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Original Article

Varied clinical patterns, physical activities, muscle enzymes, electromyographic and histologic findings in patients with post-polio syndrome in Taiwan

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Study design: A study of the clinical features, physical activity, muscle enzyme, electromyography and histopathological alternations of muscles in patients with post-polio syndrome (PPS).
Objective: To assess the varied patterns of PPS in Taiwan.
Setting: Taiwan.
Methods: Thirty-one patients who fulfill the inclusion criteria of PPS were selected for study. Clinical features, physical activity scale, serum concentrations of creatine kinase, electromyography and histopathological alterations of muscles were assessed and correlated to the causes of PPS patients.
Results: Patients with PPS in Taiwan are relatively young, with a mean age of 39.3 years. Elevated concentration of creatine kinase was found predominantly in male patients with higher physical activities. Electromyographic examinations as well as histological tests of affected muscles revealed prominent evidence of chronic and active denervation with reinnervation in PPS patients.
Conclusion: Patients with PPS in Taiwan are young. Thus, PPS should not be attributed to aging. Physical attrition with degradation of nerve terminals is considered the main cause of this disease.
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Introduction

Large groups of former polio patients experience new neuromuscular complaints decades after acute paralytic poliomyelitis. The complex symptoms described consistently by these patients encompass new muscular weakness, muscular pain, fatigue, joint pain, and respiratory difficulties. This condition has been described as post-polio syndrome (PPS).[1–3] The term and the recognition of the clinical entity, however, remain elusive. Amidst this burgeoning interest, questions about PPS as a distinct clinical entity remain. There is no definite pathognomonic test. The symptoms are subjective and fairly general; and there is no truly distinctive symptom pattern. Although the cause of PPS is not entirely clear, many hypotheses of the pathological mechanisms have been proposed. Newly affected muscles in PPS patients which were evaluated longitudinally with electrophysiological and histopathological studies have been described and showed signs of chronic and new denervation.[4–6] Other possible causes include aging with motor neuron degeneration, physical attrition, amyotrophic lateral sclerosis (ALS) of atypical form, persistent infection of polio virus,[7,8] immunopathologic mechanism,[9,10] chronic fatigue syndrome related to endocrine and neurophysiological abnormalities,[11] and dysfunction of surviving motor neurons that causes slow disintegration of the terminals of individual nerve axons.

There were several outbreaks of poliomyelitis in Taiwan during past decades,[12] and PPS encountered

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by survivors of poliomyelitis with a bewildering array of new problems has increased substantially over these years. For the varied clinical patterns of polio in this district, we were interested in the difference between PPS occurring locally and PPS reported in western countries. Patients in Taiwan were infected either in early infancy or childhood in contrast to those overseas who were infected in adulthood or in middle age.[13,14] Most survivors of poliomyelitis in Taiwan had a spinal form with weakness in the lower extremities, whereas high cord involvement with paralysis in the upper and lower extremities or associated with respiratory symptoms were common in western countries.[15] Owing to heavy traffic in cities and suburban areas, polio patients frequently use a motor pedicab for outdoor activities. Factors affecting physical activities of polio patients in Taiwan are somewhat different from those in western countries.

Because PPS appears predominantly to be a clinical diagnosis, in the present study, we examine the physical activities, serum muscle enzymes, electromyography (EMG) and morphological alterations of muscles, in an attempt to find the distinctive features of this disease.

Subjects and methods

Profile of patients

Eighty-four patients with antecedent poliomyelitis and with suspected post-polio syndrome were consecutively admitted to rehabilitation clinics of a university teaching hospital during a 5 year period from 1994 to 1998. Sixty-three out of the 84 patients (75%) were from north Taiwan including Taipei City, Chi-Long City, as well as Taipei and Tau-Yun Counties. Twenty-one patients (25%) were from central and south Taiwan. Among these patients, 23 males and eight females were diagnosed with PPS and were enrolled in this study. Their ages ranged between 28 and 51 years (mean, 39.2 years). These patients were infected with poliomyelitis even before the age of two. Their duration of the disease ranged from 26 to 50 years (mean, 36.9 years). All patients underwent an attentive neuromuscular examination and an investigation of physical activity in their daily routine and work. The diagnosis of PPS was made according to four criteria and was essentially a diagnosis by exclusion. All subjects met the following inclusion criteria: (1) a confirmed history of paralytic poliomyelitis with a partial or fairly complete neurologic and functional recovery; (2) a period of neurologic and functional stability for at least 15 years; (3) a new muscular weakness after achieving a period of stability; and (4) no other medical diagnosis to explain these health problems. Patients were excluded if they had histories of rheumatoid arthritis, heart disease, diabetes mellitus, infectious neuritis, compression neuropathy and radiculopathy. No patient was given a prescribed exercise regimen during the study period. All patients gave consent to participate in this study.

Physical activity scale

A questionnaire survey designed for epidemiologic investigation of a physical activity scale was conducted on each PPS patient within 1 week from the patient's first visit. The same questionnaire was completed by 20 normal persons, whose ages ranged from 30 to 48 years (mean, 36.2 years). The dominant activities included walking, standing, driving, sports, housework and recreations. The scores measurement was made from the duration of the activities and the activity weights of the optimal items were derived. Multiplying the amount of time spent on each activity with the respective weights and summing overall activities computed total scores. Relaxing activities such as reading and watching TV were rated zero and excluded from the scores measurement. Patients with overall scores of less than 160 were categorized as the lower physical activity group, whereas those with scores greater than 240 were categorized as the higher physical activity group.

Concentrations of creatine kinase (CK)

Concentrations of CK were measured in blood samples according to the technique of Oliver and Rosaliki, as modified by Titz[16] (normal range, 38–160 IU/l). A blood sample was taken from each patient in the morning before the needle EMG and muscle biopsy examinations. No patient had strenuous exercise or exhausting activities on the same day prior to the sample taking. During the 2 week period before the CK test, no patient had a history of medication, myocardial infarction, intramuscular injection or other muscular trauma. Isoenzymes were also tested in the blood sampling. The MM form of concentration of CK over 97% was taken.

EMG test

Conventional EMG recordings were made with concentric needle electrodes (Medelec DMC 37, UK) to measure electrical activities from affected and weak muscles of patients with PPS. Twenty motor unit action potentials (MUAPs) were recorded and analyzed for mean duration, amplitude and fractional polyphasia in each tested muscle. Fibrillations, positive sharp waves and complex repetitive discharges were counted together and considered abnormal when found at more than one site of muscular test. The experimental data were compared with the normal values obtained from our EMG Laboratory. Mean duration of MUAPs of greater than normal mean values and 2 SD, mean amplitudes of MUAPs of greater than normal mean values and 2 SD, and fractional polyphasia of greater then 20% in each of the corresponding muscle were considered abnormal.

Tests of muscle histology
Specimens from weak and atrophic muscles of PPS patients were taken via a needle biopsy. Routine stains of hematoxylin and eosin, modified Gomori-trichrome, nicotinamide adenine dinucleotide tetrazolium reductase, periodic-acid-Schiff and adenosine triphosphatase (pH 9.4) were made for light microscopy. Ultrathin sections of muscular specimens stained with uranyl acetate and lead nitrate were made for electron microscopy.

Statistics
Comparison of statistical significance between the groups was performed with Mann–Whitney (Wilcoxon), chi-square and regression tests. The maximal level of significance was $P=0.05$.

Results

Clinical findings of PPS
Symptomatic weakening muscles were found consistently in muscles previously affected with poliomyelitis, and were commonly seen in one or both lower extremities in patients with PPS. Among the 31 patients, new muscular weakness, defined as a criterion of PPS in this study, occurred in all patients. Weakness of muscle might occur in one or more muscles in each patient. These weak muscles were distributed in 17 quadriceps muscles, 11 hip flexors, six calf muscles, five tibialis anterior muscles, four adductor femoris muscles, two hamstring muscles, two hip extensor and one hip abductor muscle. Twenty-one patients (68%) had generalized fatigue. Ten patients (32%) had joint pain mostly in the knee. Seven patients (23%) had muscular pain in the calf and shoulder. There was no patient with respiratory symptoms.

Physical activity scores
The results of the principal components of physical activities and the mean scores sorted by the duration of activities and the activity weights in the 31 PPS patients and normal controls are shown in Table 1. Apart from the time spent on resting, table work, light housework and activities of daily living took most of the time spent in a day. The overall value of physical activity scores of 191.4 ± 7.9 obtained from PPS patients was lower than 212.0 ± 8.7 from normal controls (t-test, $P<0.05$). The time spent on walking and standing activities amounted to 2.12 h per day in PPS patients. Sports activities and transportation took 1.6 h per day. The amount of time spent on recreational activities was only 0.53 h per day. Physical activity scores were found to decline with age ($r=0.67$, $P<0.01$) and were consistently higher for male than female PPS patients ($P<0.05$). Eight PPS patients with scores greater than 240 were categorized as the higher physical activity group.

Concentrations of CK
The concentrations of CK in PPS patients were between 86 and 482 (mean $\pm$ 1 SD $=158\pm37$) IU/l. The total concentration of CK in serum was elevated (greater than 160 IU/l) in nine (29%) of the 31 patients. Patients with elevated CK concentration were all working males, with eight of them having higher physical activities in daily living and working (physical activity scores greater than 240). There was no significant variation in age distribution.

EMG findings
The EMG results pertaining to spontaneous activities and voluntary MUAPs are summarized in Table 2. Quantitative analysis of parameters of MUAPs showed abnormal occurrence in most of the tested muscles.

Table 1 Physical activity scale and contribution scores for PPS patients and normal controls (mean $\pm$ SD)

Physical activity	*Duration* (h/day) *PPS* (n = 31)	*Controls* (n = 20)	*Activity weight*	*Scores* *PPS*	*Controls*
Walking	0.64 ± 0.12	0.85 ± 0.24	20	12.8 ± 1.8	17.0 ± 3.9
Job involving standing	0.75 ± 0.35	0.62 ± 0.37	15	11.3 ± 4.6	9.3 ± 5.2
Job involving walking	0.73 ± 0.22	0.65 ± 0.39	20	14.6 ± 4.1	13.0 ± 8.1
Table work and computer work	5.07 ± 1.17	4.38 ± 1.09	10	50.7 ± 11.3	43.8 ± 10.4
Driving (car, pedicab)	0.83 ± 0.36	0.75 ± 0.25	15	12.5 ± 5.7	11.3 ± 3.6
Light sports	0.36 ± 0.21	0.45 ± 0.30	20	7.2 ± 4.1	9.0 ± 5.4
Moderate sports	0.28 ± 0.13	0.56 ± 0.27	30	8.4 ± 3.7	16.8 ± 7.5
Strenuous sports	0.13 ± 0.09	0.22 ± 0.12	50	6.5 ± 4.3	11.0 ± 5.4
Light housework	1.21 ± 0.35	1.55 ± 0.48	20	24.2 ± 6.8	31.0 ± 9.2
Heavy housework	0.35 ± 0.14	0.48 ± 0.11	40	14.0 ± 5.4	19.3 ± 4.1
Recreations	0.53 ± 0.25	0.75 ± 0.43	15	7.9 ± 3.6	11.3 ± 5.8
ADL (eating, bathing, toileting etc.)	2.13 ± 0.37	1.92 ± 0.41	10	21.3 ± 3.3	19.2 ± 4.2
Resting* (reading, watching TV etc.)	3.48 ± 1.44	2.95 ± 1.53	0	0	0
Overall	16.49 ± 1.51	16.13 ± 1.67		191.4 ± 7.9	212.0 ± 8.7

PPS: post-polio syndrome, ADL: activity of daily living, TV: television *Not included in physical activity, weight zero

Table 2 Electromyographic findings in weak and atrophic muscles of PPS patients

	Number of muscles with positive EMG finding	*Number of tested muscles*	*(%)*
Spontaneous activities			
fibrillations	15	52	28.8
positive sharp waves	10	52	19.2
complex repetitive discharges	7	52	13.5
contraction fasciculation	14	52	26.9
MUAPs			
increased duration (>normal mean* + 2SD)	41	52	78.8†
increased amplitude (>normal mean* + 2SD)	43	52	82.7‡
polyphasia (>20%)	24	52	46.1

PPS: post-polio syndrome, MUAPs: motor unit action potentials, EMG: electromyography, SD: standard deviation. *Normal mean values obtained from EMG Lab., National Taiwan University Hospital. †$P<0.05$, ‡$P<0.05$, by Mann–Whitney test

MUAPs with mean duration increased more than normal, mean values and 2 SD were seen in 41 (78.8%) of the 52 muscles. MUAPs with mean amplitudes increased more than normal, mean value and 2 SD were seen in 43 (82.7%) of the 52 muscles. Both abnormal duration and amplitude of MUAPs were significantly increased in affected muscles of PPS patients (Mann-Whitney test, $P<0.05$). Fractional polyphasia of more than 20% of MUAPs were found in 46.1% of the affected muscles.

Muscle histology

Tests of muscle biopsy in weak and atrophic muscles of PPS patients demonstrated the presence of chronic and acute denervation and reinnervation. Large groupings (more than 20 fibers) containing type I or type II muscle fibers were seen in nine subjects (29%). Varied muscular fiber size was found. Increased numbers of nuclei in non-atrophic fibers and 'moth-eaten' or targetoid fibers were occasionally found in fibers of normal or almost normal size. Muscle specimens taken from 12 subjects (39%) showed isolated, atrophic, angulated fibers compressed in interstices between large fibers. These small fibers that stained darkly with an enzymatic reaction were characteristic of new active denervation.[18]

Group atrophy of muscle fibers was not found, whereas internal nuclei and splitting of fibers were frequently seen in affected muscles in PPS patients. In eight (26%) of the 31 tested muscles, increased lymphocytic infiltration in perivascular and perimysial areas was observed. Fiber necrosis and phagocytosis were also found. These findings represented an inflammatory response and a continuing disease activity. Histology from an affected muscle in a PPS patient showed findings of inclusion-body myositis (IBM) consisting of infiltration of perimysial and perivascular mononuclear cells, vacuoles rimmed by basophilic materials and nuclear filamentous inclusions in muscle fibers.

Discussion

Although PPS has been recognized as a late effect of antecedent poliomyelitis, its pathomechanism is still controversial. Vivid discussion over the last two decades on the possible causes of PPS symptoms has led to widespread interest throughout the world. In the present study of PPS patients in Taiwan, we discovered that these patients are relatively young (age of less than 51 years). This finding is not compatible with the most commonly suggested notion that PPS is a result of the normal aging process. Normal aging alone cannot be responsible for this process, because neuronal loss in the spinal cord does not occur in persons aged less than 60 years.[17] In contrast, in western countries, where many PPS patients were aged more than 60 years, the pathogenesis of an aging process with neuron loss seems to be less well explained.

The symptomatic weakening in muscles of PPS patients are commonly seen in quadriceps muscles in the present study. This is because the quadriceps muscle is the main muscle frequently used in weight bearing and for keeping an upright posture and stability. It gets stressed easily in most physical activities. Muscular weakness did not appear first in the weakest muscle in polio patients with the most severe residual paralysis. On the contrary, the severely weak and atrophic muscles not frequently used in physical activities were always spared in new symptoms of PPS patients. Thirty-two per cent of the PPS patients complained of joint pain, mostly in the knee. This may be related to overstress which occurred frequently in this joint. Sixty-eight per cent of the PPS patients suffered from fatigue in the present study. This result is compatible with the findings in North America, and Scandinavia.[18–21] Serum concentrations of CK are elevated in 29% of PPS patients. This finding reveals that muscular damage does not occur consistently in all PPS patients. In the present study of muscle enzymes, nine patients had elevated concentrations of CK and an astonishing finding is that eight of these patients are male and have higher physical activities. This demonstrates a close correlation between physical activity and muscular damage, and indicates that physical attrition may play a significant role in causing PPS.

In the present histological tests of PPS patients, no clusters of atrophic fibers (group atrophy) were found, but a few single scattered angulated and dark fibers stained with enzymatic reaction were observed. These findings are compatible with a new active denervation and degeneration of individual nerve terminals in motor units of PPS patients. Physical attrition may

possibly cause integrated dysfunction of individual nerve terminals rather than anterior horn cells, because cell bodies are overloaded and unable to maintain metabolic demands of their pathologically increased number of sprouts.[9,22] The clinical features of PPS resemble neither classic motor neuron disease nor ALS in rapid progression, bulbar weakness, and signs of corticospinal tract dysfunction are conspicuously absent. Histological tests also failed to support neuron death with the fading of whole motor units as seen in ALS.

The present study of a PPS patient accompanied with IBM is possible evidence of pathogenesis associated with viral infection and myopathy. Inflammatory myopathy of this chronic form is characterized histopathologically by nuclear and cytoplasmic filamentous inclusions and vacuoles rimmed by basophilic materials in muscle fibers.[23] Mendell and colleagues[24] have demonstrated a prominent evidence of amyloid deposits in microfilaments of IBM. Intracellular deposition of amyloid might alter muscle proteins that accumulate within cytoplasm. Both PPS and IBM are possible results of amyloid myopathy associated with viral infection.

The EMG findings in this work showed increased duration and amplitude of MUAPs that reflect profuse reinnervation by sprouts from regenerating neurons in muscle previously affected by poliomyelitis. These findings are compatible with those of Stalberg, Grimby[6] and Rodriques[25] on single-fiber EMG with increasing fiber densities and on macro-EMG with increasing MUAP size. Spontaneous activities such as fibrillation and positive sharp waves were observed in 20% to 30% of the tested muscles in this study. This phenomenon may be related to new denervation of nerve terminals; it has been known anecdotally for years that spontaneous activities persisted for decades after the paralytic episode. From the electrophysiologic point of view, it is not easy to differentiate between these two events by the amount and frequency of occurrence of spontaneous activities. Fasciculation potentials occurred during voluntary contraction of muscles as contraction fasciculation were seen in 26.9% of the PPS patients. This remains speculative. Its prevalence was unclear in differentiation from true fasciculation by its pattern of firing.

In conclusion, certain histological variations in muscle biopsies of PPS patients appear to be specific for recent denervation and may assist in clinical diagnosis. PPS patients are young in Taiwan, and thus PPS should not be regarded as a result of an aging process. Physical attrition with degradation of nerve terminals is probably the main cause of this disease.

References

1 Munsat TL. Poliomyelitis – new problems with an old disease. *N Engl J Med* 1991; **324:** 1206 – 1207.
2 Dalakas MC. The post-polio syndrome as an evolved clinical entity: definition and clinical description. *Ann NY Acad Sci* 1995; **753:** 68 – 80.
3 Halstead LS, Silver JK. Nonparalytic polio and postpolio syndrome. *Am J Phys Med Rehabil* 2000; **79:** 13 – 18.
4 Rodriques AA, Agre JC, Franke TM. Electromyographic and neuromuscular variables in unstable postpolio subjects and control subjects. *Arch Phys Med Rehabil* 1997; **78:** 986 – 991.
5 Lange DJ. Post-polio muscular atrophy, an electrophysiological study of motor unit architecture. *Ann NY Acad Sci* 1995; **753:** 151 – 157.
6 Stalberg E, Grimby G. Dynamic electromyography and muscle biopsy changes in a 4-year follow-up study of patients with a history of polio. *Muscle Nerve* 1995; **18:** 699 – 707.
7 Julien J *et al*. Postpolio syndrome: poliovirus persistence is involved in the pathogenesis. *J Neurol* 1999; **246:** 472 – 476.
8 Stone R. Post-polio syndrome: remembrance of viruses past. *Science* 1994; **264:** 909.
9 Dalakas MC. Pathogenetic mechanisms of post-polio syndrome: morphological, electrophysiological, viological, and immunological correlations. *Ann NY Acad Sci* 1995; **753:** 167 – 185.
10 Rao U *et al*. Prevalence of low plasma IGF-I in poliomyelitis survivors. *J AM Geriatr Soc* 1993; **41:** 697 – 702.
11 Bruno RL, Sapolsky R, Zimmerman JR, Frick NM. Pathophysiology of a central cause of post-polio fatigue. *Ann NY Acad Sci* 1995; **753:** 257 – 275.
12 Kim-Farley RJ *et al*. Outbreak of paralytic poliomyelitis, Taiwan. *Lancet* 1984; **2:** 1322 – 1324.
13 Agre JC, Rodriquez AA, Sperling KB. Symptoms and clinical impressions of patients seen in a post-polio clinic. *Arch Phys Med Rehabil* 1989; **70:** 367 – 370.
14 Ramlow J *et al*. Epidemiology of the post-polio syndrome. *Am J Epidemiol* 1992; **136:** 769 – 786.
15 Bach JR. Evaluation and management of post-polio respiration sequelae: non-invasive options. In: Halstead LS, Grimby G (eds). *Post-polio syndrome*. Hanley & Belfus: Philadephia, 1995, pp. 89 – 111.
16 Titz NW. *Textbook of Clinical Chemistry*. 1st edn. Saunders: Philadephia, 1986.
17 Tomlison BE, Irving D. The numbers of limb motor neurons in the human lumbosacral cord throughout life. *J Neurol Sci* 1977; **34:** 213 – 219.
18 Agre JC *et al*. A comparison of symptoms between Swedish and American post-polio individuals and assessment of lower limb strength – a four-year cohort study. *Scand J Rehabil Med* 1995; **27:** 183 – 192.
19 Stanghelle JK, Festvag LV. Postpolio syndrome: a 5 years follow-up. *Spinal Cord* 1997; **35:** 503 – 508.
20 Wekre LL, Stanghelle JK, Lobben B, Oyhaugen S. The Norwegian polio study 1994: a nation-wide survey of problems in long-standing poliomyelitis. *Spinal Cord* 1998; **36:** 280 – 284.
21 Lonnberg F. Late onset polio sequelae in Denmark. Presentation and results of a national-wide survey of 3607 polio survivors. *Scand J Rehabil Med* 1993; **28**(Suppl.): 7 – 15.
22 Gandevia SC, Allen GM, Middleton J. Post-polio syndrome: assessments, pathophysiology and progression. *Disabil Rehabil* 2000; **22:** 38 – 42.

23 Semino-Mora C, Dalakas MC. Rimmed vacuoles with beta-amyloid and ubiquitinated filamentous deposits in the muscles of patients with long-standing denervation (postpoliomyelitis muscular atrophy): similarities with inclusion body myositis. *Hum Pathol* 1998; **29:** 1128–1133.
24 Mendell JR, Sahenk Z, Gales T, Paul L. Amyloid filaments in inclusion body myositis, novel findings provide insight into nature of filaments. *Arch Neurol* 1991; **48:** 1229–1234.
25 Rodriquez AA *et al*. Electromyographic and neuromuscular variables in post-polio subjects. *Arch Phys Med Rehabil* 1995; **76:** 989–993.