirmed diagnosis in 50% of these patients and resulted in therapy. Forty six patients (68.6%) had a preoperative diagnosis of polyneuropathy of unknown etiology. Specific pathological results were found in 12 of these patients (26.1%), diagnosis was made in 11 patients (23.9%) including diabetic neuropathy (1 patient), sarcoidosis (1 patient), vasculitis (5 patients), toxic neuropathies (3 patients), and HMSN II (1 patient). In one patient a renal failure was known, a metabolic neuropathy could be confirmed histologically, but new findings could not be derived. In nine patients (19.6%) the results lead to therapy. The remaining seven patients were diagnosed as having other kinds of neuropathy. These included hereditary neuropathies (suspected Friedreich’s ataxia) and metabolic neuropathies, in two cases with proved inflammatory neuropathy steroid therapy could be started. In all, diagnostic consequences arose in 32.8%, therapeutic consequences in 26.9%.

Out of the 67 patients in whom a sural nerve biopsy had been performed, we were able to follow up 47 patients (70.1%) from 2 to 60 months after operation (mean 24.4 months). Of the remaining 20 patients, 7 had died, and 13 could not be reached. Postoperative or long-term complications are listed in Table 2. There were three patients (6.4%) with wound infections, and four patients (8.5%) with delayed wound healing (4–12 weeks). Pain in the scar area and reduction of sensitivity was determined in 15 (31.9%) and 12 (25.5%) patients, respectively. At the time of follow-up investigation 14 patients (29.8%) were still suffering from pain, 22 (46.8%) from dysesthesia. A persistent sensory loss was stated in 34 cases (72.3%). Only 24 patients (51.1%) would submit to biopsy again.

4. Discussion

According to Dyck and Lofgren [1] the sural nerve is the most suitable nerve for biopsy, fulfilling the following criteria: affected by the neuropathy, constant in its location and readily accessible, either a pure sensitive or a pure motor nerve, long enough so that 6–10 cm of the same fascicles can be removed, located where entrapment and pressure are not common, and suitable for conduction velocity studies in vitro. Pollock et al. [7] compared fascicular and whole sural nerve biopsies, concluding that whole nerve biopsies should be recommended since it has greater diagnostic potential without producing larger sural sensory loss. As only little information is available in the literature regarding value of sural nerve biopsies, we evaluated 67 patients with neuropathy after whole sural nerve biopsy, with regard to indications, diagnostic and therapeutic value, and long-term complications. In our series, specific histologic findings were made in 34%, a diagnostic consequence arose in 33%, and a therapeutic consequence in 27% of the patients. This roughly corresponds to the results of Neundörfer et al. [3]. Among 56 patients 15 cases (27%) were diagnosed by histology alone, in 21 cases (37%) non-specific histological findings contributed valuable diagnostic information, and the remaining 20 cases (36%) continued to be unclear. Similar, Argov et al. [8] reported a contribution of the final diagnosis in 20 out of 53

Table 1. Histologic findings, diagnostic and therapeutic value of sural nerve biopsies

<table>
<thead>
<tr>
<th>Suspected diagnosis</th>
<th>No. of patients (%)</th>
<th>Specific histologic findings</th>
<th>Diagnostic consequence</th>
<th>Therapeutic consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory-demyelinating neuropathies</td>
<td>14 (20.9)</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Polyneuropathy of unknown etiology</td>
<td>46 (68.6)</td>
<td>12</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>Hereditary neuropathies</td>
<td>2 (3.0)</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>5 (7.5)</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>67 (100)</td>
<td>23 (34.3)</td>
<td>22 (32.8)</td>
<td>18 (26.9)</td>
</tr>
</tbody>
</table>
nerve biopsies (38%), and Oh [9], reviewing a series of 385 biopsies, found specific findings in 24% of the cases. Gabriel et al. [10] prospectively studied 50 patients with peripheral neuropathy. Nerve biopsy revealed an otherwise unsuspected diagnosis in 14% of the patients, in 70% the biopsy findings contributed nothing. Rappaport et al. [2] examined 60 patients after sural nerve biopsy. Vasculitis was suspected in 29 patients (48%), diagnosis was confirmed in 6 of the patients (20%). In 27 patients (45%) the etiology of neuropathy was unclear. 12 patients (44%) in this group had sural nerve pathology, but no change in therapy was required. At all 25 patients (42%) remained undiagnosed after biopsy. In contrast, Chia et al. [11] could reach a definite diagnosis in 94 out of 100 patients older than 65 years when combining clinical and histological data. However, according to Midroni and Bilbao [12], doing a clinicopathological correlation in 239 cases, biopsy is essential for patient management in 21% and helpful in an additional 22%. In our series inflammatory-demyelinating neuropathies were suspected in 14 patients (20.9%), including suspected vasculitis in 8 cases. Specific histological findings confirmed diagnosis in 50% of these patients and resulted in therapy. In 46 patients (69%) the origin of polyneuropathy was unknown. Specific pathological results were found in 12 of these patients (26%), merely, 76% of these patients remained undiagnosed, and 80% without therapy. Based on our study we agree with other authors [2,5,13,14] that nerve biopsy should be done in carefully selected cases, only. Thus indications for sural nerve biopsy are mainly inflammatory neuropathies, collagenoses and immunologic neuropathies (e.g. vasculitis, sarcoidosis), and possibly hereditary neuropathies (e.g. amyloidosis), as nerve biopsy in the latter was progressively replaced by less invasive molecular genetic techniques. Accordant with Deprez et al. [14], who showed that only 20% of nerve biopsies provided contributive information in the absence of any pre-biopsy diagnosis, we also emphasize the need for a thorough clinical work-up. The performance of sural nerve biopsy should be the last of the diagnostic measures, when the diagnosis has remained unclear despite all other investigations, not least because of the significant complication rate. In our series there were 3 patients (6%) with postoperative wound infections, 4 patients (9%) with delayed wound healing, 15 patients (32%) with pain in the scar area, and 12 patients (26%) with reduction of sensitivity after biopsy, which is comparable to other authors. Rappaport et al. [2] found wound infections in 6 out of the 60 patients (10%), and delayed wound healing in 7 patients (12%). Neundörfer et al. [3] described pain in 28 out of the 56 patients (50%), paresthesia in 30%, tactile dysesthesia in 32%, and reduction of sensitivity in 46 out of the 56 patients (82%), immediately after the operation. Dahlén et al. [4] only had 1 patient with a minor wound rupture 13 days post-biopsy, but 11 out of the 31 patients (35%) stated pain in the operated area, and loss of sensation in the operated area was present in 27 out of the 31 patients (87%). Chronic pain in the distribution of the sural nerve was described in 14 of our patients (30%), others noted an incidence of such pain in 0% [7] to 58% [6]. Similar differences can be found in persistent dysesthesia with 30% [3] to 60% [7], 47% (22 out of the 67 patients) in our series. In contrast, the majority of patients stated a persistent sensory loss over the lateral aspect of the ankle and foot in several studies [3,6,7] (93–100%), which is to be expected in virtually all patients to some degree after nerve biopsy. Persistent numbness was present in 72% of the patients in our study. So patients must be properly informed about the risks of sural nerve biopsy, especially because of the persistent problems.

In conclusion we think that sural nerve biopsy should be limited to inflammatory neuropathies, collagenoses and immunologic neuropathies, and possibly hereditary neuropathies, as nerve biopsy in the latter was progressively replaced by less invasive molecular genetic techniques. In cases of polyneuropathy of unknown etiology, in which near 70% remained undiagnosed after biopsy, we cannot recommend sural nerve biopsies. Because of the high complication rates and poor results nerve biopsies should be done only in carefully selected cases after thorough clinical work-up.

**Table 2**

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound infection</td>
<td>3 (6.4)</td>
</tr>
<tr>
<td>Delayed wound healing</td>
<td>4 (8.5)</td>
</tr>
<tr>
<td>Pain in scar area</td>
<td>15 (31.9)</td>
</tr>
<tr>
<td>Reduction of sensitivity</td>
<td>12 (25.5)</td>
</tr>
<tr>
<td>Chronic pain in sural nerve distribution</td>
<td>14 (29.8)</td>
</tr>
<tr>
<td>Persistent dysesthesia</td>
<td>22 (46.8)</td>
</tr>
<tr>
<td>Persistent sensory loss</td>
<td>34 (72.3)</td>
</tr>
</tbody>
</table>

**References**


