Clinical aspects of nerve damage in leprosy
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Chapter 4

Change of Sensation in Leprosy by Selective Meshing of the Epineurium

From: Change of Sensation in Leprosy by Selective Meshing of the Epineurium
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Submitted for publication
SUMMARY

At present the administration of prednisone remains the first choice of treatment for early loss of protective sensation in leprosy. However, in cases where sensation is not restored by corticosteroid therapy, a definite improvement of sensation can still be obtained by a new microsurgical approach known as “selective meshing of the epineurium (SME)”.

This improvement is the best (a moderate and definite improvement in 70% of the nerves) when the operation is performed within six months after loss of sensation, is still definite in 43% of the nerves when operated within five years and in 32% of the nerves when operated within 10 years after loss of sensation. The results of 195 nerves operated on in 95 patients are presented.

The outcome of nerve decompressions by selective meshing of the epineurium may even be better when performed earlier after the initial loss of sensation.

There is a need to reconsider prednisone regimens and the timing and indications for nerve decompression by a selective meshing of the epineurium.

INTRODUCTION

In leprosy neuritis the involved nerve may be affected in two ways. First, all the fascicles in a nerve may be destroyed by the acute granulomatous reaction and this damage is irreversible. The second possibility is that the endoneurial fluid pressure increases causing oedema and consequently obstruction of the venous outflow through the epineurium. This may be to such an extent that it leads to microvascular insufficiency (ischaemia) and consequently loss of nerve function. When the cause of the oedema is eliminated at an early stage these effects are rapidly reversible, but when the oedema is long lasting the nerve tissue can be invaded by connective tissue cells and organized to a fibrous scar. This may explain why severe nerve pain and loss of nerve function in leprosy often fails to respond to corticosteroid therapy only although varied success rates of steroid therapy have been reported, and why the lack of improvement seems to correlate well with the severity and the duration of the neuritis.

In cases where the response to conventional steroid therapy is not up to the level of functional recovery, surgical intervention can be contemplated, albeit that surgical decompression of the affected nerve has not always enjoyed a favourable press as illustrated by Graham Green in his novel ‘A burned out case’, 1961 (p.12):

She had made her mouth with a mauve lipstick, which went badly with the black skin, and her right breast was exposed, for she had been feeding her baby on the dispensary steps. **Her arm was scarred for half its length where the doctor had made an incision to release the ulnar nerve, which had been strangled by its sheath. Now the girl was able with an effort to move her fingers a further degree.** The doctor wrote on her card, for the sister’s attention; “Paraffin wax “ and turned to the next patient.
In the past nerve decompression to prevent the fascicles from being strangulated by the sclerosed epineurium was looked upon as a deliberate infliction of injury because the epineurium as well as the matrix in which nerve fascicles are embedded, were divided. In ENL neuritis sometimes the epineurium was stripped off the compressed fascicles\(^4\). This technique is likely to damage the interconnected intrinsic microvascular systems in the epineurium, perineurium and endoneurium, a system upon which impulse transmission and axonal transport are dependent.

In 1993 when faced with a patient who's neuritis did not respond to prednisone treatment, Anandaban Hospital performed a nerve decompression using a new microsurgical approach, which would better respect the epineural blood vessels. Since then good results have been obtained from this procedure, later named “nerve decompression by selective meshing of the epineurium (SME)”.

MATERIALS AND METHODS

**Numbers:**
The SME was performed on 105 patients with a total of 208 affected nerves (91 ulnar nerves, 68 median nerves and 49 tibial nerves). When more than one nerve per patient needed decompression this was in general done in the same session. A control study was done on a matched group (for type of leprosy, age and duration of loss of sensation) of 100 non-operated patients.

**Selection of patients for surgery:**
Only included were those who had at least 3 points (see assessment) loss of sensation per nerve in the hand and/or foot and who had received no corticosteroids in the past two months. All of these nerves previously failed to improve with a standardised course of prednisone of 40 mg/day for three weeks, after which the dosage was reduced by 5 mg per week. Because of time constraints at the always-crowded outpatients department we focussed on loss of sensation and therefore intrinsic muscle weakness was not included in the selection criteria.

**Assessment of sensation:**
Ideally we would have liked to use the Semmes Weinstein filaments for sensory testing. Earlier we had tested the different sets obtained from the same supplier (Hansens Disease Centre, Carville, U.S.A. that were used by our physio-assistants. Because of too wide a variation in the forces needed for bending the same calibres of filaments of the different sets, the Semmes Weinstein monofilaments were not used in this study. A sort-like finding was earlier described in literature\(^5,6\).

The inter-observer reliability was much better when sensory testing was done with the ball pen test. For this only pressure was applied for making a minimal, just visible indentation.
Two experienced physio-assistants independently did this in two consecutive sessions, at the following intervals:

1. Within one week preoperatively.
2. At one week, two weeks, three weeks, one month, three months, six months, one year and two years postoperatively.

Sensation was measured three times at two sets of three standardised points in the hand each covering the median and ulnar nerve territories, and at three standardised points in the foot covering the area supplied by the posterior tibial nerve. These points were agreed upon at the Neuritis Workshop in Karigiri, South India (fig.1).

**Fig. 1.** The standardised points for testing the ulnar, median and posterior tibial nerves.

**Scoring of the sensation per nerve** was as follows:

- **Normal sensation:** 2 points
  
  When there was a correct response at least once within 2 cm of the test point.
  
- **Partial sensation:** 1 point
  
  When there was no correct response within 2 cm, but at least twice a response within 4 cm of the test point.

- **No sensation:** 0 points
  
  When there was no correct response within 2 cm, or maximally one single response within 4 cm of the test point.

As every nerve was tested at 3 points, the maximum score for each nerve was 6 points.
Recording of the change of sensation:
The result of the decompression by selective meshing of the epineurium (SME) was marked as follows:

- **Definite result:** 3 to 6 points improvement.
- **Moderate result:** 2 points improvement.
- **No result:** further decreased sensation or 0 or 1 point improvement.

Surgical procedure:
The operation was performed by the senior author under regional anaesthesia, with a tourniquet inflated at a pressure of 250 mm respectively 350 mm/Hg for the arm respectively the leg, with the help of magnifying glasses (4.5 times) and a number 15 surgical blade.

Fig. 2. The epineurial blood vessels and the incisions for the selective meshing of the epineurium (SME).
Fig. 3. The incision for the decompression of the Ulnar Nerve

Over the ulnar nerve at the elbow an S-skin incision is made from about 8 cm proximal of the medial epicondyl, over the cubital tunnel, and over the first 5 cm of the flexor carpi ulnaris muscle.

Proximally external neurolysis is done by carefully freeing the ulnar nerve from under the medial intermuscular septum and the fibres of the arcade of Struthers. Hereafter the aponeurotic roof of the cubital tunnel is incised while preserving the ulnar collateral artery and leaving the soft tissue attachment in the depth of the groove intact in order to prevent later luxation of the nerve. After this the fibrous arcade over the flexor ulnaris muscle is incised. While flexing the elbow, the free gliding capacity of the nerve in the groove is checked. Subsequently internal decompression of the enlarged nerve is done by selective meshing of the epineurium while carefully sparing its vascular plexus and the extrinsic blood vessels. Decompression is done at the superficial, medial and lateral site of the affected nerve leaving the bottom of the groove undisturbed. For this with a number 15 surgical blade partially overlapping incisions of about 2 mm lengths are made in the epineurium, between the epineural blood vessels (fig. 2) which remain clearly visible as the extremities are only briefly elevated before inflating the tourniquet. This expansion of the constricted epineurium parallels the resulting expansion after meshing a skin graft and is done until a proper refill of the epineural vessels is observed.

Only in those cases where there is a tendency for ventral luxation of the nerve over the epicondyl, a double, winged medial epicondyl based fascial flap is used to reconstruct the roof of the cubital tunnel this of cause without again constricting its blood supply.

No indication was ever found for performing a medial epicondylectomy and the ventral transposition of the nerve. The procedure is finalised by closure in layers.
The median nerve is approached through a S-curved, 3 to 4 cm longitudinal incision just proximal of the carpal tunnel, as much as possible paralleling the ulnar side of the palmaris longus tendon. In this way there is the least chance of damaging the palmar cutaneous branch of the median nerve. The antebrachial fascia is incised over the full length of the enlarged nerve and the transverse carpal ligament is divided at the ulnar side in case the nerve is also affected inside the tunnel. In the latter situation the limited open approach is used which saves the structures superficial to the roof of the carpal tunnel. The selective meshing of the epineurium and closure are done as described above.
The tarsal tunnel is approached through a curved incision which starts about 8 -10 cm proximal to the tip of the medial malleolus, then reaches the malleolus about 3 cm posterior of its tip and after this bends to ventral to the point of bifurcation of the medial and lateral plantar nerves. After opening the deep fascial layer proximally, the tibial nerve and vessels are identified and the tarsal tunnel is opened. Dissection is continued as far as the bifurcation of the lateral planter and the medial plantar nerves and the branching off of the medial calcaneal branches. At the level of the bifurcation a vascular plexus often surrounds the tibial nerve. Over the length of the enlarged nerve the selective meshing of the epineurium and closure are done as described above with special attention not to damage the network of the extrinsic blood supply.

The whole procedure will take about 20 minutes per nerve after which a compression bandage is applied. The joints are elevated for one week. Limited joint exercises are started by the physiotherapy department the day after the operation in order to prevent adhesion formation and thus to preserve the gliding function of the nerves.

Parameters:
The following parameters were recorded:

1. Preoperative time of loss of sensation.
2. Postoperative time before change of sensation was noticed.
3. Classification.
4. Presence of M. lepra in the fascicle biopsies.
5. Presence of M. lepra in the skin-smears.
7. IgM anti-phenolic-glycolipid-1 (PGL-1) titre in serum.

The information on preoperative time of loss of sensation was retrieved from the patient's record. The fascicle biopsies were prepared with fresh FMA fixative and after this they were stained by the modified Job & Chacko method with the reduced use of ethyl alcohol. Skin smears were stained in the standard way using carbol-fuchsin and 1 % hydrochloric acid in 70 % ethanol. For the lepromin test lepromin A (3x10⁶ bacilli in 100 µl; supplied by the Immunology of Leprosy Programme of the World Health Organisation) was injected intradermally on the volar aspect of the forearm, and the degree of induration at 3-4 weeks was measured. Induration of greater than or equal to 3mm was considered positive. IgM anti-phenolic-glycolipid-1 (PGL-1) antibodies were measured at Anandaban's Mycobacterium Research Laboratory by enzyme linked immunosorbant assay (ELISA), with disaccharide bovine serum albumin at a concentration of 250 ng/ml as the glucoconjugate and serum diluted 1:300. Samples with absorbency greater than 0.199 (mean absorbency plus 3 SD of serum from 91 healthy Nepali control subjects) were considered positive.

Statistics:
The differences in proportions of change in sensation were tested by the chi-squared test.
RESULTS

Anandaban Hospital provides clinical treatment to leprosy patients who sometimes come from as far away as Tibet. Ten operated patients were lost for the follow up. Ultimately data could be collected from 95 patients (64 males and 32 females, with ages ranging from 16 to 54 years) in whom a total of 195 nerves were operated on. The average follow up time was 25.9 months (24.0-28.7 months). Of the control group 4 patients were lost for the follow up.

Table 1:
Duration of preoperative loss of sensation and the postoperative change of sensation when divided in no result (NR), moderate result (MR) and definite result (DR):

<table>
<thead>
<tr>
<th></th>
<th>Less than 6 months</th>
<th>6 months-1 year</th>
<th>1 to 5 years</th>
<th>5 to 10 years</th>
<th>More than 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR (n=89)</td>
<td>30 %</td>
<td>27 %</td>
<td>47 %</td>
<td>54 %</td>
<td>50 %</td>
</tr>
<tr>
<td>MR (n=27)</td>
<td>4 %</td>
<td>13 %</td>
<td>10 %</td>
<td>14 %</td>
<td>23 %</td>
</tr>
<tr>
<td>DR (n=79)</td>
<td>66 %</td>
<td>60 %</td>
<td>43 %</td>
<td>32 %</td>
<td>27 %</td>
</tr>
</tbody>
</table>

n= number of nerves that were operated on.

Table 2:
Out of 117 fascicle biopsies the relation between M.lepra in the decompressed nerve and the postoperative change of sensation when divided in no result (NR), moderate result (MR) and definite result (DR):

<table>
<thead>
<tr>
<th></th>
<th>M.lepra in the decompressed nerve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>not present</td>
</tr>
<tr>
<td>NR (n=52)</td>
<td>32 %</td>
</tr>
<tr>
<td>MR (n=18)</td>
<td>19 %</td>
</tr>
<tr>
<td>DR (n=47)</td>
<td>9 %</td>
</tr>
</tbody>
</table>

n= number of nerves that were operated on.
Table 3:
Relation between M.leprae in the skin-smears and the postoperative change of sensation when divided in no result (NR), moderate result (MR) and definite result (DR):

<table>
<thead>
<tr>
<th></th>
<th>M.leprae in the skin smears</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
</tr>
<tr>
<td>NR (n=89)</td>
<td>22 %</td>
</tr>
<tr>
<td>MR (n=27)</td>
<td>11 %</td>
</tr>
<tr>
<td>DR (n=79)</td>
<td>67 %</td>
</tr>
</tbody>
</table>

n= number of nerves that were operated on.

Table 4:
Relation between the lepromin test and the postoperative change of sensation when divided in no result (NR), moderate result (MR) and definite result (DR):

<table>
<thead>
<tr>
<th></th>
<th>Lepromin test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>positive</td>
</tr>
<tr>
<td>NR (69 nerves)</td>
<td>55 %</td>
</tr>
<tr>
<td>MR (23 nerves)</td>
<td>18 %</td>
</tr>
<tr>
<td>DR (48 nerves)</td>
<td>27 %</td>
</tr>
</tbody>
</table>

n= number of nerves that were operated on.

Table 5:
Relation between the PGL-1 antibodies in the serum and the postoperative change of sensation when divided in no result (NR), moderate result (MR) and definite result (DR):

<table>
<thead>
<tr>
<th></th>
<th>PGL-1 antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>positive</td>
</tr>
<tr>
<td>NR (81 nerves)</td>
<td>29 %</td>
</tr>
<tr>
<td>MR (26 nerves)</td>
<td>15 %</td>
</tr>
<tr>
<td>DR (78 nerves)</td>
<td>56 %</td>
</tr>
</tbody>
</table>

n= number of nerves that were operated on.
Table 6:
Relation between classification, duration of the preoperative loss of sensation, and the postoperative change of sensation when divided in no result (NR), moderate result (MR) and definite result (DR):

<table>
<thead>
<tr>
<th>Classification of Leprosy</th>
<th>Loss of sensation &lt; 1 year</th>
<th>Loss of sensation &gt; 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paucibacillary</td>
<td>Multibacillary</td>
<td>Paucibacillary</td>
</tr>
<tr>
<td>NR (56 nerves)</td>
<td>31 %</td>
<td>52 %</td>
</tr>
<tr>
<td>MR (19 nerves)</td>
<td>10 %</td>
<td>16 %</td>
</tr>
<tr>
<td>DR (48 nerves)</td>
<td>59 %</td>
<td>32 %</td>
</tr>
</tbody>
</table>

n= number of nerves that were operated on.

At the end of the follow-up there was a further decrease in sensation in seven patients in whom 12 nerves had been operated on. Six of them had multibacillary leprosy and five sustained one or more recorded episodes of type 2 reaction after the time of nerve decompression. In the control group there was a decrease of sensation in 43 patients (97 nerves), while in 7 patients (15 nerves) improvement was found.

The degree of improvement after selective meshing of the epineurium is significantly higher when the nerve decompression is performed within 6 months after loss of sensation than when done after 5 years (p<0.01).

Although, the significance could not be proven, improvement seems better when M.leprae are demonstrated in nerves, in skin smears, when there is anti-PGL-1 positivity, lepromin negativity (all signs of multibacillary leprosy) and in the early phase of multibacillary leprosy. In 35 patients M.leprae was found in one or more nerves while the skin smears were negative. On the other hand in seven patients no M.leprae was found in the nerve(s), while the skin smear was positive. In a total of 18 patients the serum anti-PGL-1 titre was positive while the skin smear was negative. Of these anti-PGL-1 positivity was found in two patients who had been smear negative for more than 5 years, suggesting a possible relapse. In 13 patients the anti-PGL-1 was negative while the skin smear was positive.

DISCUSSION

In those patients in whom no improvement of sensory nerve function loss was observed after corticosteroid therapy, a moderate and definite improvement (2-6 points per nerve) could be obtained in about 70 % of the nerves when surgical decompression was done by selective meshing of the epineurium.
This compares favourably with the control group in which such an improvement was found in only 7% of the affected nerves. This difference is significant (p<0.05) and it may signify that after unsuccessful corticosteroid therapy the chances of spontaneous improvement of sensation are very slim. There is an inexplicably wide variation in the reported efficacy of only prednisone therapy for nerve function loss. In a study conducted in our hospital, an over-all improvement was found in 37% of the nerves.

In leprosy when nerve decompressions by the selective meshing of the epineurium are done at an early stage of loss of sensation, the recovery is significantly better than when done at a later stage. This corresponds with previous reports on non-leprosy nerve decompressions, e.g. the carpal tunnel release and when done for nerve function loss in leprosy. Our findings suggest that nerve decompressions performed in patients with multibacillary leprosy who had a loss of sensation of less than 1 year duration and in whom SME was performed, had better recovery of sensory loss.

This can be explained by the fact that in early multibacillary leprosy the neuritis in general is less severe and advanced than in paucibacillary leprosy and the oedema formation is therefore easier to reverse. In longstanding multibacillary leprosy the low-grade inflammation in the nerve persists for years leading to progressive scar formation. At that advanced stage it tends to respond less well to decompression than in paucibacillary leprosy, where the neuritis in general is confined to the earlier phase of the disease except in cases of type 1 reaction, relapse, or downgrading of the disease.

In a number of treated patients who had become skin smear negative, acid-fast bacilli were found in the nerve biopsy together with serum anti-PGL-1 positivity.

This demonstrates that nerves may be the last tissue to be cleared from bacilli and that until this process is completed, cell wall antigens will be released that can evoke an immune response.

The reliability of Semmes Weinstein monofilaments for the assessment of sensation in leprosy can be enhanced when for each patient a same observer will use the same one set. At the time of the study this was not feasible in our busy hospital and the reliability of the monofilaments, in contrast to a well-performed ball pen test, failed to meet our standards. This situation is rather similar to e.g. the one observed in most of the other countries where leprosy is endemic.

CONCLUSIONS

At present the administration of prednisone remains the first choice of treatment for early loss of sensation in leprosy. But when this fails a definite improvement of sensation can still be obtained by selective meshing of the epineurium. This improvement is the best (a moderate and definite improvement in 70% of the nerves) when the operation is performed within six months after loss of sensation, is still definite in 43% of the nerves when operated within five years and in 32% of the nerves when operated within ten years after loss of sensation.
Even after failed corticosteroid therapy the results of our nerve decompressions by selective meshing of the epineurium were significantly better than our results of corticosteroid therapy only, and may even be better when performed complementary to corticosteroid treatment and much earlier after the initial loss of sensation.

Therefore there is a need to reconsider prednisone regimens and the timing and indications for nerve decompression by a selective meshing of the epineurium.

**Illustrations:**
1. The standardised points for testing the ulnar, median and posterior tibial nerves.
2. The epineurial blood vessels and the incisions for the selective meshing of the epineurium (SME).
3. The incision for the decompression of the ulnar nerve.
4. The incision for the decompression of the median nerve.
5. The incision for the decompression of the tibial nerve.

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