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Experiences from Studies on Quiet Nerve Paralysis in Leprosy Patients

H Srinivasan[1] and MD Gupte[2]

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In leprosy, nerve trunk damage and paralysis are most often associated with antecedent attacks of acute or sub acute neuritis. (Bryceson & Pfaltzgraff 1979) 'Quiet Nerve Paralysis' (QNP) was first proposed by Srinivasan et al, as the most common onset of nerve trunk paralysis occurring quietly without clinical and subclinical neuritis. Though widely accepted, there is paucity of hard authentic data on epidemiology and management of this condition. We report findings from a study in 12 adjoining villages in Sriperumbudur taluk in Chengalpattu district in a population of 23,905. We observed QNP as an integral aspect of leprosy in pure neuritic, borderline tuberculoid, borderline lepromatous and lepromatous forms. Routine examination of sensory and motor territories of all nerve trunks of the extremities, irrespective of thickening, is needed. Standardizing of methods for clinical examination and data processing is important to eliminate errors of misclassification. We developed a seven-grade nerve function deficit scale as a practical and sensible tool to track major changes. There is a distinct need to study larger population of patients to get conclusive results. We propose several hypotheses regarding QNP pathogenesis. Given the situation we cannot make any recommendation for the management of QNP.

Key words : Quiet Nerve Paralysis, Leprosy, Neuropathy, Steroids, MDT

Introduction

In most peripheral neuritides the neuropathy is 'silent' in that the patient is unaware of anything being wrong till very late. In leprosy, however, it has been the general impression that nerve trunk damage and paralysis is most often associated with concomitant or immediately antecedent attacks of acute or subacute neuritis of the

[1] H Srinivasan , FRCS (London), FRCS (Edinburgh), Former Director, National JALMA Institute for Leprosy and other Mycobacterial Diseases (ICMR), Agra, India

[2] MD Gupte, MD, Former Director, National Institute of Epidemiology (ICMR)- *CJIL Field Unit for Leprosy (ICMR) at time of this work*, Avadi, Chennai, Tamil Nadu, India

Correspondence : MD Gupte, Address : K 502, Westend Village, Right Bhusari Colony, Paud Road, Kothrud, Pune 411038, Maharastra, **Email :** mohandgupte@gmail.com

This unpublished work was presented by Dr MD Gupte at IAL Digha Conference, November 2017 and dedicated to memory of Late Padmashri Dr H Srinivasan. Dr Srinivasan (1929-2015), was an outstanding surgeon, academician and innovator & above all a wonderful human being. He inspired many of us and will continue to inspire many coming generations of leprologists and medical professionals. Tributes to this great individual who also contributed as editor of our journal for several years.

– VM Katoch, Hon. Editor, Indian Journal of Leprosy.

concerned nerve trunk.

Occurring either alone or as part of reactional episodes, with significantly increased tenderness and pain in the affected nerve trunk (Bryceson & Pfaltzgraff 1979a). Srinivasan et al pointed out in 1982 that nerve trunks often became paralysed in leprosy patients 'quietly' without manifest clinical acute or subacute neuritis and suggested that this was probably the most common mode of onset of nerve trunk paralysis. They proposed the name 'Quiet Nerve Paralysis' for this condition. The concept and fact of Quiet Nerve Paralysis (QNP) seems to have found ready acceptance among leprologists and leprosy workers including the sixth WHO expert committee on leprosy (WHO 1989), although terms like 'silent neuritis' and 'silent neuropathy' are used by some to refer to this condition. In our view, 'Quiet Nerve paralysis' is more appropriate, since 'neuritis' has already an established usage among clinicians to refer to clinically recognized episodes of acute or subacute neuritis with increased pain and tenderness in the nerve trunks, and 'neuropathy' indicates only a pathological state involving nerves, which need not necessarily be associated with paralysis of a nerve trunk.

Despite the general acceptance of the existence of QNP there has been no publication other than that of Srinivasan et al mentioned earlier to provide further information on the epidemiology, natural history or management of this condition. One cannot make broad generalizations from that study because it was based on a hospital clinic attending population, with all the biases associated with such a selected sample. Therefore, in this paper we will first examine available information and assess whether QNP really exists and how common it is. We shall then outline the lessons learnt by us from our on-going studies at the CJIL Field Unit at Avadi, Madras. Lastly, we shall be making some comments relevant to the issue of QNP.

QNP exists and it is common

Studies on deformities and disabilities have generally focused their attention on the epidemiology and pattern of deformities and not on their mode of onset. Hence there is a paucity of information on this subject. Nevertheless, available information is examined below.

A detailed retrospective study of leprosy patients detected in Bobbili in Andhra Pradesh during 1963-72 carries some information directly relevant to our subject, although that study itself was designed to examine the relationship between treatment with dapsone and occurrence of deformities (Gupte 1979). In that study of 2608 newly detected patients followed up for a number of years, 117 patients had developed deformities during the period of observation, out of a total of 2222 patients who were known to have had no deformities initially. Table 1 shows the relationship between the occurrence of reactions (which would also include neuritis) and deformity.

It is seen that, while the risk of developing deformity was, very much higher in those who developed reactions, we also find that in 75% of

Table 1 : Relationship between the occurrence of reactions and deformities in 2222 originally undeformed patients (Gupte 1979)

	Reactions	No Reactions	Total
Deformity developed	29	88	117
Remained undeformed	57	2048	2105
Total	86	2136	2222

those who developed deformities (88 out of 117) there was no history or record of reactions, indicating that, most probably, most of these were instances of QNP.

Srinivasan et al (1982) reported that in an unpublished prospective non-interventional study (in the field) of about 500 'high risk' patients, 58 patients developed motor paralytic deformity over a period of two years, and in 47 (81%) of them onset of paralysis was not associated with a remembered episode of neuritis of the concerned nerve trunk. They also reported that in a subsequent enquiry of about 100 patients with paralytic deformity, about 67% of the patients reported that their deformities developed “just like that", suddenly or gradually, without acute or subacute neuritis of the concerned nerve, suggesting that these, or, most of these, were instances of QNP.

It is the common experience of clinicians that a proportion of patients with pure neuritic type of leprosy present with nerve damage and deformity, without concomitant or immediately antecedent clinical acute or subacute neuritis of the concerned nerve trunk. Evidently such cases would also be instances of QNP. Uplekar and Antia (1986), in their detailed study of 12 cases of pure neuritic leprosy, found only 3 presenting with acute neuritis. Since relevant information is not given, presumably at least some if not all of the retaining 9 cases were instances of QNP. In one series of 108 patients having pure neuritic leprosy reported by Kaur et al (1991), 34 had motor paralysis or paresis and deformity and about 70 had sensory loss "limited to the distributions of nerve trunks". Only five of these 108 patients were reported to have had 'nerve pain'. Even assuming (relevant information is not available in the paper) that all these 5 had motor paresis or sensory deficit, we find that they formed only a very small proportion of those developing sensory or sensori-motor paralysis. Thus the available data indicate that QNP exists and that it is the most common mode of onset of nerve trunk paralysis and deformity in leprosy patients. Presumably the remaining great majority were instances of QNP.

Studies on QNP

Studies of QNP in the field need to be carefully designed and carried out. By definition 'Quiet Nerve Paralysis' starts insidiously and so the affected patients will not be reporting on their own in the early stages. Therefore, they will have to be searched for among those with active leprosy. Some kind of preliminary examination of these cases needs to be carried out for identifying the high risk group, among whom cases of QNP are likely to be found. Those patients coming in the high risk group will then have to be assessed in detail for identifying those with QNP, i.e. those with functional deficit of a major nerve trunk. This requires using nerve function tests which are reliable in the sense of having high reproducibility. These tests should also be practicable in the field. Further, such assessment also requires availability of personnel competent to carry out the tests, interpret the result interpret the results and record the findings. Lastly, an objective scale of nerve function deficit for use in the field is required for expressing and recording the degree of nerve damage, in numerical terms, for easy future comparison which will be necessary for assessing the natural history of the condition as well as the effect of any intervention. During 1989-1990 we carried out some Pilot studies in a rural area in Chengalpattu district in South India, primarily to develop reliable methodology, and we report here some of the experiences and the lessons learnt.

The methodology used was as follows. An area was chosen and a baseline survey of the population was carried out, to identify prevalent

(active) cases of leprosy. The identified prevalent cases were then examined in order to select those at high risk of having QNP for further detailed examination. Identification of thickening of designated nerve trunks (ulnar, median, common peroneal and posterior tibial) was used for this purpose since it was thought that thickening would precede clinically recognizable damage to the nerve trunk. Patients who thickening of any of the above had named nerve trunks were then examined in detail, in the field, for nerve function deficit. The examination for nerve function deficit was carried out blind (without the examiner knowing which nerves were thickened) by a physiotherapy technician specially trained by one of us in the techniques of examination and recording the results. Sensibility was assessed in the hands by feather for perception of fine touch, pin for perception of pain and thermal sense tester (Srinivasan & Stumpe 1989) for perception of heat. In the sole, only perception of coarse touch (pressure) and perception of pain on deep pressure were tested, using ball pen. Motor paralysis was assessed by the standard voluntary muscle testing method and motor power was recorded in the six grades 0 to 5 MRC scale. For palmar and plantar intrinsic muscles, however, their power was recorded as normal, weak or paralysed (grades 2, 1 and 0 respectively).

Nerve function deficit status of each nerve was ranked in a seven grade (grades 0 through 6) scale as shown in Table 2 below. A proforma was developed for recording the information and was pretested before final use.

Table 2 : Nerve function deficit grading used in the field

Grade	Description
0.	Normal. No sensory loss. No motor loss
1.	Loss of only one modality of sensation
2.	Partial (area wise or modality wise) sensory loss
3.	Complete (area - and modality wise) sensory loss
4.	Partial sensory & partial motor loss
5.	Complete sensory & partial motor loss
6.	Complete sensory-motor loss

Table 3 : First reproducibility exercise (380 nerves)

I Exam.Grade	II Examination grade							Total
	0	1	2	3	4	5	6	
0	86	17	6	12	1	1	-	123
1	12	4	1	-	-	-	-	17
2	16	5	12	11	-	-	-	44
3	31	11	21	77	-	7	-	147
4	1	-	-	1	1	-	-	3
5	3	1	-	4	1	22	1	32
6	2	-	-	2	-	5	13	22
Total	151	38	40	107	3	35	14	388

Concordance: 55%

We had assumed that the methods used for assessment of nerve function deficit were reliable, in the sense of having high reproducibility. Nevertheless, we carried out studies to test this assumption in the following manner. Initially, the same patients were re-assessed 3-4 weeks later by the same examiner, blindly, without his being aware of nerve thickening status or the previous assessment results. At one year, the reproducibility exercise was repeated and two assessments were carried out, by the same examiner, with a time interval of about 3 weeks between the two, on 34 patients (272 nerve trunks) in another area, again blindly. Table 3 shows the results of the first reproducibility exercise. It can be seen that in the first reproducibility exercise, the assessments coincided in only 55% of instances. When one grade difference was considered permissible, 75% of the results were within the permissible zone. The situation was much better in the second reproducibility exercise (Table 4).

At the second exercise there was 82% concordance between the two assessments (Kappa = 0.67) and when one grade difference was permitted, 87% of the results fell within the permissible zone. We learn from these studies that: (i) mere training is not sufficient to ensure high reproducibility, (ii) that some experience in carrying out these tests under field conditions is necessary for achieving acceptable reproducibility, (iii) that even with experience, reproducibility is of the order of 80% to 85% only, and (iv) that while assessing follow-up results one should therefore take this source of error into account.

It is pertinent to mention in this connection that,(i) in assessing for 'reproducibility error', a very large number in the '0' category (normal nerves) will dilute the error, leading to its underestimation, (ii) errors relating to category '6' (complete sensori-motor paralysis) are likely to be minimal, and (iii) that categories 1 to 5 (incomplete paralysis of the nerve trunk) are the most important from the point of view of standardizing the data for 'reproducibility error'.

We had selected an area of 12 adjoining villages in Sriperumbudur taluk of Chengalpattu district (South India) for these studies. The enumerated population in these 12 villages was 23905. In the baseline survey 21604 (90.4) were examined, and 244 prevalent (active) cases of leprosy (138 males including 37 children and 106 females including

Table 4 : Second Reproducibility exercise (272 nerves)

I Exam.Grade	II Examination grade							Total
	0	1	2	3	4	5	6	
0	159	-	4	9	-	1	-	173
1	3	2	4	-	-	-	-	9
2	7	-	14	2	-	-	-	23
3	7	1	1	30	-	1	-	40
4	-	-	-	-	-	-	-	0
5	3	-	-	2	2	11	-	18
6	-	-	-	-	1	1	7	9
Total	179	3	23	43	3	14	7	272

Concordance: 81.9% Kappa: 0.67.

34 children) were identified. These 244 patients included 6 indeterminate, 10 pure neuritic, 178 tuberculoid, 18 borderline tuberculoid and 32 borderline lepromatous or lepromatous cases of leprosy. As mentioned earlier, these patients were next examined by experienced paramedical workers for thickening of the designated nerve trunks (ulnar, median, common peroneal and posterior tibial nerves), and 62 patients (25%) were identified as having thickening of one or more of the above named nerve trunks. Fifty-five (89% of these 62 were males (including 4 children). Thus nerve thickening was found in 50% and 11% of the adult males (51/101) and male children (4/37) respectively, and in 8% and 3% of adult females (6/72) and female children (1/34) respectively in this population of 244 leprosy patients.

Multiple nerve thickening (thickening of 3 or more number of nerve trunks) was found in 39 (58%) of the study subjects, all of them being adult males.

Table 5 shows the distribution of nerve trunk thickening according to type of leprosy in these 244 patients.

It is evident that any nerve thickening as well as multiple nerve thickening are related to type of leprosy, being more common in pure neuritic, and the more extensive borderline and lepromatous tubes than in the more limited tuberculoid and indeterminate tubes of leprosy.

As may be expected, ulnar nerve was the one to be most frequently thickened (83 out of 124 nerves or 67%) followed by common peroneal nerve (71 out of 124 nerves or 57%). Compared to these two nerves, thickening was identified very much less often in the case of median and posterior tibial nerves (31 out of 124 (25%) and 28 out of 124 (22.6%) respectively).

Nerve function deficit data

Fifty-three of the 62 patients with thickening, of one or more nerves could be assessed in detail for evidence of nerve damage and all but one were found to have some nerve damage (deficit grade 1 to 6). Complete information regarding both thickening and functional status was available for 389 of the 424 nerve trunks of these 53 patients. Two hundred sixty-four of the 389 nerve trunks (67.8%) showed evidence of damage and function deficit. Table 6 shows the relation between thickening and damage in these 389 nerves.

It can be seen from Table 6 that 95% of thickened nerves and 51% of nerves identified as not thickened showed evidence of nerve function

Table 5 : Nerve trunk thickening according to type of leprosy in 244 leprosy patients

Type of leprosy	No. of patients	1 or 2 nerves thickened	3 to 8 nerves thickened	% with any nerve	%with multiple nerve thickening
Indeterminate	6	--	--	- -	--
Pure Neuritic	10	3	4	70	40
Tuberculoid	178	16	--	9	--
Borderline Tuberculoid	18	4	4	44	22
Borderline Lepromatous & Lepromatous	32	3	28	97	87
All types	244	26	36	25	15

deficit of varying degree in these 53 patients. It is also worth noting that in these patients thickened nerves contributed only 54.5% (144 out of 264) of all damaged nerves.

We had selected eliciting nerve trunk thickening as the preliminary test on the assumption that nerve trunk thickening generally preceded damage and so the risk of damage to the nerve trunk would be low in the absence of thickening. Furthermore, we had also assumed that while thickening would indicate a higher risk of damage, only a proportion, probably a fairly substantial proportion, of the thickened nerves would actually be damaged. Our findings showed that besides almost all thickened nerves substantial proportions (51%) of non-thickened nerves were also damaged in this patient population! It thus appeared that looking for nerve trunk thickening as the preliminary test for nerve trunk involvement and damage would not be a sensitive enough procedure for identifying the population at high risk for QNP. This meant that the more demanding detailed examination for nerve function deficit would be necessary even for preliminary surveys aimed at identifying a target population for studying QNP. In order to be sure on this matter we conducted yet another study.

Since the 237 non-thickened nerves (of which 51% showed evidence of damage) were from patients who had one or more thickened nerve trunks, in the new study we decided to examine the functional status of nerve trunks in about 100 patients having no thickening of any nerve trunk. Actually, 91 such patients (having indeterminate or tuberculoid leprosy) were examined and 17 of them (19%) showed some evidence of nerve damage, Of the 728 nerve trunks examined in these 91 patients, only 29 (4%) showed evidence of damage.

Furthermore, in the first set of 53 patients having one or more thickened nerves, 43 of the 152 thickened nerves (28%) showed severe damage (deficit grades 4 to 6); and 12 of the 237 non-thickened nerves (5%) showed severe damage. In contrast, of the 728 non-thickened nerves from 91 patients having no thickening of any nerve, only 5 nerves (0.7%) showed severe damage. These findings bring out an important fact not hitherto appreciated, viz., the risk of damage (and severe damage) in non-thickened nerves increases considerably in patients having thickening of some nerves. Second, these findings also show that our initial assumption that thickening of nerve trunk indicated an increased risk of damage was not wholly incorrect. Our findings show that we may still use elicitation of nerve thickening as a preliminary test for identifying the population at risk of nerve damage; but, in the identified high risk patients the other, non-thickened, nerves must also be carefully examined for functional deficit. We may also mention here that it is in the borderline

Table 6 : Nerve thickening and damage (389 nerves)

Damage Status	Thickening Status		Total
	Thickened	Not thickened	
Damaged	144	120	264
Not damaged	8	117	125
Total	152	237	389

Proportion of thickened nerves showing damage = 95%
Proportion of non-thickened nerves showing damage = 51%

lepromatous and pure neuritic types of leprosy that thickening of nerve trunks occurs most often and that in patients with these types of leprosy, one should examine all nerve trunks, both thickened and non-thickened ones, for functional deficit.

Effect of steroid therapy

This study was also planned to be an intervention study with the objective of assessing the usefulness of steroid therapy in QNP. Hence persons with nerve damage from six of the 12 villages (29 patients) were put on steroid therapy for three months, and similar patients from the other six villages (29 patients) were kept as control. Both groups received MDT as per the NLEP norms. Patients on steroid therapy received 40 mg of prednisolone daily (single dose) for the first two weeks, 30 mg daily for the next six weeks and the dosage was progressively reduced over the subsequent next four weeks after which steroid therapy was terminated. Daily steroid intake was not supervised. Patients were provided with a week's stock of steroids at a time and were instructed regarding how many tablets they should take daily for that week. Patient compliance was monitored by random pill counting. Nerve damage status was assessed by the same trained examiner at three months intervals. All assessments were done blind, without the examiner being aware of earlier assessment findings.

We came across some important methodological and operational problems during the course of this study. First, a substantial proportion of patients in the steroid group (11 out of 29 patients) could not be given prednisolone because of prescribed contraindications like chronic cough, hyperacidity and plantar ulceration. Second, random check using pill counting among those who received steroid therapy showed that a proportion of these patients (6 out of 18) were not consuming the tablets as prescribed. Thus only 41% of the patients in the steroid group (12 out of 29) had actually consumed steroid tablets as prescribed. Third, a comparison of the initial nerve function deficit status showed that the two groups (MDT only and MDT plus regular steroid) were not comparable in this regard (Table 7).

Since the 'MDT only' and 'MDT + steroid' groups were not comparable in their initial nerve function deficit status, three comparable subsets from each group (grade '0', grades 1-3 and grades 4-6) were compared separately regarding the changes in their nerve function status. The differences between pairs of these three comparable subsets were found to be statistically not significant, as shown in the three Tables 8, 9, and 10.

These findings suggest that steroid therapy did not have any noticeable beneficiary effect in this study population.

Table 7: Initial nerve function deficit status in the two (MDT and MDT+ steroid) groups (232 nerves)

Group	Initial nerve function deficit grade			Total
	0	1-3	4-6	
MDT only	69	85	14	168
MDT+ steroid	17	32	15	64
Both groups	86	117	29	232

$P < 0.005$

Table 8 : Comparison of MDT only and MDT+ steroid (Regular) groups for change in nerve function status - Initial status: grade 0 (86 nerves)

Group Subjects	Nerve function status		Total
	Static	Worsened	
MDT only	64	5	69
MDT+ steroid < (Regular)	16	1	17
Both groups	80	6	86

P = 0.41 (Fisher's exact): differences not statistically significant

Table 9 : Comparison of MDT only and MDT+ steroid (Regular) groups for change in nerve function status - Initial status: grades 1, 2, 3 (117 nerves)

Group Subject	Nerve function status			Total
	Improved	Static	Worsened	
MDT only	43	33	9	85
MDT+ steroid < (Regular)	11	16	5	32
Both groups	54	49	14	117

P > 0.25; differences not statistically significant

Table 10 : Comparison of MDT only and MDT+ steroid (Regular groups for change in nerve function status - Initial status grades 4, 5 and 6 (29 nerves)

Group Subset	Nerve function status		Total
	Improved	Static/Worsened	
MDT only	9	5	14
MDT+Steroid < (Regular)	5	10	15
Both groups	14	15	29

P > 0.35; differences not statistically significant.
Fisher's exact P = 0.14

Effect of MDT on QNP

Next, we examined the changes in nerve function status in patients (168 nerves) in the QNP study receiving only MDT, and found that, after standardizing the data for 'reproducibility error; improvement in nerve function status had occurred more frequently in these patients receiving MDT than could be accounted for by the reproducibility error factor, whereas worsening noted after MDT could be accounted for by reproducibility error.

In order to confirm this conclusion, another small study was carried out. In this study, involving another set of 24 patients (192 nerves) from another area, a comparison of the follow-up findings after standardizing for 'reproducibility error' showed that while improvement in nerve function after MDT could have occurred due to the reproducibility error, the worsening noted after MDT was more than could be accounted for by reproducibility error. Incidentally, it was also found that when the nerve function deficit grades

in these patients were translated into WHO disability grades (0 to 3) (WHO 1969), this difference (increased worsening) was not seen. It appeared from this study that nerve function status worsened to some extent under MDT, which was picked up by the nerve function deficit scale devised by us, but the change was not big enough to be detected by the WHO disability grading system.

These conflicting findings in these two studies, one showing improvement and the other showing worsening of QNP following MDT suggest that the sample sizes in these studies were probably not large enough to provide consistent results.

Comments

Available information indicates that QNP occurs in all types of leprosy, except the Indeterminate as currently defined (IAL 1982), particularly in patients with extensive leprosy. Patients with pure neuritic leprosy as well as borderline tuberculoid, borderline lepromatous and lepromatous patients are the most vulnerable group. In these patients, the clinical examination should include, as a routine, examination of sensory and motor territories of all the nerve trunks of the extremities irrespective of their thickening status. That is the only way to recognize QNP in the early stage. The peripheral leprosy workers need to be trained in this regard. It also appears that QNP may occur in untreated patients, patients under treatment as well as those relapsing after successful treatment (Srinivasan et al 1982). Treatment in this context refers to antileprosy chemotherapy, viz., dapsone monotherapy. The situation under multidrug therapy (MDT) is not known, but it may not be very different.

We may consider the following six hypotheses regarding the aetiology/pathogenesis of QNP:

(i) QNP is an integral part of the disease process itself; (ii) QNP is a complication caused by certain immunological phenomena related to the disease like increased CMI or deposition of immune complexes or local release of noxious biological substances; (iii) QNP is an epiphenomenon due to the operation of other factors not related to the disease process; (iv) (In cases under treatment QNP or its worsening (in some cases) is an inescapable side effect of any effective anti-leprosy treatment; (v) QNP occurs from a combination of (some or all of) the above causes; and (vi) QNP is the common and result and there are subsets within QNP according to the cause. These hypotheses are briefly examined below:

(i) QNP is an integral aspect of leprosy:

QNP is present in many cases of pure neuritic leprosy and some cases of other types of leprosy, even at the time of diagnosis of the disease. This as well as the occurrence of complete or partial recovery of the paralysed nerve after the institution of antileprosy treatment would suggest that the nerve paralysis in these cases was part and parcel of manifestation of leprosy. More frequent occurrence of QNP in the more extensive types of leprosy (in which the bacillary population is also greater) would further suggest that the condition is related to bacterial load and not so much to systemic CMI-related factors like delayed hypersensitivity. Multiplication of bacilli in the Schwann cells and their consequent destruction, the resulting segmental demyelination, as well as the inflammatory cell response to *M. leprae* and its antigens (Ridley & Job 1985; Job, Selvapandian & Rao 1991; Job & Dharmendra 1985) could well account for QNP. Failure of steroid therapy to reverse the nerve paralysis would support this hypothesis.

(ii) QNP is a complication due to immunological phenomena related to the disease:

These immunological phenomena typically manifest as ENL and reversal reactions (Type 2 and 1 of Jopling respectively) and when they occur in the nerve trunk, there is clinical neuritis. It is well documented that such clinical neuritis increases the risk of nerve damage manifold. There does not seem to be any particular reason why the same processes cannot be operating continuously on a small scale and at a low subclinical level and cause insidious damage resulting in QNP. Non-responsiveness of nerve paralysis to antileprosy chemotherapy and recovery with steroid therapy would support this hypothesis.

(iii) QNP is an epiphenomenon:

It is possible that in some patients at least other neuropathic factors, not directly related to the disease process, operate to damage the already diseased nerves and accentuate the neuropathy to cause increased nerve damage and paralysis. The drug(s) administered for curing the disease, some unspecified nutritional deficiencies (e.g. Zinc) or metabolic abnormalities, local anatomic factors like entrapment, repeated bending strains or repeated minor trauma suggest themselves as possible such extraneous factors. Since Srinivasan and Noordeen (1966) drew attention to the possibility of a role for dapsone therapy in causing or worsening of deformities in leprosy, others (Gupte 1979, Radhakrishna & Nair 1987, Sebille et al 1987, Sirsat et al 1987) have shown that this is not an unrealistic or far-fetched proposition. Recovery after simple decompression of the nerve (Parikh et al 1968; Vaidyanathan and Vaidyanathan 1968) after cessation of dapsone therapy (Sebille et al 1987, Sirsat et al 1987) would support this hypothesis. A variety of factors not related to leprosy, ranging from emotional crisis and surgical trauma to small pox vaccination, intercurrent infections and administration of some drugs like potassium iodide and diethylcarbamazine (Ramu & Dharmendra 1978, Bryceson & Pfaltzgraff 1979b) are said to precipitate reactions in which neuritis is often a feature. It is possible that some such factors may operate in the pathogenesis of QNP also, in some cases, may be at a subclinical level.

(iv) QNP is an inescapable side effect of effective treatment of leprosy:

Treatment of leprosy is based on administering mycobactericidal drugs. This has two different kinds of consequences: (a) reduction of bacterial load and consequent improvement in the CMI of the individual, and (b) destruction of bacilli and consequent release of intracellular mycobacterial antigens. The two types of reactions (Reversal reactions and ENL reactions respectively) are generally considered to be the sequalae of these two consequences. Therefore any effective treatment, whether dapsone monotherapy, multidrug therapy or immunotherapy is considered capable of precipitating reactional episodes of one type or the other. The same logic also applies to occurrence of acute neuritis in isolation without any other manifestation of reaction. If these generally accepted ideas are correct, we may also accept the idea that, in some individuals at least, these processes may operate at a low subclinical level in the nerve trunk and damage the nerve insidiously, i.e. cause QNP, just because they are getting effective mycobactericidal treatment.

The last two hypotheses (v and vi above) only postulate that in any given case more than one aetiological factor may be operating (hypothesis v), or, that in any given case nerve damage occurs due to one factor, but QNP as a whole is a heterogeneous group containing a number of subsets of cases, each subset having one common aetiological factor.

Only detailed studies can help us unravel the situation and provide us with some definite understanding of this interesting and important clinical phenomenon. This brings us to the next issue for consideration, viz., further studies of this condition.

Study of QNP

There is practically no information available in the literature regarding the aetiology, epidemiology, natural history and management of QNP. That this is so despite the fact that QNP is the most common mode of onset of nerve damage, deformity and disability in leprosy is indeed surprising. One reason for this situation may be that most clinicians are not aware of this condition/ or/ its importance, or, they consider it as an integral part of leprosy. 'Another reason could be the traditional medical perception of leprosy as an infectious disease caused by a mycobacterium and that treatment in this context means just mycobactericidal chemotherapy. According to this perception factors relating to the onset of deformity are not per se a major concern of the clinician unless they like reactions and acute neuritis are also seriously bothering the patient. A third reason could be the consideration that studies of this condition present many operational and methodological problems.

Our own limited experience shows that the study should be properly planned, and that the personnel should not only be trained in the techniques of detailed assessment for nerve damage but should have obtained considerable experience in the use of these techniques under field conditions and achieved maximum reproducibility, for the data to become meaningful. We would also like to stress the necessity for standardizing the data in order to eliminate errors arising from deficiency in reproducibility.

The seven grade nerve function deficit scale that we have used in our studies for assessing the degree of nerve function deficit appears practicable and sensitive enough to track major (and so practically relevant) changes in nerve function deficit. The 0-3 WHO disability grading scale will not do for studying QNP as it is not sensitive enough.

Lastly, our experience shows that we need to study much larger populations of patients than done by us so far, in order to get some conclusive results.

In the present state of our knowledge we cannot make any recommendations regarding the kind of interventions that will be useful and so on the management of QNP. Only future studies can clarify this aspect of QNP.

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