での筋硬度の変化については、施術前が平均18.8±6.3(SD)、施術後が18.1±3.0で有意差はなかった(対応のあるt検定、p=0.488)(図1)。

4. 施術後のアンケート

今回の鍼、あんま・マッサージ施術体験者の全員が施術を受けて良かったと回答し、今後のスモン検診時も継続的な施術を希望していた。

考　察

スモン検診での鍼治療、あんま・マッサージ施術は、平成18年度に茨城県において初の試みを行い、患者の反応は非常に好評であり、本年度の実施の要望も強かった。今回のアンケートの結果も好評であり、肩こり、下肢が軽くなるなど症状の緩和にある程度貢献でき、検診に従事する医療スタッフと患者の交流という面で非常に有用と考えられた。さらに新規の検診受診者が1名増え、患者サービスが実を結んだ結果といえる。

今回は、鍼治療、あんま・マッサージ施術の前後で簡易型の筋硬度計を使用して筋のこりや張りを評価する客観的指標とした。筋硬度計の精度や臨床評価の意義に関しては、今回の検討では十分な予備的評価をしていないが、これまで同様の機器を用いた報告[4, 5]や機器メーカーの資料等を参考にした。筋硬度計の軟部組織の硬度に対する測定値は絶対値ではなく相対的なものであり、被験者により測定条件で異なり統計的な評価は困難と思われる。また、今回の測定できた患者数は非常に少数であり、結果としても前後での明らかな有効性は証明できなかった。しかし、患者の自覚症状の改善やアンケートにて良好な結果を得たことより、スモン検診時の鍼治療、あんま・マッサージ施術は患者にとって有効な方法と考えられる。

結　論

今回のスモン検診時に実施した鍼治療、あんま・マッサージ施術の第一の目的は、患者サービスと患者・医療者間の交流であり、アンケート結果からも今回の目的の一部は果たせたと考えられる。また、このような検診時に付加価値をつけた患者サービスは、スモン検診参加へのモチベーションの維持のために有効であり、今後も継続の方向で考えている。

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スモン患者において全額公費負担制度は十分には機能していない

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要　旨

スモン患者においては全額公費負担制度が十分には機能していないことが、アンケート調査を通じて判明した。医療従事者に今後も粘り強く啓発活動を行ってゆく必要がある。

目　的

スモン恒久対策の観点からスモン患者の治療費については全額公費負担が適用されている。しかしスモン患者・家族からは実地臨床の場においては必ずしもこのことが周知徹底されていない、と聞くことがある。そこで今回特定疾患研究事業がスモン患者に適正に行われているか否かを検討するために、兵庫県下のスモン患者にアンケート調査を実施した。

対象と方法

兵庫県下に在住のスモン患者80名にアンケート調査用紙を郵送し、無記名で回答を回収した。

質問項目を**表1**に記す。

結　果

46名(57.5%)から回答を得た。

これまでスモン患者ということで診療を拒否されたり、いやな思いをしたことはあるか、との質問には「ある」と答えた患者が16名(35%)で、「ない」と答えた患者は30名(65%)であった(**表2**)。

「ある」と答えた患者にその時期を質問したところ、発症後間もないころから2006年まで、とかなりのばらつきがあった(**表3**)。さらにそのことに関しどう思ったか、どう行動したか、と質問したところ**表4**に示すような回答を得た。その中には、医師とけんか状態になったという患者がいる一方で、わかってもらえないなら仕方がないと思った、説明しても無駄、個人では対応できない、どうしようもない、といった諦めの気持ちの患者が多かった。さらに気分が悪くなった、悲しくつらかった・子供に申し訳ないと思った(出産時)、今も傷ついている、と精神的に苦痛を訴えた患者もいた。また一般患者として診てほしい、との希望を述べる患者や医師のスモンに対しての理解度に差が

表1　質問項目

① これまでスモン患者ということで診療を拒否されたり、いやな思いをしたことはあるか。

② ①で「ある」と答えた患者に
　いつのことか
　そのことに関しどう思ったか、どう行動したか

③ スモン以外の病気について、診療費を請求されたことがあるか。

④ ③で「ある」と答えた患者に
　その病気は何か
　いつのことか
　そのことに関しどう思ったか、どう行動したか

表2

これまでスモン患者ということで診療を拒否されたり、いやな思いをしたことはあるか。	
ある	ない
16名　(35%)	30名　(65%)

表3　時期

発症後間もないころ	1978年
数十年前	1980年
だいぶ前	2001年
数年前	2004年
1965年ころ	2005年
1971年	2006年
1972年	

表4　どう思い、どう行動したか

一般患者として診てほしい
気分が悪くなった
悲しくつらかった。子供に申し訳ないと思った（出産時）
仕方がないと思った
医師のスモンに対しての理解度に差があると思った
わかってもらえないなら仕方がないと思った
説明しても無駄
医師とけんか状態になった
今も傷ついている
個人では対応できない
どうしようもない
スモンが忘れられる時代かなあと思った
スモンを医師が理解してない
諦めて転医した

表5

スモン以外の病気について、診療費を請求されたことがあるか。	
ある	ない
19名　（44%）	24名　（56%）

有効回答数：43名

表6　その病気は何か

風邪	甲状腺機能低下症	骨粗鬆症
糖尿病	高脂血症	湿疹
頸椎症	腰椎症	白内障
緑内障	肛門ポリープ	C型肝炎
狭心症	完全房室ブロック	

あると思った、スモンを医師が理解してほしい、スモンが忘れられる時代かなあと思った、などスモンの風化を危惧する意見も聞かれた（表4）。

次にスモン以外の病気について診療費を請求されたことの有無を質問したところ、有効回答数43名中、「ある」と回答した患者は19名（44%）いた（表5）。そこで「ある」と回答した患者にどういう病気のときに請求されたかを質問したところ風邪に始まり種々の疾患にわたることがわかった（表6）。さらにその時期について聞いたところ、1990年ころ、2001年、2004年、2005年、2007年と比較的最近のことであった（表7）。

表7　時期

1990年ころ
2001年
2004年
2005年
2007年

表8　どう思い、どう行動したか

根気よく説得したが平行線だった
スモン手帳を見せたら理解してくれた
スモンの申請は難しい・面倒、といわれた
お金を払わないことに引け目を感じる
医師によっての違いを感じた
事務職員は医師に言ってくれたが、医師が認めなかった
わかってもらえなかった
諦めた
県の健康局疾病課の理解が乏しく感じる
肩身が狭い感じがした
スモン患者の取り扱いを医療機関はよくわかっていないと感じた
スモンをよく知らない医師がとても多い

またそのことについてどう思い、どう行動したか、との問いにはスモン手帳を見せたら理解してくれた、との回答があった。しかしこの回答意見は少数で、表8に示すように悲観的な回答が多かった。

考　察

スモン恒久対策の観点からスモン患者の治療費については全額公費負担が適応されている。しかし必ずしもこのことは周知徹底されておらず、混乱を生じているとの不満をスモン患者から聞くことがある。そこで今回兵庫県下在住のスモン患者にアンケート調査を実施した。

スモン患者ということで診療を拒否されたり、いやな思いをしたことがある患者が16名（35%）いた。その時期は発症後間もないころから2006年まで、とかなりのばらつきがあった。発症後間もないころは病因についてさまざまな学説があり、受診時の対応に不愉快なことがあったことは想像できるが、最近においてもそのようなことがあったことは驚きである。

医師とけんか状態になったという患者がいる一方で、わかってもらえないなら仕方がないなどといった

諦めの気持ちの患者、精神的に苦痛を訴えた患者がいることに医療従事者は留意すべきである。

医師のスモンに対しての理解度に差があると思った、スモンを医師が理解してほしい、スモンが忘れられる時代かなあと思ったなどスモンの風化を危惧する意見も聞かれた。スモンの風化に関しては以前本班会議でも報告したことがあるが[1]、本研究班を中心に医療者に対して今後も引き続き粘り強く啓発活動を行ってゆかなければならない。

スモン以外の病気について、診療費を請求されたことがあるかとの質問には、「ある」と回答した患者が19名(44%)いた。その疾患群は多岐にわたっていることがわかった。その時期は1990年ころ～2007年と比較的最近のことであった。そのときスモン手帳を見せたら理解してくれた、との回答があった。しかしこの回答意見は少数で、根気よく説得したが平行線だった、諦めた、肩身が狭い感じがした、など悲観的な回答が多かった。

平成18年2月2日付で厚生労働省健康局疾病対策課から全国健康関係主管課長会議資料が提出された。その中でスモン患者には特定疾患研究事業として補助率10/10による全額公費負担が適用されていることの確認が明記されている。しかし臨床の現場では十分に認識されていないことが今回の調査で明白になった。今後本研究班を中心にしてさらなる啓発の必要性を痛感する。

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研究成果の刊行に関する一覧表

平成19年度研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
A Matsumoto, Y Tajima, H Sasaki	Electrophysiological studies in peripheral nerve function with subacute myelo-optico-neuropathy	JPNS	12 (S)	56-57	2007
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M Nagayoshi, N Iwata, K Hachisuka	Factors associated with life satisfaction in Japanese stroke outpatients	Disabil Rehabil	30 (3)	222-230	2008

研究成果の刊行物・別刷

neuropathy, papilloedema, increased platelet count and CSF proteins, and decreased thyroid function. Spine MRI revealed C2 vertebral body osteosclerotic myeloma. VEGF levels, very high at onset, dramatically decreased after auto-PBSCT, but returned high in the relapse phase. She has been treated with local radiotherapy and follow up is ongoing. To date this is the first case of relapse of POEMS syndrome after successful autologous auto-PBSCT.

A BRAZILIAN FAMILY WITH CMT2/dHMN AND ANTICIPATION

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Charcot-Marie-Tooth type 2 (CMT2) is an axonal, autosomal dominant, motor and sensory neuropathy that results from mutations in more than 10 different genes. Mutations in at least 2 of them result in both CMT2 or distal hereditary motor neuronopathy (dHMN) that occasionally coexist in the same family. Age at onset varies from 1 to 63 years and the possible existence of anticipation has been found in some families, but never confirmed. We describe a Brazilian family with CMT2/dHMN and strong evidence of anticipation. We examined 14 affected and 3 at-risk members. EMG was carried out in 10 members. We defined age at onset as the time when the patient first noted any impairment related to the neuropathy. This is a 5 generation family with at least 26 affected persons (13 females, 13 males). In the first generation (GI) there were no affected persons, while in the second generation (GII) there were 3 affected and 10 non-affected members; in GIII 10 and 20, respectively, in GIV 8 and 16, and in GV there is only one affected member. Mean age at onset from GII to GV were 50 years, 41 years, 14 years and 4 years, respectively; while age variation in parent-child pairs was 23 years from GII to GIII, 19 years from GIII to GIV, and 10 years from GIV to GV. Disease severity also increased with the generations. The oldest patient (81 years old) is still well and independent, while the younger patient (7 years) is unable to walk independently and has very weak hands. All affected members have distal motor weakness, predominantly affecting the legs. Mild proximal weakness is present in some patients. Sensation was clinically normal in 5 patients, and their sensory nerve action potentials (SNAP) were also normal. Five other patients had a mildly decreased SNAP amplitudes. The remaining patients clearly had typical CMT2. We describe a family whose clinical phenotypes ranged from CMT2 to dHMN, in which the phenomenon of anticipation is an important characteristic. *Funded by CNPq, FAPESP and FAEPA.*

NEUROFASCIN: A TARGET FOR ANTIBODY MEDIATED AXONAL INJURY IN PERIPHERAL NEUROPATHIES

Mathey EK[1], Williams KR[2], Rasband MN[3], Willison HJ[4], Armati PJ[1], Pollard JD[1], Linington C[2]. [1]University of Sydney, Sydney, Australia; [2]University of Aberdeen, Aberdeen, Scotland UK; [3]University of Connecticut, Farmington, CT, USA; [4]University of Glasgow, Glasgow, Scotland UK.

Irreversible axonal loss is recognized as the major pathological correlate to chronic disability in inflammatory demyelinating diseases of both the central and peripheral nervous systems. The degree of axonal loss in a number of inflammatory peripheral neuropathies has a significant impact on the speed of recovery from a relapse, lasting clinical deficits and overall prognosis. Although axonal injury is a major factor contributing to the development of chronic disability in peripheral demyelinating neuropathies (PDNs), the mechanisms involved remain obscure. We recently identified the axonal/axoglial proteins neurofascin (NF155/NF186) as potential autoantibody targets in clinically definite multiple sclerosis and now postulate that these antibodies could also be relevant to PDNs. NF155/186 are alternatively spliced products of the neurofascin gene and are localised within the polarized domains of the myelinated axon that centre around the node of Ranvier in both the central and peripheral nervous systems. The frequency/titre of autoantibody responses to neurofascin in subgroups of patients with demyelinating and axonal neuropathies was determined by ELISA and the pathophysiological relevance assessed in vivo in rats with experimental autoimmune neuritis (EAN). Disease was initiated using a low dose of neuritogenic T cells followed by the adoptive transfer (i.p.) of 0.5 mg of either a pan NF specific or control IgG2a monoclonal antibody (mAb) at disease onset. The NF-specific mAb exacerbated disease severity and was associated with deposition of the transferred antibody at the nodes of Ranvier. Confocal microscopy demonstrated that the anti-NF mAb co-localises with voltage gated sodium channels at the nodes of Ranvier, but not with NF-155 at the paranodes. These results identify neurofascin as a target for autoantibody-mediated axonal injury in peripheral demyelinating disease, a mechanism that might play a critical role in the development of axonal injury.

ELECTROPHYSIOLOGICAL STUDIES IN PERIPHERAL NERVE FUNCTION WITH SUBACUTE MYELO-OPTICO-NEUROPATHY

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Subacute myelo-optico-neuropathy (SMON) is the neurological intoxication of Clioquinol, and SMON has affected about 10,000 patients in Japan. Since Clioquinol formulations were released in 1970, we have treated the patients with SMON. Their peripheral neuropathy has been regarded as the major symptom of SMON. However, in the electrophysiological examination for recent cases of SMON, we rarely find peripheral neuropathy. We studied the neural conduction dysfunction at the lumber root level in 37 patients with SMON (47–74 years old). For this purpose, we applied transcutaneous magnetic stimulation to L5 nerve roots and elicited the motor evoked potentials (MEPs) from M.Ext.Hall., and calculated the conduction time of lumber root from the difference between the latencies of MEPs elicited from M.Ext.Hall. and the peripheral nerve conduction

time calculated using F-wave and M-wave latencies. In normal controls, the lumber root conduction times were 6.1 ± 2.5 msec and in SMON patients, the conduction times were 11.3 ± 3.9 msec. The conduction times at the lumber root level in SMON were significantly delayed compared to the normal values. The magnetic coil stimulates the lumbar nerve root at the exit of intervertebral foramen, so the latency difference between the peripheral nerve conduction time and the latency of MEP by magnetic stimulation reflects the conduction time from the lumber nerve root in intervertebral foramen to spinal motor neurons. We concluded that the conduction dysfunction at the proximal side of lumber root was the responsible focus of the peripheral neuropathy in SMON 35 years after onset. Furthermore, in our studies, 5 patients had the recovery of conduction velocities on the distal side of peripheral nerve compared to the results carried out during years from 1970 to 1975. These facts suggest that the conduction function on the distal side of peripheral nerve recovered with dysfunction remaining on the proximal side of nerve roots. However, the results involve only 5 patients, therefore it is necessary to search for similar cases.

PERINEURIOMA: A FOCAL, MOTOR PREDOMINANT, BENIGN NERVE TUMOR OF THE YOUNG

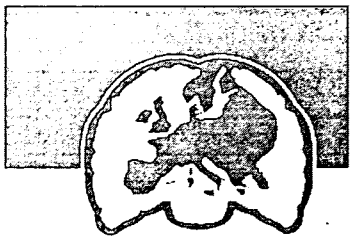
Mauermann ML[1], Dyck PJ[1], Kuntz NL[1], Amrami KK[1], Spinner RJ[1], Bosch EP[2], Engelstad JK[1], Dyck PJB[1]. [1]Mayo Clinic, Rochester, MN; [2]Mayo Clinic, Scottsdale, AZ, USA.

The objective of this study was to review the clinical, laboratory, electrophysiological and radiological characteristics of perineurioma. Perineurioma is a benign tumor due to focal proliferation of perineurial cells. The natural history and clinical features have not been systematically studied. Mayo Clinic clinical and pathological databases were searched from 1985–2006. Identified biopsied specimens were reviewed. Cases in which the outer leaflets of pseudo-onion bulbs were reactive for epithelial membrane antigen and non-reactive for S100 protein were included. Twenty-eight of 424 identified cases were pathologically confirmed as perineurioma. Median age at time of evaluation was 19 years (range 2–56 years). There were 15 adults and 13 children; 15 women and 13 men. Median time from symptom onset to evaluation was 24 months (range 0.5–normal (7 of 7) MRI demonstrated fusiform nerve enlargement with T2 hyperintensity in 26 of 28 patients. Targeted biopsy, usually at the site of MRI abnormality, was diagnostic in all cases. Conclusions: 1) Perineurioma is a benign peripheral nerve tumor that presents with focal nerve enlargement and causes problematic morbidity. 2) It usually presents in young people as an insidious, slowly progressive, motor predominant neuropathy. 3) Although always focal, one-quarter of cases involve more than one nerve and are radiculoplexus neuropathies. 4) While motor predominant, mild sensory symptoms and findings are common. 5) Targeted fascicular nerve biopsy, at the site of MRI abnormality, is needed for diagnosis. 6) Because intensive evaluation is needed for diagnosis, perineurioma is probably under-recognized.

POSTGANGLIONIC SUDOMOTOR, ADRENERGIC AND CARDIOVAGAL ABNORMALITIES ARE COMMON IN HEREDITARY SENSORY AND AUTONOMIC NEUROPATHY TYPE I AND DO NOT PREDICT MUTILATING INJURY

Mauermann ML, Dyck PJ, Low PA, Klein CJ. Mayo Clinic, Rochester, MN, USA.

Our objective was to study autonomic dysfunction in hereditary sensory and autonomic neuropathy type I (HSANI) kindreds without RAB7 and with and without SPTLC1 mutation. Mutilating injuries of the feet and hands commonly occur in HSANI. The extent of these injuries likely relates to the severity of sensory loss, but undoubtedly also relates to other variables. Here we focus on the putative role of sudomotor and other autonomic dysfunction in HSANI. Two genes (SPTLC1 and RAB7) have been identified as causative among some families but genetic heterogeneity is noted. We reviewed the charts of 25 HSANI kindreds previously studied (Klein et al., 2005). Probands had undergone extensive testing for neuropathy as well as genetic evaluation for mutations of SPTLC1 and RAB7. Detailed autonomic testing including postganglionic sudomotor, adrenergic and cardiovagal parameters were available in 19 and 11 had thermoregulatory sweat tests (TST). Six had mutilating acropathy with foot fractures, ulcers and amputations. Eighteen of 19 studied had abnormalities of autonomic testing. TST in 10 of 11 studies had distal anhidrosis (1%–9%); global anhidrosis (100%) in one. QSART identified in 6 of 7 post ganglionic sudomotor abnormalities more extensive than predicted by



20th ECNP Congress
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Estimation of prevalence of major depression in patients with subacute myelo-optico-neuropathy

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Introduction: Subacute myelo-optico-neuropathy (SMON) is a disease characterized by subacute onset of sensory and motor disturbance in the lower half body combined with visual impairment caused by clioquinol intoxication. In Japan, owing to the governmental banning of the use of clioquinol in 1970, the new patients diagnosed as having SMON have almost disappeared. Afterward, the number of SMON patients has gradually decreased. Now, about 3,000 patients with SMON are alive in Japan suffering from physical and mental sequela of clioquinol intoxication. Since there was no clinical study related to the psychological problems of SMON patients, we estimated the prevalence of major depression in patients with SMON through the structured interview by the psychiatrists, simultaneously applying Beck's depression inventory (BDI) questionnaires.
Materials and Methods: Psychiatric conditions were evaluated in 26 patients (9 males, 17 females, mean age 70.7 years) with SMON living in Kyoto prefecture through the structured interview by the psychiatrists using the BDI questionnaires. The BDI questionnaires were applied on 106 patients (mean age 73.5 years) with SMON and 92 age-matched healthy persons (mean age 75.8 years). Clinical symptoms of SMON were evaluated using medical checkup records established by the SMON Research Committee. Mental status were evaluated applying the Mini Mental State Examination (MMSE).
Results: The mean scores of BDI questionnaires obtained from SMON patients were significantly high compared with the healthy persons of the same age. The numbers of SMON patients who's total BDI scores exceeded 25 points were sixteen (15%) out of 106. On the other hand, 2 (2%) out of 92 healthy persons exceeded 25 points of total BDI scores. In male SMON patients, the total BDI scores significantly correlated with age and reversely correlated with the MMSE scores. In contrast to that, the BDI scores of the female patients did not correlate with age nor MMSE scores, but significantly correlated with the degree of dysesthesia of lower extremities, duration of SMON disease and reversibly correlated with the total scores of the Barthel index.
Discussions: The structured interview by psychiatrists using BDI questionnaires on SMON patients living in Kyoto showed that the patients with more than 25 points of BDI questionnaires were suffering from major depression. There were no patients with major depression with less than 25 points. Therefore, we used the cut-off point of 25/24 of BDI questionnaires as the discrimination of the presence or absence of major depression. Applying this tentative criterion, the prevalence of major depression is more than seven times of prevalence compared to the aged people. The causative

factors of major depression may relate to the long suffering periods of SMON sequela including dysesthesia sensation and disabilities of daily life.
Conclusion: The prevalence of major depression of SMON patients was estimated about 15% of patients, which percentage was seven times as many as the prevalence of major depression of the people of the same age. The mental cares with maintenance of daily activity should be considered for the SMON patients.

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ORIGINAL ARTICLES: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Investigation of visual disorders of subacute myelo-optico-neuropathy (SMON) patients 32 years after onset: Questionnaire-based survey and ophthalmological examination

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An investigation of subacute myelo-optico-neuropathy (SMON) patients (20 male and 132 female, aged 31–93 years) was conducted in December 1998 using a self-administered questionnaire. Following this survey, ophthalmological examinations were performed on 33 patients between 1998 and 2000. The questionnaire-based survey revealed that the prevalence of patients with cataracts was 52.0%, and those with glaucoma was 9.4%. By dividing the patients into two groups, according to the levels of visual disturbances at the time of onset of SMON, we found that the prevalence of glaucoma was higher in the group with visual disturbances than in the group with normal vision. However, the prevalence of cataracts, optico-neuritis and fundus hemorrhage was not considerably different between the two groups. Ophthalmological examinations (e.g. intraocular pressure test, visual field test, slit lamp microscopy test, funduscopic examination) revealed that 63.6% of patients had cataracts, and 12.1% had glaucoma (9.1% for normal tension glaucoma). The ophthalmological examination revealed that the prevalence of normal tension glaucoma in the SMON patients tended to be higher than in other surveys in the general population of Japan. SMON patients need follow-up ophthalmological examinations, especially for glaucoma, on a nationwide scale.

Keywords: clioquinol, glaucoma, subacute myelo-optico-neuropathy (SMON).

Introduction

Subacute myelo-optico-neuropathy (SMON) due to 5-chloro-7-iodo-8-hydroxy-quinoline (clioquinol, chinoform) broke out in Japan around 1960–1970. Clioquinol was a frequently used amoebicidal and antibacterial drug in Japan. Cases of SMON started with subacute onset of sensory and motor disorders in the lower half of the body and visual disturbances. The total

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number of patients reached over 9000 according to a national survey in 1970. As for prognosis, relapse was rare, and the disease came to a standstill even in the more severe cases after the withdrawal of clioquinol. Some patients died, but 3500 patients survived and suffered sequelae of SMON.[1,2]

Subacute myelo-optico-neuropathy patients who have overcome acute or subacute conditions complain today of many complications, such as paresthesia and dysesthesia, and paraplegia of the lower extremities. Complications were present in 93% of SMON patients in a national survey conducted in 2002.[3] Complications that occurred with a high prevalence were cataracts (56.2%), hypertension (40.2%), vertebral disease (35.5%) and gastrointestinal disease (27.6%). However, it is not clear whether these conditions, particularly visual disorders, are sequelae of SMON or due to the results of aging. It is also unclear whether other new visual disorders resulting from clioquinol occur with aging. We herein report the status of visual disorders of SMON patients according to a self-administered questionnaire and ophthalmological examination, and discuss the prevalence of cataract and glaucoma in SMON patients.

Methods

Questionnaire-based survey

Subacute myelo-optico-neuropathy patients (20 male, 132 female) living in Aichi Prefecture are registered by the SMON Research Committee, and take the general SMON examination once every 3 years. An investigation of these patients was conducted in December 1998 using a self-administered questionnaire. The questionnaire was sent to SMON patients, and consent was received from each patient to participate in this study. All SMON patients received health management allowances from the Organization for Adverse Drug Reactions Relief. The questionnaire consisted of questions concerning the years of SMON duration from onset, level of visual disturbance at onset of SMON, level of visual disturbance and ophthalmological diseases at present, and patients' age and gender. The level of SMON patients' visual disturbances were checked by neurologists, who conducted a general SMON examination. In the examinations, patients had both eyes open and used either the naked eye or had correction with their own glasses, but no other special correction was assigned. Visual disturbances were classified into six levels: total blindness, light discrimination, hand discrimination, finger discrimination, vision impairment, and normal vision. The number of patients with ophthalmological diseases such as cataracts, glaucoma, or fundus hemorrhage, was estimated based on the clinical diagnosis by the ophthalmologists with whom SMON patients were in consultation.

Ophthalmological examination

From 1998 to 2000, ophthalmological examinations were performed on 33 SMON patients (three male, 30 female) who replied to the questionnaire mentioned above. Ophthalmological examinations included tests of visual acuity, total refraction, intraocular pressure, visual field, slit lamp microscopy and funduscopic examination. Finally, ophthalmological diagnosis of patients was made by ophthalmologists based on the questionnaire, summary sheet, medical history from clinical charts and ophthalmological examination. In this paper, a patient was considered to be suffering from glaucoma if he or she had in one or both eyes incidence of: (i) glaucomatous cupping of the optic disc; (ii) visual field defects of the Bjerrum or Roenne nasal step type; and (iii) iridotomy from glaucoma.

The questionnaire investigation and ophthalmological examinations were conducted by doctors in the SMON Research Committee, supported by the Ministry of Health, Labor and Welfare of Japan.

Results

Questionnaire-based survey

We received 126 replies from patients (19 male, 107 female) by mail. Patients' ages ranged 31–93 years, and the average age was 71.5 years. There were 18 patients aged under 59 years, 27 patients aged 60–69 years, 54 patients aged 70–79 years, and 28 patients aged at 80 years or more. The average duration period since the onset of SMON was 32 years.

At the time of onset of SMON, the visual disturbances in the 126 patients was either total blindness (three patients), light discrimination (four), hand discrimination (one), finger discrimination (11), slight vision impairment (66) and normal vision (42), as shown in Table 1. At the onset of SMON, the percentage of patients with total blindness, and light, hand or finger discrimination was 15.0%, the percentage with slight vision impairment was 52.0% and the percentage with normal vision was 33.1%.

In this questionnaire study, the visual disturbances in the 126 patients was total blindness (one patient), light discrimination (one), hand discrimination (none), finger discrimination (six), slight vision impairment (96) and normal vision (23), as shown in Table 1. The percentage of patients with total blindness, and light, hand or finger discrimination was 6.2%, the percentage with slight vision impairment was 72.4% and the percentage with normal vision was 18.1%.

The percentage of patients with total blindness, and light, hand or finger discrimination at the time of the

study was lower than the percentage at the onset of SMON, as shown in Table 1. The percentage of patients with slight vision impairment at the time of the study was higher than the percentage at the onset of SMON. The percentage of patients with normal vision at the time of the study was lower than the percentage at the onset of SMON.

The number (prevalence) of patients with ophthalmological diseases was 66 (52.0%) with cataracts, 12 (9.4%) with glaucoma (type of glaucoma unknown), nine (7.1%) with fundus hemorrhage, six (4.7%) with optic-neuritis and 27 (21.3%) with other conditions, as shown in Table 3. Calculating the prevalence of cataract according to age group, the prevalence was 5.5% in patients aged under 59 years, 40.7% in patients aged 60–69 years, 64.8% in patients aged 70–79 years and 69.9% in patients aged at 80 years or more. Calculating the prevalence of glaucoma according to age group, the prevalence was 11.1% in patients aged under 59 years, 3.7% in patients aged 60–69 years, 9.3% in patients aged 70–79 years and 10.7% in patients aged 80 years or more.

We divided the patients into two groups according to the level of visual disturbances at the onset of SMON: a visual disturbances group and a normal vision group. The visual disturbances group included patients with all four disturbances: finger discrimination, hand discrimination, light discrimination and total blindness. The prevalence of glaucoma in the visual disturbances group was higher than that in the normal vision group, as shown in Table 2. However, the prevalence of cataracts, optico-neuritis and fundus hemorrhage was not considerably different between the two groups, as shown in Table 2.

Table 1 Comparison between the level of visual disturbances at the time of onset of subacute myelo-optico-neuropathy (SMON) and at present ($n = 127$)

Visual disturbances at present	Total	Visual disturbances at the onset					
Total blindness [TB]	1 (0.8)						1
Light discrimination [LD]	1 (0.8)					1	
Hand discrimination [HD]							
Finger discrimination [FD]	6 (4.9)		3	2		1	
Slight vision impairment [SVI]	96 (75.6)	26	58	5		2	2
Normal vision [NV]	23 (18.1)	16	5	4	1		
	127 (100)	42 (33.1)	66 (52.6)	11 (8.7)	1 (0.8)	4 (3.1)	3 (2.4)
		NV	SVI	FD	HD	LD	TB

( ), % of total. [ ], abbreviation of type of visual disturbances.

Table 2 Prevalence of ophthalmological diseases at the onset of SMON

Ophthalmological diseases	Levels of visual disturbances		
	Normal vision ($n = 42$) *n* (%)	Visual disturbances† ($n = 86$) *n* (%)	Total ($n = 127$) *n* (%)
Cataract	20 (48.8)	46 (53.5)	66 (52.0)
Glaucoma	1 (2.4)	11 (12.8)**	12 (9.4)
Fundus hemorrhage	3 (7.1)	6 (7.0)	9 (7.1)
Neuritis	1 (2.4)	5 (5.8)	6 (4.7)
Others§	11 (26.2)	16 (18.6)	27 (21.3)

†Refers to slight vision impairment, finger, hand and light discrimination and total blindness in Table 2. **A significant difference at $P = 0.01$ level in prevalence between normal vision and visual disturbances. §Degeneration of retina, flying mosquito, Sjögren syndrome, eye dryness, retinal detachment, and herpes.

Table 3 Visual test abnormality of patients ($n = 33$)

Abnormal visual field	No. of patients
1–2 concentric contraction	8
Glaucomatic disorder	3
Central scotoma	2
Depression (whole)	2
Depression (upper)	1
Enlarged Mariotte blind spot	2

Table 4 Fundus abnormality of patients ($n = 33$)

Abnormal fundus	No. of patients
Glaucomatous fundus changes	3
Macular disorder	3
Atrophy or degeneration retina and/or choroids	2
Atrophy or depigmentation of optic nerve	2
Small hemorrhage	1

Ophthalmological examinations

Ophthalmological examinations were performed on 33 SMON patients (three male, 30 female) in the years 1998–2000. Patients' ages ranged 32–89 years, and the average age was 67.3 years. There was one patient aged under 49 years, eight patients aged 50–59 years, eight patients aged 60–69 years, nine patients aged 70–79 years and seven patients aged 80 years or more.

Five out of 33 patients had corrected visual acuity of less than 0.7. Intraocular pressures were within normal limits in all patients. The numbers of patients with abnormal visual field were: eight for concentric contraction; three for glaucomatic disorder; three for depression; two for central scotoma; and two for enlarged Mariotte blind spot, as shown in Table 3.

Funduscopic examination revealed glaucomatous fundus changes in three patients, macular disorder in three patients, atrophy or degeneration of retina and/or choroids in two patients, atrophy or depigmentation of optic nerve in two patients, and a small hemorrhage in one patient, as shown in Table 4.

Finally, we diagnosed glaucoma in four patients (normal tension glaucoma [NTG] in three and another type of glaucoma in one), cataracts in 21, optic atrophy in two, macular degeneration in two, and retinal degeneration, vitreous opacity and fundus hemorrhage in one patient each, as shown in Table 5. The prevalence of cataracts was 63.6%, and that of glaucoma was 12.1% (9.1% in NTG) in ophthalmological examinations.

Table 5 Ophthalmological diagnosis of patients ($n = 33$)

Diagnosis	No. of patients (%)
Abnormal refraction	31 (93.9)
Near sight	11
Far sight	17
Irregular sight	6
Glaucoma	4 (12.1)
Normal tension glaucoma	3
Others	1
Cataract (including artificial glasses)	21 (63.6)
Optic atrophy	2 (6.1)
Macular degeneration (including suspected)	2 (6.1)
Retinal degeneration	1 (3.0)
Vitreous opacity	1 (3.0)
Fundus hemorrhage	1 (3.0)

Discussion

As indicated by the name of the disease, subacute myelo-optico-neuropathy, 32.6% of patients complained of visual disturbances (total blindness, light, hand and finger discrimination) at the onset of SMON in this questionnaire survey. The percentage of complaints of visual disturbances has decreased to 6.3%, as revealed by this questionnaire survey performed approximately 32 years after onset. However, the patients suffered from many ophthalmological diseases as comorbidities, in addition to typical SMON neurological symptoms, such as paresthesia and dysesthesia, and paraplegia of the lower extremities. According to a national SMON questionnaire survey,[3] cataracts had the highest prevalence (56.2%) among the major coexistent ophthalmological diseases in SMON patients (mean age, 72.9 years). The prevalence of cataracts, 52.0% in the present questionnaire survey, and 63.6% in the present ophthalmological examination, was not greatly different from that in the national SMON survey,[3] though the severity of cataracts is not clear in the questionnaire survey. It was reported in a Japanese cataract survey in the general population[4] that the prevalence of cataracts (lens opacification including early senile changes) was 68.9% in people aged 60–69 years, 81.8% in people aged 70–79 years and 98.1% in people aged at 80 years or more. A review[5] shows that the prevalence of lens opacities was 57.6% in people aged 65–74 years in the Framingham eye study, and the prevalence of senile lens changes was 73.2% in people aged 65–74 years and 91.1% in people aged 75–85 years in the National Health and Nutrition Examination Survey. The prevalence of cataracts was

40.7% in patients aged 60–69 years, 64.8% in patients aged 70–79 years, and 67.4% in patients aged at 80 years or more in the present questionnaire survey and 63.0% in patients in the present ophthalmological examination, which were almost the same as in three cataract surveys mentioned above. However, we can not compare these cataract prevalences precisely, because there were some variations in diagnostic criteria or equipment used in the diagnosis of cataracts.

The prevalence of glaucoma was 9.4% in this questionnaire-based survey and 12.1% in this ophthalmological examination disregarding the type of glaucoma. One survey[6] published in Japanese showed that the prevalence of glaucoma in the SMON patients who lived in other districts in Japan was 4.2% in a questionnaire survey, and 8.3% in an examination of a small number of patients (120 patients in a questionnaire survey and 12 patients in examination). However, glaucoma is today usually classified into five types: (i) primary open angle glaucoma (POAG); (ii) normal pressure glaucoma (NPG; criteria as for POAG with intraocular pressure [IOP], <21 mmHg]; (iii) primary angle-closure glaucoma (PACG); (iv) secondary glaucoma; (v) and ocular hypertension.[7] It is preferable to compare prevalences of the same type of glaucoma between groups. The number (prevalence) of glaucoma in this examination was three (9.1%) in NTG. The age-specific prevalence of NTG in this examination was 12.5% in patients aged 50–59 years, 0% in patients aged 60–69 years, 11.1% in patients aged 70–79 years and 14.3% in patients aged at 80 years or more. In comparison, the prevalence of NTG is 3.6% in the general population older than 40 years in Japan. Age-specific prevalences were 1.7% in people aged 40–49 years, 2.4% in people aged 50–59 years, 4.4% in patients aged 60–69 years, 7.9% in people aged 70–79 years and 5.7% in people aged at 80 years or more.[8] In another study[9] in Japan, the prevalence of NTG was 2.0% in the general population. Age-specific prevalences were 0.9% in people aged 30–49 years, 2.1% in people aged 50–69 years, and 4.0% in people aged 70 years or more. In other glaucoma surveys, the overall prevalence or age-specific prevalences of NTG are not shown. However, there is not considered to be a large difference between the prevalence of NTG and POAG or OAG, because NTG is equal to POAG when a few cases with elevated IOP are excluded from POAG. The Framingham eye study[10] reported that the prevalence of open-angle glaucoma (OAG) was 2.6%. Age-specific prevalences were 1.2% in people aged 52–64 years, 4.1% in people aged 65–74 years and 4.0% in people aged 75–85 years. The Rotterdam Study[11] reported that the prevalences of definite and probable OAG was 3.2%. Age-specific prevalences were 1.6% in people aged 55–59 years, 2.1% in people aged 60–64 years, 3.2% in people aged 65–69 years, 4.5% in people aged 70–74 years, 5.3% in people aged 75–79 years and 6.3% in people aged at 80 years or more. A survey conducted in India[12] reported that the prevalence of POAG was 1.6%. Age-specific prevalences were 0.6% in people aged 40–49 years, 1.6% in people aged 50–59 years, 2.6% in people aged 60–69 years, 3.6% in people aged 70–79 years and 3.6% in people aged at 80 years or more. The West Bengal Glaucoma Study[13] also reported that the prevalences of POAG was almost the same as those mentioned above. We cannot discuss the prevalence of NTG from the standpoint of statistics because of the small amount of data. However, the prevalence of NTG in SMON patients tended to be higher than that in other surveys in the general population.

In this questionnaire-based survey, the prevalence of glaucoma was 9.4%, although the classification of glaucoma was unknown. This value of 9.4% also tended to be higher than that of other surveys in the general population. We divided the SMON patients into two groups according to the level of visual disturbances at the time of onset of SMON. The questionnaire-based glaucoma prevalence in the visual disturbance group was higher than that in the normal vision group. This difference in the prevalence between the groups is interesting. However, the present data does not provide for further analysis.

There are several reports[14,15] on the visual condition of SMON patients at the onset of the disease. These reports described optic atrophy based on funduscopic examination, and central scotoma and concentric contraction from the visual field test. These abnormalities were also observed in the SMON patients in this examination. In addition to these abnormalities, fundus glaucomatous change was observed in three out of 33 patients. It is said that some patients with low-tension glaucoma have later increases in intraocular pressure, while others remain with low tension, and that there is a cause and effect relationship between optic nerve damage and elevated intraocular pressure.[16] We should follow the intraocular pressure of SMON patients in the future. Three patients had been diagnosed with glaucoma before this examination, and one patient's glaucoma was discovered during this examination.

Subacute myelo-optico-neuropathy patients need follow-up ophthalmological examinations, especially for glaucoma, on a nationwide scale.

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[Original]

Disability and Lifestyle of Subacute Myelo-Optico-Neuropathy and Stroke Patients and Elderly Persons Living at Home: A Comparison of the Barthel Index Score and the Frenchay Activities Index Score

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Abstract : To evaluate subacute myelo-optico-neuropathy (SMON) and stroke patients and elderly persons by using the Barthel Index (BI) and Frenchay Activities Index (FAI) and to reveal the disability and lifestyle of SMON patients, cross sectional comparison study was performed. Forty SMON patients, 92 age-matched stroke patients with the same level of BI score and 92 age-matched elderly persons living at home were subjected in this study. The SMON patients responded to a self-administered BI and FAI at their yearly health counseling, and the score of the BI and FAI of stroke outpatients and elderly persons were sampled from the databases. The differences in age distribution and sex ratio between the three groups were analyzed by the χ^2 test and one-way analysis of variance, respectively, and the differences in BI and FAI between the three groups were analyzed by the Kruskal-Wallis test, followed by the Mann-Whitney test. The BI total score of the SMON patients was the same as that of the stroke patients and lower than that of the elderly persons. The 4 items of self-care index and 2 items of mobility index in the SMON patients were rated significantly higher and lower than the stroke patients respectively, and all items except eating and toileting in the SMON patients were rated lower than elderly persons (Mann-Whitney test, $P<0.05$). The FAI scores in the SMON patients were lower than the elderly persons and higher than the stroke patients. These results suggest that the scores of the BI and FAI differentiated the features of disability and lifestyle of the SMON patients from those of stroke patients and elderly persons.

Key words : stroke, subacute myelo-optico-neuropathy, Frenchay Activities Index, Barthel Index.

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Introduction

Subacute myelo-optico-neuropathy (SMON) is a disease induced by the ingestion of clioquinol (5-chloro-7-iod-8-hydroxyquinoline), an intestinal antibacterial drug[1], and its clinical features are 1) subacute onset, 2) persistent symmetrical dysesthesia, usually affecting the lower trunk and legs, 3) spastic or spastic/ataxic paraparesis or, more rarely, hypotonic weakness in the lower limbs, 4) occasional visual impairment, and 5) preceding abdominal symptoms[2]. A large number of SMON were observed throughout Japan from 1955 till 1970, reaching nearly 10,000, and 220 cases were also reported from outside Japan[2-4]. Although new cases of SMON dramatically decreased in number after the governmental banning of the use of clioquinol in 1970, the number of surviving SMON patients was 2,936 in 2002, who received health management allowances from the Organization for Adverse Drug Reaction Relief.

A survey which was conducted 32 years after the banning of this drug revealed that the severities of impairment of vision, walking and sensation were overall milder than those at the onset[5], but the SMON patients are coming to need more social support, because the complications and comorbidities are now becoming important as a disability in daily life. At the present time the pathogenesis of SMON has been elucidated. It may be worthwhile to pay close attention to such patients in order to evaluate the disability and lifestyle of the SMON patients and to examine what kind of interventions, especially rehabilitation and social supports, are able to provide them with satisfactory relief. Because the number of SMON patients is far smaller than that of stroke patients living at home, it is favorable if the SMON patients can make use of the social support system for stroke patients and elderly persons who are living at home. First of all, we planned to evaluate activities of daily living (ADL) of the SMON patients using the Barthel Index (BI) [6], which is frequently used as an ADL scale in the fields of rehabilitation medicine and social welfare, and with the Frenchay Activities Index (FAI) [7], which is a higher social indicator for stroke patients[8] or a scale for lifestyle [9], in order to examine whether these scales could differentiate the features of SMON patients from stroke patients and elderly persons.

Therefore, the purpose of this study was to evaluate SMON patients, age-matched stroke patients living at home with the same level of the BI score, and age-matched elderly persons living at home by using the BI and FAI, and then compare the scores between them.

Subjects and Methods

As a project of the SMON Research Group sponsored by the Bureau of Health, Welfare and Labor of the Japanese Government, we have provided health counseling at the clinic or by home visits every year for registered SMON patients living in the Kitakyushu and Chikuho areas. The subject group consists of 40 SMON patients living at home who received health counseling between 1997 and 2005 (SMON group). In the case of those who received health counseling several times, we decided to use their initial evaluation values. The age distribution and sex ratio are described as follows: 50 – 59 years old, 6 (male 3/female 3);

60−69 years old, 8 (3/5); 70−79 years old, 16 (5/11); 80−89 years old, 10 (6/4).

In order to involve stroke patients living at home as a disease control, among the 1,070 people in the database of a national survey on disability characteristics of stroke patients in the chronic stage, 869 patients who were living at home and had no missing values were decided upon as the population[10]. Under conditions in which the age distribution and sex ratio matched approximately those for the SMON group and the BI score of each age group in the stroke group was equal to or larger than the lowest BI score by each age group in the SMON group, 92 patients (Stroke group) were randomly sampled using the RANDOM command of a statistical software package (SPSS 8.1J, SPSS Japan, Tokyo). The age distribution and sex ratio of the Stroke group were as follows: 50−59 years old, 15 (7/8); 60−69 years old, 19 (7/12); 70−79 years old, 35 (12/23); 80−89 years old, 23 (14/9).

In order to include elderly persons as a control, among the 1,000 people on the list of voters for Yahatanishi-ku, Kitakyushu, who were randomly sampled for the study to obtain standard values for BI and FAI, 748 people who agreed to the survey and had no missing values were chosen as the population [11]. Without setting conditions for BI, 92 subjects (Control group) were randomly sampled in a manner similar to that for the Stroke group, and the age distribution and sex ratio of the control group were the same as for the stroke group.

The BI used in the present study is the self-administered modification [12] for an epidemiological survey, based on the Granger version of BI [13]. The following has been reported: 1) an evaluation of the ability of basic ADL [13]; 2) 13 evaluation items, which are the same as the Motor scores for the Functional Independence Measure [14]; 3) its confirmed validity and reliability as a self-administered evaluation method [12,14]; and 4) the standard values for middle-aged and elderly persons living at home in Japan [15].

The FAI used as a lifestyle index is the self-administered modification [16] for an epidemiological survey, based on Holbrook's activities index [7]. The following has been reported: 1) evaluate the higher social activities [8], that is, lifestyle [9] ; 2) make a semiquantitative evaluation of a total of 15 items regarding the practice level on a scale of 4 from 0 to 3 [7]; 3) its confirmed validity and reliability as a self-administered evaluation method [16] ; and 4) the standard values for middle-aged and elderly persons living at home in Japan [11,17].

Regarding the BI and FAI for the SMON group, the evaluation form was provided to patients in the health counseling. After the forms were filled out by the patients, physicians confirmed the presence or absence of missing values during the examination. Additional questions were posed and corrections were made as needed. Thereafter, the forms were collected. The present study on the SMON group and previous surveys for the Stroke group and the Control group were appropriately conducted in accordance with guidelines for epidemiological surveys by the Bureau of Health, Labor and Welfare. Among the obtained data, personally identifiable data was all deleted, and the rest was kept anonymous in an untraceable manner to compile a database. The evaluation values were analyzed using SPSS8.1J. For the three groups, the age distribution and sex ratio were compared using a one-way analysis of variance and χ^2 test. The evaluation values for the BI and FAI were compared among the three groups using the Kruskal-Wallis test. For comparison of the SMON group and Stroke group, and the SMON group and Control group, the Mann-Whitney test was