Journal of Neurology, Neurosurgery, and Psychiatry 1989;**52**:1420–1423

Short report

Hypothyroidism and polyneuropathy

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SUMMARY The prevalence and characteristics of polyneuropathy were assessed using standard clinical and electrophysiological criteria in 39 consecutive outpatients with primary hypothyroidism, 15 of whom were previously untreated. Subjective complaints, mainly paraesthesiae, were recorded from 25 cases (64%) and objective findings supporting a clinical diagnosis of polyneuropathy were present in 13 (33%). Using standard electrophysiological criteria, a definite diagnosis of polyneuropathy was made in 28 cases (72%). The commonest sites of abnormal nerve conduction were the sensory nerves, especially the sural nerve. Polyneuropathy was generally mild. None of the clinical and biochemical indicators of hypothyroidism were significantly correlated with the electrophysiological signs of peripheral nerve impairment or the diagnosis of polyneuropathy.

Neurological complications in hypothyroid patients are a well established finding.[1] Diffuse peripheral neuropathy was thought to be common,[2–7] but as precise diagnostic criteria for polyneuropathy were generally lacking, the true prevalence of polyneuropathy in hypothyroidism has been imprecise.

The aims of the current study were: (1) to assess the degree of impairment of the principal electrophysiological parameters of nerve function in a representative sample of hypothyroid ambulatory patients; (2) to calculate the prevalence of polyneuropathy using standard electrophysiological criteria for diagnostic purposes; (3) to identify the clinical and/or biochemical indicators of hypothyroidism most commonly correlated with polyneuropathy.

Material and methods

Every subject with a diagnosis of primary hypothyroidism attending the outpatient service for endocrine disorders of the General Hospital of Monza during a 14-month period (1 November 1985 to 31 December 1986) was considered for inclusion in the study. A diagnosis of hypothyroidism was made when triiodothyronine (TT3) and/or thyroxine (TT4) were below the normal limits (0·7 ng/ml and 4 mcg/dl respectively), and thyrotropin (TSH) was above normal (4·5 mU/ml) in two independent assays. Patients were excluded if those criteria could not be completely satisfied, and when hypothyroidism was secondary to pituitary disease. Hormone replacement for thyroid insufficiency was not a criterion for exclusion. A history was taken and complete medical examination carried out for every patient. Information was collected on the date of the diagnosis, the presence of other disorders causing polyneuropathy, and current treatment, including hormone replacement. During the day of the interview a blood sample was taken for assays of the commonest parameters of thyroid function (TT3, TT4, their free fractions FT3 and FT4, TSH, and antithyroglobulin antibody levels), and a detailed neurological investigation (clinical and electrophysiological) was made.

Clinical investigation included a set of screening questions referring to the principal symptoms of polyneuropathy (that is, muscle cramps, restless legs syndrome, "burning feet", muscle pain, problems with object handling, impairment of standing and/or gait, and "glove and stocking" paraesthesiae) and a standard neurological examination.

A clinical diagnosis of polyneuropathy was made when there was evidence of bilateral impairment of strength and/or sensation and/or deep tendon reflexes in the upper and/or lower extremities with symmetrical (or nearly symmetrical) distribution.

The electrophysiological examination was done on the right limbs with constant monitoring of skin and room

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Received 20 January 1989 and in revised form 24 May 1989.
Accepted 27 June 1989

temperature: skin temperature was maintained between 32–34°C and room temperature about 22–24°C. Motor nerve conduction velocities were measured with standard surface stimulating and recording techniques in ulnar, median and peroneal nerves. Sensory nerve conduction velocities were measured orthodromically in ulnar and median nerves (5th and 2nd finger-wrist), and antidromically in sural nerve (lateral malleolus-sura). Motor and sensory action potential amplitude and distal latency were measured in the same nerves.

All electrophysiological parameters (conduction velocity (CV), distal motor latency and potential amplitude) were compared with standard values obtained in age-matched controls in the same laboratory (60 subjects aged 15 to 75 years). The normal limits of CV and distal latency were set at 2·5 SD from the mean values for these controls. The action potential was considered abnormal if the amplitude was below the lowest value found in the controls. An electrophysiological diagnosis of polyneuropathy was made when CV and/or distal latency and/or potential amplitude were abnormal in at least two separate nerves.

The mean values for each electrophysiological parameter in hypothyroid patients and controls were compared using Student's *t* test. Differences between subgroups of patients according to disease duration, aetiology, and replacement treatment were tested by one-way analysis of variance and chi-square test. Correlations between parameters of thyroid function and selected electrophysiological findings were calculated by linear regression analysis.

Results

A total of 44 patients met the diagnostic criteria for hypothyroidism. Five of them, however, presented other concurrent disorders or factors causing polyneuropathy: diabetes (1), uraemia (1), collagen disease (1), cancer chemotherapy (1), anticonvulsant (barbiturate) treatment (1). These patients were excluded from further analysis. The sample comprised 31 females and 8 males with a median age of 49 years. The commonest diagnosis was idiopathic hypothyroidism (17), followed by surgical (10) and radiation (9) hypothyroidism. Disease duration (expressed as the interval between diagnosis and inclusion in the study) ranged from less than one month to 35 years (median 2·2 years). Replacement therapy was being given to 24 cases at the time of the visit.

TT3 and TT4 bioassays were done in all cases, TSH in all but one, FT3 and FT4 in all but three. With reference to local standard limits, values were abnormal as follows: three cases (TT3), eight cases (TT4), 22 cases (TSH), 11 cases (FT3), 11 cases (FT4), and 15 cases (anti-thyroglobulin antibodies).

One or more symptoms leading to the diagnosis of polyneuropathy were present in 25 cases (64%), the commonest being paraesthesiae (20 cases), followed by muscle cramps (10), muscle pain (7), and problems with object handling (2). Neurological examination was abnormal in 13 cases (33%). In none of the cases was the defect asymmetrically distributed. Impairment of deep tendon reflexes was the commonest finding (11 cases), followed by muscle weakness (2), sensory impairment (1), muscle atrophy (1), hypotonia (1), and autonomic dysfunction (1).

A definite electrophysiological diagnosis of polyneuropathy was made in 28 cases (72%). Nineteen of these patients (68%) had symptoms suggestive of polyneuropathy and ten (36%) were positive on neurological examination. The electrophysiological parameters in hypothyroid patients and age-matched controls are compared in table 1. CV was abnormal in the sural nerve in 69% of the cases, and in the median sensory nerve in 13%, but rarely in the other nerves.

Table 1 *Hypothyroidism and polyneuropathy. Electrophysiological findings*

Variable	*Hypothyroid patients (mean, SEM)*	*Controls (mean, SEM)*	*p*	*No cases (%) with abnormal electrophysiological findings**
Conduction velocity (msec)				
Median motor	56·2, 0·7	58·3, 0·6	0·03	1 (2·6)
Median sensory	52·7, 1·3	56·9, 0·6	0·00	5 (12·8)
Ulnar motor	59·3. 0·8	59·7, 0·6	0·71	2 (5·1)
Ulnar sensory	55·4. 1·2	57·6, 0·7	0·11	2 (5·1)
Sural	47·4, 0·9	60·7, 0·6	0·00	27 (69·2)
Peroneal	50·0, 0·9	52·2, 0·4	0·03	1 (2·6)
Latency (msec)				
Median motor	3·7, 0·2	3·3, 0·0	0·03	5 (12·8)
Ulnar motor	2·5, 0·0	2·4, 0·0	0·24	— (—)
Peroneal	4·1, 0·1	4·0, 0·1	0·30	14 (35·9)
Amplitude				
Median motor	14·0, 1·0	14·4, 0·7	0·75	2 (5·1)
Median sensory	8·2, 0·7	11·4, 0·6	0·00	8 (20·5)
Ulnar motor	12·8, 0·8	12·0, 0·5	0·44	2 (5·1)
Ulnar sensory	7·1, 0·8	11·0, 0·6	0·00	10 (25·6)
Sural†	15·6, 2·1	20·3, 1·6	0·07	8 (20·5)
Peroneal	8·0. 1·0	8·8, 0·6	0·46	4 (10·3)

*See text for explanation
†Action potential was undetectable in 1 case which was excluded from the calculations.

Table 2 *Hypothyroidism and polyneuropathy. Disease characteristics and treatment in patients with and without polyneuropathy*

	*Polyneuropathy**		*No polyneuropathy**	
Variable	*No*	*(%)*	*No*	*(%)*
Aetiology of hypothyroidism†				
Surgical/radiation	13	68·4	6	31·6
Idiopathic	13	76·5	4	23·5
Congenital	2	66·7	1	33·3
Disease duration (years)†				
<1	11	73·3	4	26·7
1–5	9	69·2	4	30·8
6–10	4	80·0	1	20·0
>10	4	66·7	2	33·3
Replacement therapy†				
no	10	66·7	5	33·3
yes	18	75·0	6	25·0

*See text for explanation
†Disease characteristics and treatment were not significantly different in patients with and without polyneuropathy

Distal latency was most commonly impaired in the peroneal nerve (36%). Action motor and sensory potential amplitude was decreased in up to 26% of the cases (ulnar sensory nerve). In general, polyneuropathy was considered mild in 25 cases (16 of which had normal neurological findings) and moderate to severe in three.

Aetiology of hypothyroidism, disease duration and replacement therapy did not seem predictive of peripheral nerve impairment, with the exception of low sural CV among those receiving replacement therapy ($F = 4{\cdot}42$; $p = 0{\cdot}04$) and lower median and ulnar sensory action potential amplitude in subjects with surgical or idiopathic hypothyroidism ($F = 4{\cdot}72$; $p = 0{\cdot}01$). Likewise, no correlation was found between disease characteristics and treatment and diagnosis of hypothyroidism (table 2) and between sural CV (selected as the most sensitive indicator of peripheral neuropathy) and TSH ($R = -0{\cdot}11$; $p = 0{\cdot}48$), TT3 ($R = -0{\cdot}13$; $p = 0{\cdot}42$), TT4 ($R = -0{\cdot}18$; $p = 0{\cdot}29$), FT3 ($R = -0{\cdot}09$; $p = 0{\cdot}58$), or FT4 ($R = -0{\cdot}17$; $p = 0{\cdot}30$).

Discussion

Our data, drawn from a representative sample of outpatients with thyroid dysfunction, tend to confirm the assumption that polyneuropathy is relatively common in hypothyroidism. In fact, the estimated prevalence rate of polyneuropathy diagnosed electrophysiologically is 718 cases per 1,000 hypothyroid population. Yet almost two-thirds of our cases might have escaped notice had only a clinical examination been done. Thus in unselected hypothyroid patients polyneuropathy is often a mild disorder, and is occasionally only a subclinical entity. Subjective complaints, such as paraesthesiae and pain in the extremities, are commonly reported in hypothyroid patients[4 8–10] and were also frequent in this study. This observation leads to the assumption that symptoms of peripheral nerve impairment in hypothyroid patients are a fairly sensitive predictor of polyneuropathy. Hypothyroid polyneuropathy tends mainly to be sensory, as shown here and confirmed by other reports.[6 9 11 12] However, our findings cannot be considered conclusive as standard needle electromyography was not done. Abnormalities of conduction, latency and nerve potential amplitude in the median nerve may be evidence of a carpal tunnel syndrome and lead to the assumption that entrapment at the wrist is part of a more widespread involvement of the peripheral nervous system.[3 7] The small number of cases available probably prevented us from finding any significant correlation between polyneuropathy and long lasting hypothyroidism, specific disease patterns, or control of thyroid function by replacement therapy.

Financial support from FIDIA is gratefully acknowledged.

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