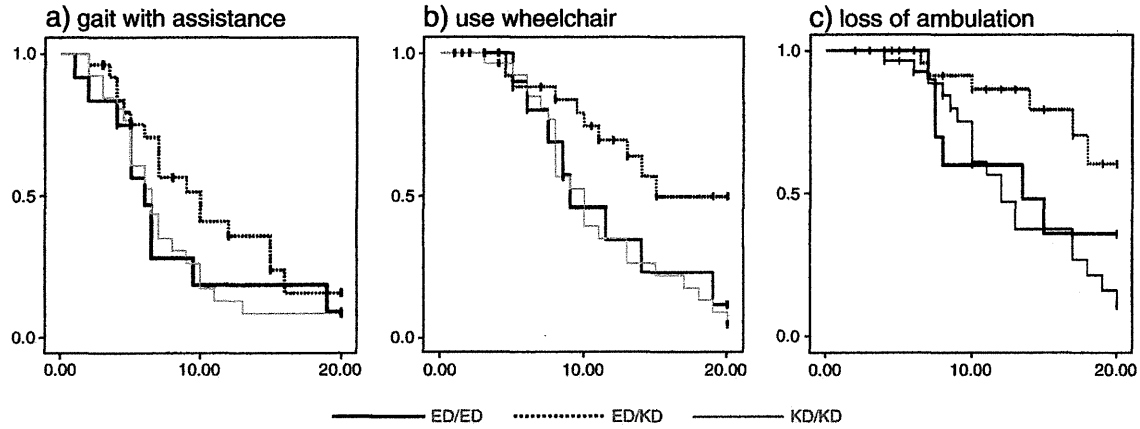

Fig. 1. Kaplan–Meier analysis of time from disease onset to (a) walking with assistance, (b) wheelchair use, and (c) loss of ambulation. Significant differences between ED/KD and KD/KD genotypes were identified. Age at disease onset was significantly different between ED/ED participants and ED/KD and KD/KD participants.

population, although p.D176V was the second most common mutation carried by 29 of our participants. In addition, a high variability was observed regarding age at disease onset and disease progression, underscoring the role of a yet-to-be identified factor(s) in determining disease phenotype.

The recruitment of participants from PADM and highly specialized neurology hospitals is a potential source of selection bias and thus a limitation of this study. These participants are likely to be more motivated because they are more severely affected compared to the general patient population. Furthermore, patients with lower disease severity may not yet be diagnosed with GNE myopathy. Therefore, our study may not accurately reflect the general patient population. Nevertheless, we believe our findings provide important information as our study population covers a broad range in age (22 to 81 years) and symptoms (minimal to wheelchair-bound). Finally, recall bias may also affect results presented in this retrospective study. Therefore, future studies should be performed with an emphasized prospective design.

In conclusion, our study shows that the KD/KD genotype (*i.e.*, p.V572L homozygous mutation) is associated with a more severe phenotype compared to compound heterozygous ED/KD mutations. Because only a small number of participants could walk, future studies should include ambulation-independent motor tests to yield a more comprehensive clinical overview in GNE myopathy patients with different genotypes.

Supplementary data to this article can be found online at doi:10.1016/j.jns.2012.03.016.

Conflict of interest

We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Acknowledgments

We thank members of the Patients Association for Distal Myopathies (PADM) for their help. This work was partly supported by the Research on Intractable Diseases of Health and Labor Sciences Research Grants; Comprehensive Research on Disability Health and Welfare Grants, Health and Labor Science Research Grants; Intramural Research Grant (23-4, 23-5) for Neurological and Psychiatric Disorders of NCNP; and a Young Investigator Fellowship from the Translational Medical Center, NCNP.

References

[1] Nonaka I, Sunohara N, Satoyoshi E, Terasawa K, Yonemoto K. Autosomal recessive distal muscular dystrophy: a comparative study with distal myopathy with rimmed vacuole formation. Ann Neurol 1985;17:51–9.
[2] Argov Z, Yarom R. "Rimmed vacuole myopathy" sparing the quadriceps. A unique disorder in Iranian Jews. J Neurol Sci 1984;64:33–43.
[3] Nishino I, Noguchi S, Murayama K, Driss A, Sugie K, Oya Y, et al. Distal myopathy with rimmed vacuoles is allelic to hereditary inclusion body myopathy. Neurology 2002;59:1689–93.
[4] Eisenberg I, Avidan N, Potikha T, Hochner H, Chen M, Olender T, et al. The UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase gene is mutated in recessive hereditary inclusion body myopathy. Nat Genet 2001;29:83–7.
[5] Kayashima T, Matsuo H, Satoh A, Ohta T, Yoshiura K, Matsumoto N, et al. Nonaka myopathy is caused by mutations in the UDP-N-acetylglucosamine-2-epimerase/N-acetylmannosamine kinase gene (GNE). J Hum Genet 2002;47:77–9.
[6] Keppler OT, Hinderlich S, Langner J, Schwartz-Albiez R, Reutter W, Pawlita M. UDP-GlcNAc 2-epimerase: a regulator of cell surface sialylation. Science 1999;284:1372–6.
[7] Malicdan MC, Noguchi S, Nishino I. Recent advances in distal myopathy with rimmed vacuoles (DMRV) or hIBM: treatment perspectives. Curr Opin Neurol 2008;21:596–600.
[8] Noguchi S, Keira Y, Murayama K, Ogawa M, Fujita M, Kawahara G, et al. Reduction of UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase activity and sialylation in distal myopathy with rimmed vacuoles. J Biol Chem 2004;279:11402–7.
[9] Broccolini A, Gidaro T, De Cristofaro R, Morosetti R, Gliubizzi C, Ricci E, et al. Hyposialylation of neprilysin possibly affects its expression and enzymatic activity in hereditary inclusion–body myopathy muscle. J Neurochem 2008;105:971–81.
[10] Salama I, Hinderlich S, Shlomai Z, Eisenberg I, Krause S, Yarema K, et al. No overall hyposialylation in hereditary inclusion body myopathy myoblasts carrying the homozygous M712T GNE mutation. Biochem Biophys Res Commun 2005;328:221–6.
[11] Malicdan MC, Noguchi S, Nonaka I, Hayashi YK, Nishino I. A Gne knockout mouse expressing human GNE D176V mutation develops features similar to distal myopathy with rimmed vacuoles or hereditary inclusion body myopathy. Hum Mol Genet 2007;16:2669–82.
[12] Malicdan MC, Noguchi S, Hayashi YK, Nonaka I, Nishino I. Prophylactic treatment with sialic acid metabolites precludes the development of the myopathic phenotype in the GNE myopathy mouse model. Nat Med 2009;15:690–5.
[13] Argov Z, Eisenberg I, Grabov-Nardini G, Sadeh M, Wirguin I, Soffer D, et al. Hereditary inclusion body myopathy: the Middle Eastern genetic cluster. Neurology 2003;60:1519–23.
[14] Tomimitsu H, Shimizu J, Ishikawa K, Ohkoshi N, Kanazawa I, Mizusawa H. Distal myopathy with rimmed vacuoles (DMRV): new GNE mutations and splice variant. Neurology 2004;11:1607–10.
[15] Yabe I, Higashi T, Kikuchi S, Sasaki H, Fukazawa T, Yoshida K, et al. GNE mutations causing distal myopathy with rimmed vacuoles with inflammation. Neurology 2003;12:384–6.
[16] Chu CC, Kuo HC, Yeh TH, Ro LS, Chen SR, Huang CC. Heterozygous mutations affecting the epimerase domain of the GNE gene causing distal myopathy with rimmed vacuoles in a Taiwanese family. Clin Neurol Neurosurg 2007;109:250–6.
[17] Ro LS, Lee-Chen GJ, Wu YR, Lee M, Hsu PY, Chen CM. Phenotypic variability in a Chinese family with rimmed vacuolar distal myopathy. J Neurol Neurosurg Psychiatry 2005;76:752–5.

Please cite this article as: Mori-Yoshimura M, et al. Heterozygous UDP-GlcNAc 2-epimerase and *N*-acetylmannosamine kinase domain mutations in the *GNE*..., J Neurol Sci (2012), doi:10.1016/j.jns.2012.03.016

[18] Hagemans ML, Winkel LP, Van Doorn PA, Loonen MC, Hop WJ, Reuser AJ, et al. Clinical manifestation and natural course of late-onset Pompe's disease in 54 Dutch patients. Brain 2005;128:671–7.
[19] Oskoui M, Levy G, Garland CJ, Gray JM, O'Hagen J, De Vivo DC, et al. The changing natural history of spinal muscular atrophy type 1. Neurology 2007;69: 1931–6.
[20] Sienko Thomas S, Buckon CE, Nicorici A, Bagley A, McDonald CM, Sussman MD. Classification of the gait patterns of boys with Duchenne muscular dystrophy and their relationship to function. J Child Neurol 2010;25:1103–9.
[21] Eisenberg I, Grabov-Nardini G, Hochner H, Korner M, Sadeh M, Bertorini T, et al. Mutations spectrum of GNE in hereditary inclusion body myopathy sparing the quadriceps. Hum Mutat 2003;21:99.

Please cite this article as: Mori-Yoshimura M, et al. Heterozygous UDP-GlcNAc 2-epimerase and *N*-acetylmannosamine kinase domain mutations in the *GNE*..., J Neurol Sci (2012), doi:10.1016/j.jns.2012.03.016

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Neuromuscular Disorders 23 (2013) 176–179

www.elsevier.com/locate/nmd

Case report

Prednisolone-sparing effect of cyclosporin A therapy for very elderly patients with myasthenia gravis

Seika Nakamura [a], Satoshi Kaneko [a,*], Akiyo Shinde [b], Jun-ichi Morita [a], Kengo Fujita [a], Satoshi Nakano [c], Hirofumi Kusaka [a]

[a] *Department of Neurology, Kansai Medical University, Osaka, Japan*
[b] *Department of Neurology, Tenri Yorozu Hospital, Nara, Japan*
[c] *Department of Neurology, Osaka City General Hospital, Osaka, Japan*

Received 18 July 2012; received in revised form 6 October 2012; accepted 3 November 2012

Abstract

Three very elderly (over 80 years old) patients having generalized myasthenia gravis without thymoma were treated with cyclosporin A and followed for up to 24 months. Cyclosporin A therapy quickly improved myasthenia gravis symptoms in all cases, which allowed a rapid reduction in the prednisolone dose and improvement of prednisolone-related hyperglycemia and hypertension. Combination therapy with prednisolone and low-dose cyclosporin A not only improved the clinical symptoms of the very elderly myasthenia gravis patients but also resulted in a rapid reduction in prednisolone dosage and prednisolone-related side effects. Attention should be paid to cyclosporin A-related renal dysfunction.

Keywords: Corticosteroids; Cyclosporin A; Elderly; Myasthenia gravis

1. Introduction

The annual incidence of myasthenia gravis (MG), especially late-onset MG, has been reported to be increasing [1]. However, there is not yet established any clinical evidence suggesting how to treat these very elderly patients with immunosuppressive agents.

Among many immunosuppressive agents, cyclosporin A (CsA) has been proven to be effective on MG based on the results of several clinical trials [2,3]. CsA therapy quickly improves MG symptoms [4] and slightly affects glucose tolerance [5,6], but increases serum creatinine especially in elderly patients. However, participants of these trials were up to 70 years old; and there are few reports on the effectiveness of CsA in very elderly MG patients.

Herein we report effectiveness and side effects of long-term combination therapy with prednisolone (PSL) and CsA on 3 very elderly (over 80 years old) patients having generalized MG patients without thymoma and who also required high dose of PSL.

2. Case report

Case 1: An 83-year-old woman noticed ptosis initially, then mild dysphagia. She was diagnosed as having Myasthenia Gravis Foundation of America (MGFA) class IIb [7]. She also had type 2 diabetes, diabetic retinopathy and hypertension. Only an anticholinesterase drug was administered because of her age and complications. However, dysphagia progressed in 2 months and her symptoms became worsened to MGFA class IIIb, with 12 points on the MG-ADL scale [8] and 21 points for the QMG score [7]. Her anti-AChR Ab titer was 23 nmol/L. PSL was started at 5 mg every other day, and was titrated up to

* Corresponding author. Address: Department of Neurology, Kansai Medical University, 10-15, Fumizonocho, Moriguchi, 570-0074 Osaka, Japan. Tel.: +81 66992 1001; fax: +81 66993 9468.
E-mail address: kanekosa@takii.kmu.ac.jp (S. Kaneko).

0960-8966/$ - see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.nmd.2012.11.003

Table 1
Clinical characteristics of myasthenia gravis (MG) patients treated with low-dose cyclosporin A (CsA).

Case	Sex	Age (years)	Months since MG onset	Medication before start of CsA therapy	PSL-related complications	MGFA class before/after CsA treatment	Anti-AChR-Ab (nmol/L) before/after CsA treatment	Reduction in PSL dosage by CsA
1	F	83	4	Pyridostigmine 12 mg PSL 80 mg AD	Hyperglycemia Hypertension	IIb/0	23/9.4	94%
2	F	81	6	Ambenonium 15 mg PSL 100 mg AD	Hyperglycemia Hypertension	IIa/0	5.7/0.6	93%
3	F	84	38	Distigmine 5 mg PSL 100 mg	Hypertension Depression	IIb/IIa	5.2/1.6	65%

PSL prednisolone, AD alternate day.

80 mg every other day by 4 weeks. As the PSL dose increased, hyperglycemia appeared and so insulin therapy was added to the treatment. Dysphagia persisted 4 weeks after initiation of PSL therapy and she needed help for her daily life activities. In order to achieve further improvement and a reduction in the PSL dose, CsA at 3 mg/kg/day was added. Her clinical symptoms improved in 2 weeks and so tapering of the PSL dose was started. After 4 weeks of CsA treatment, she became independent in her daily life. Her clinical symptoms improved, the QMG score dropped to 3 points, the MG-ADL scale became 1 point, and she was classified as MGFA class I. PSL was able to be stopped by 15 months after the start of CsA treatment, and exacerbation of MG symptoms was not observed. The anti-AChR Ab titer was reduced to 8.3 nmol/L after 6 months of CsA treatment. The CsA trough level was in 40–190 ng/mL and her serum creatinine level did not become elevated. The hyperglycemia was improved as the PSL dose was lowered, and her blood sugar was well controlled under 4–6 units of insulin per day (Table 1).

Case 2: An 81-year-old woman was admitted because of ptosis for 3 months. She had ptosis and diplopia but little weakness in her limbs on admission. Initial treatment of 120 mg of pyridostigmine failed to improve her eye symptoms, and so the treatment was switched to 15 mg of ambenonium, which also failed to improve them. Her general symptoms were mild and she was designated as MGFA class IIa with 13 points for the QMG score and 7 points on the MG-ADL scale. However, the ptosis gradually became so severe that she could not open her eyes. In order to improve the ptosis, PSL was started at 6 months after her initial MG symptoms. PSL was titrated starting from 5 mg every other day, but hyperglycemia appeared. Temporary insulin therapy and subsequent oral antidiabetic agent (80 mg of gliclazide) were needed. She became hypertensive, and so an antihypertensive agent was added. Titration of PSL continued up to 100 mg every other day improved her QMG score within 3 weeks from 13 to 9 points, but was not adequately effective for her ptosis and diplopia. To promote clinical improvement and reduce the PSL-related side effects, CsA at 3 mg/kg/day were started, while continuing the PSL; and her QMG score was further improved from 9 to 6 points in 2 weeks. Daily fluctuation of her ptosis still persisted, and so PSL treatment was switched from alternative days to an everyday regimen at the dosage of 40 mg. This regimen was effective for her ptosis and daily fluctuation which disappeared within several days. Tapering of the PSL dose was started at the rate of 2.5 mg in 2 weeks. Four weeks after CsA treatment, she was categolized as MGFA class I, with 5 points for the QMG score and 3 points on the MG-ADL scale. PSL was able to be discontinued after 14 months of CsA therapy, and she remained asymptomatic thereafter. Hyperglycemia and hypertension were improved along with reduction in PSL dose, and treatment with antidiabetic and antihypertensive drugs was stopped. Her anti-AChR Ab titer was reduced from 5.6 to 0.6 nmol/L by 6 months after. CsA trough level was in 60–140 ng/mL, and no elevation of serum creatinine was observed during the treatment.

After discontinuation of PSL, case 1 and case 2 were followed up for more than 9 and 10 months, respectively, without relapse of MG symptoms.

Case 3: An 81-year-old woman noticed left ptosis. Diagnosis of ocular-type MG was made, and 5 mg of distigmine successfully controlled her ocular symptoms. Three years after the onset of diplopia, general weakness appeared at the age of 84, followed by dysphagia and dysarthria occurring within 1 month, and so she was admitted to our hospital. She was categorized as being MGFA class IIIb and registered 16 points on the MG-ADL scale. Her anti-AChR Ab titer was 27 nmol/L. PSL was started from 5 mg every other day, but a myasthenic crisis occurred at day 3 of treatment; and so she was mechanically ventilated. Methylprednisolone pulse therapy and 7-times immunoabsorption improved the weakness, and she was withdrawn from mechanical ventilation 2 weeks later. PSL at 100 mg every other day was administered for 5 weeks but failed to improve her dysphagia and she developed PSL-related depression. For further improvement of her MG symptoms and reduction in PSL-related side effects, CsA treatment was started at the dosage of 3 mg/kg/day. Two weeks later her MG symptoms improved, and tapering of the PSL dosage was started. The PSL dose could be reduced from 100 to 80 mg every other day within 2 weeks. Her MG symptoms were now at MGFA class IIa, with 4 points on the MG-ADL scale, and she was discharged. The titer of

anti-AChR Ab at discharge was 1.6 nmol/L. The CsA trough level was 30–160 ng/mL, but her serum creatinine rose from 1.0 to 1.48 mg/dL after 13 months of CsA treatment. Despite the reduction in the CsA dose to 1 mg/kg/day, her serum creatinine still continued to elevate, reaching 1.65 mg/dL at 15 months after the start of CsA therapy. Therefore the CsA had to be discontinued. One month after the discontinuance, her serum creatinine level improved to 1.08 mg/dL and stayed invariably at the level. The PSL was then tapered to 20 mg every other day, and she was able to maintain her activity of daily life without any side effects.

3. Discussion

The prevalence of MG patients has been reported to be increasing among very elderly people [9,10]. Elderly patients with MG have variable manifestations, ranging from mild ocular to severe bulbar and/or respiratory involvement [11]. They also have a higher mortality and full remission is rare [12]. They respond relatively well to immunosuppressive therapies [13,14], but attention should be given to side effects [15]. Hepatic and renal functions of very elderly patients are limited, and they tend to have multiple complications such as hypertension, diabetes mellitus, hyperlipidemia and osteoporosis. Taking PSL-rerated side effects into consideration [16], long-term and high-dose PSL therapy [17] is not appropriate for elderly patients.

Immunosuppressive agents have been reported to be comparatively effective for treatment of elderly patients with MG. For instance, improvement of clinical symptoms during therapy with 5 mg/kg of CsA becomes apparent within 1–2 weeks, as shown in a study on 20 MG patients having a mean age of 51.6 ± 12.1 years [4]. Nagane et al. reported that 16 out of 18 MG patients ranging in age from 42 to 68 years were able have their PSL dose reduced more than 50% within two years after the addition of CsA to the PSL therapy [6]. The dosage of CsA in that study was initially started at 4.3 ± 1.0 mg/kg, then gradually reduced to 3.3 ± 0.7 mg/kg at 6 months, 3.0 ± 0.6 mg/kg at 12 months, and 2.6 ± 0.8 mg/kg at 24 months; but its immunosuppressive effect was sufficient. However, there is no clinical trial for very elderly (over 80 years old) patients having their MG treated with PSL and CsA.

Our 3 cases were at high risk for PSL-related side effects. PSL therapy only was not sufficient to improve their clinical symptoms. Especially Case 3 developed a myasthenic crisis and was treated with PSL-pulse therapy and immunoabsorption, but her symptomatic improvement was limited. In contrast, the effectiveness of CsA on her clinical symptoms appeared within a few weeks. Twelve months after the introduction of CsA treatment, the dosage level of PSL was able to be reduced 94% in Case 1, 95% in Case 2 and 65% in Case 3.

CsA has been reported to have side effects of nephrotoxicity, hyperglycemia and hypertension [4]. Especially elderly people should be carefully considered for its indication and dosage. Many clinical trials [2,3,18–20] have shown that renal dysfunction due to CsA therapy is a major side effect but that it is reversible after a reduction in or discontinuance of the CsA dose. The present 3 cases were treated with CsA at 3 mg/kg or less, and its trough concentration was kept under 200 ng/mL. Cases 1 and 2 did not show any elevation of their serum creatinine level. However, Case 3 had a 40-year history of hypertension and showed a consequent elevation of creatinine to 1.0 mg/dL during treatment with CsA at 3 mg/kg. Therefore, her CsA therapy had to be discontinued at 14 months of treatment. Her clinical symptoms were stable with low-dose PSL after discontinuance of the CsA therapy, and so the introduction of CsA therapy was beneficial for her with regard to reduction in the PSL dose. Her serum creatinine returned to the previous level after discontinuance of CsA therapy.

CsA has been reported to alleviate PSL-related hyperglycemia [6]. Conversion from tacrolimus to CsA for posttransplant diabetes mellitus has been reported to be beneficial as CsA causes an improvement in glucose metabolism [5]. Among calcineurin inhibitors, CsA may be suitable for diabetic patients. Early introduction of CsA to spare the use of PSL should be considered. Cases 1 and 2 showed hyperglycemia as their PSL dose was increased, and they needed to be treated with insulin. Further worsening of hyperglycemia was not observed after introduction of the CsA therapy, which quickly improved MG symptoms, resulting in a rapid reduction in the PSL dose and improvement of hyperglycemia. After cessation of PSL treatment, CsA therapy was continued on these patients; but no elevation of blood sugar was observed.

Transient hypertension was observed in Case 2, but it improved along with the reduction in the PSL dose. Hypertension can be caused by CsA treatment, but in our study the CsA dose was low enough that no CsA-related hypertension was observed.

Combination therapy of PSL and low-dose CsA for very elderly MG patients was safe and effective. CsA had a PSL-sparing effect and was able to reduce PSL-related side effects. MG symptoms were stable for a long period after cessation of PSL treatment. Elevation of serum creatinine should addressed especially in patients with preexisting renal dysfunction; but we found it to be reversible and the function to improve after discontinuance of CsA. Low-dose CsA therapy was safe and effective for very elderly MG patients, and should be considered in the early stage of severe form of MG, especially when high dose of PSL is required, to reduce the PSL dosage level and PSL-related side effects.

To establish safe and effective therapy for MG patients over 65 years of age at onset, prospective multicenter

studies on the presentation, clinical course, response and outcome to treatments are needed.

References

[1] Casetta I, Groppo E, De Gennaro R, et al. Myasthenia gravis: a changing pattern of incidence. J Neurol 2010;257:2015–9.

[2] Tindall RS, Rollins JA, Phillips JT, Greenlee RG, Wells L, Belendiuk G. Preliminary results of a double-blind, randomized, placebo-controlled trial of cyclosporine in myasthenia gravis. N Engl J Med 1987;316:719–24.

[3] Tindall RS, Phillips JT, Rollins JA, Wells L, Hall K. A clinical therapeutic trial of cyclosporine in myasthenia gravis. Ann NY Acad Sci 1993;681:539–51.

[4] Utsugisawa K, Nagane Y, Suzuki S, Suzuki N. Monitoring treatment with cyclosporine microemulsion in myasthenia gravis. Eur J Neurol 2008;15:598–604.

[5] Bouchta NB, Ghisdal L, Abramowicz D, et al. Conversion from tacrolimus to cyclosporin is associated with a significant improvement of glucose metabolism in patients with new-onset diabetes mellitus after renal transplantation. Transplant Proc 2005;37:1857–60.

[6] Nagane Y, Suzuki S, Suzuki N, Utsugisawa K. Two-year treatment with cyclosporine microemulsion for responder myasthenia gravis patients. Eur Neurol 2010;64:186–90.

[7] Jaretzki A, Barohn RJ, Ernstoff RM, et al. Myasthenia gravis: Recommendations for clinical research standards. Task force of the medical scientific advisory board of the myasthenia gravis foundation of America.. Neurology 2000;55:16–23.

[8] Wolfe GI, Herbelin L, Nations SP, Foster B, Bryan WW, Barohn RJ. Myasthenia gravis activities of daily living profile. Neurology 1999;52:1487–9.

[9] Matsuda M, Dohi-Iijima N, Nakamura A, et al. Increase in incidence of elderly-onset patients with myasthenia gravis in Nagano Prefecture. Jpn Intern Med 2005;44:572–7.

[10] Somnier FE. Increasing incidence of late-onset anti-AChR antibody-seropositive myasthenia gravis. Neurology 2005;65:928–30.

[11] Mantegazza R, Baggi F, Antozzi C, et al. Myasthenia gravis (MG): epidemiological data and prognostic factors. Ann NY Acad Sci 2003;998:413–23.

[12] Aarli JA. Myasthenia gravis in the elderly: Is it different? Ann NY Acad Sci 2008;1132:238–43.

[13] Pascuzzi RM, Coslett HB, Johns TR. Long-term corticosteroid treatment of myasthenia gravis: report of 116 patients. Ann Neurol 1984;15:291–8.

[14] Nagane Y, Suzuki S, Suzuki N, Utsugisawa K. Factors associated with response to calcineurin inhibitors in myasthenia gravis. Muscle Nerve 2010;41:212–8.

[15] Evoli A, Batocchi AP, Minisci C, Di Schino C, Tonali P. Clinical characteristics and prognosis of myasthenia gravis in older people. J Am Geriatr Soc 2000;48:1442–8.

[16] Truhan AP, Ahmed AR. Corticosteroids: a review with emphasis on complications of prolonged systemic therapy. Ann Allergy 1989;62:375–91.

[17] Schneider-Gold C, Gajdos P, Toyka KV, Hohlfeld RR. Corticosteroids for myasthenia gravis. Cochrane Database Syst Rev 2005:CD002828.

[18] Goulon M, Elkharrat D, Lokiec F, Gajdos P. Results of a one-year open trial of cyclosporine in ten patients with severe myasthenia gravis. Transplant Proc 1988;20:211–7.

[19] Bonifati DM, Angelini C. Long-term cyclosporine treatment in a group of severe myasthenia gravis patients. J Neurol 1997;244:542–7.

[20] Lavrnic D, Vujic A, Rakocevic-Stojanovic V, et al. Cyclosporine in the treatment of myasthenia gravis. Acta Neurol Scand 2005;111:247–52.

平成25年度　班会議プログラム

厚生労働科学研究費補助金（難治性疾患等克服研究事業(難治性疾患克服研究事業)）

希少難治性筋疾患に関する調査研究班
(H24-難治（難）--一般-028)

「　ＩＢＭ分科会　」
H25 年度 会議プログラム

研究代表者：　東北大学大学院医学系研究科　神経内科学

青木　正志

日　　時　　平成 26 年 1 月 31 日(金) 10:00～11:55

会　　場　　都市センターホテル　701 会議室

東京都千代田区平河町 2-4-1

http://www.toshicenter.co.jp/

お願い：演題発表時間 15 分（発表 10 分、討論 5 分）
発表者はご自身の PC をご持参くださいますようお願いいたします。

研究班事務局：加藤 昌昭、鈴木 直輝、武藤久美子
〒980-8574 宮城県仙台市青葉区星陵町 1-1
東北大学大学院医学系研究科　神経内科学
TEL 022-717-7189　FAX 022-717-7192

開会挨拶　　10:00～10:05　　研究代表者　　青木 正志

封入体筋炎に関する班員研究発表　　10:05～12:30

Session I　　10:05～10:50　　座　長　　青木正志

1. 封入体筋炎に対する経静脈的免疫グロブリン療法の効果（10:05～10:20）

研 究 分 担 者：森 まどか
所　　属：国立精神・神経医療研究センター病院 神経内科
研 究 協 力 者：○森まどか 1)（もりまどか），西川敦子 1*)，山本敏之 1)，大矢 寧 1)，小林 庸子 2)，西野一三 3)，村田美穂 1)
研究協力者所属：1）国立精神・神経医療研究センター病院　神経内科
2）同病院　リハビリテーション科
3）同神経研究所　疾病研究第一部
*現・大阪市立総合医療センター神経内科

2. 封入体筋炎に対する長期継続免疫グロブリン静注(IVIG)療法の有用性（10:20～10:35）

研 究 分 担 者：村田　顕也
所　　属：和歌山県立医科大学 神経内科
研 究 協 力 者：○村田顕也 1)（むらたけんや），高　真守 1)，阪田麻友美 1)，森めぐみ 1)，中山宜昭 1)，檜皮谷泰寛 1)，梶本賀義 1)，近藤智善 2)，伊東秀文 1)
研究協力者所属：1）和歌山県立医科大学　神経内科
2）リハビリテーション花の舎病院

3. IBM の診断における補助検査の有用性（10:35～10:50）

研 究 分 担 者：梶　龍兒
所　　属：徳島大学 神経内科
研 究 協 力 者：○松井尚子（まついなおこ），島谷佳光，野寺裕之，和泉唯信，梶 龍兒
研究協力者所属：徳島大学神経内科

＊＊＊＊＊＊＊＊　　休憩　　10:50 ～ 11:00　　＊＊＊＊＊＊＊＊

Session Ⅱ　11:00～11:45　　座　長　　西野一三

4. 封入体筋炎筋組織における p62/SQSTM1 の発現と nucleophagy（11:00～11:15）

研 究 分 担 者：日下　博文
所　　属：関西医科大学　神経内科
研 究 協 力 者：○中野　智１）（なかの　さとし），中村聖香１），日下博文２）
研究協力者所属：1）大阪市立総合医療センター　神経内科
2）関西医科大学　神経内科

5.（11:15～11:30）

研 究 分 担 者：山下　賢
所　　属：熊本大学医学部附属病院　神経内科
研 究 協 力 者：○山下 賢(やました　さとし)1)，俵　望 1)，森　麗 1)，西田泰斗 2)，
内野克尚 1)，永利聡仁 3)，栗﨑玲一 3)，中西俊人 1)，堀 寛子 1)，
平原智雄 1)，渡邉聖樹 1)，上山秀嗣 2)，山下太郎 1)，前田 寧 1)，
安東由喜雄 1)
研究協力者所属：1）熊本大学医学部附属病院　神経内科
2）国立病院機構熊本再春荘病院　神経内科
3）国立病院機構熊本南病院　神経内科

6.（11：30～11：45）

研 究 分 担 者：樋口　逸郎
所　　属：鹿児島大学医学部保健学科理学療法学専攻　基礎理学療法学講座
研 究 協 力 者：○橋口昭大（はしぐちあきひろ）1)，袁　軍輝 1)，稲森由恵 1)，白石匡史 1)，
高嶋　博 1)，樋口逸郎 2)
研究協力者所属：1）鹿児島大学大学院医歯学総合研究科　神経内科・老年病学講座
2）鹿児島大学医学部保健学科理学療法学専攻　基礎理学療法学講座

閉会挨拶　　11:45～11:50　　研究代表者　　青木 正志

12：10～12：50　「希少難治性筋疾患に関する調査研究班」今後の研究方針に関する打ち合わせ

12：50～　「希少難治性筋疾患に関する調査研究班」班会議　受付け開始

厚生労働科学研究費補助金（難治性疾患等克服研究事業(難治性疾患克服研究事業)）

希少難治性筋疾患に関する調査研究班

（H24-難治等（難）-一般-028）

H25 年度 班会議プログラム

研究代表者：　東北大学大学院医学系研究科　神経内科学

青木　正志

日　　時　　平成 26 年 1 月 31 日(金) 13:00～16:00

会　　場　　都市センターホテル　701 会議室

東京都千代田区平河町 2-4-1

http://www.toshicenter.co.jp/

お願い：演題発表時間 20 分（発表 15 分、討論 5 分）
発表者はご自身の PC をご持参くださいますようお願いいたします。

研究班事務局：加藤 昌昭、鈴木 直輝、武藤久美子
〒980-8574 宮城県仙台市青葉区星陵町 1-1
東北大学大学院医学系研究科　神経内科学
TEL 022-717-7189　FAX 022-717-7192

開会挨拶　　13:00～13:05　　研究代表者　　青木 正志

Session I 13:05～13:45　　座　長　　西野一三

1. 封入体筋炎　update　と分科会の取り組み（13:05～13:25）

研 究 代 表 者：○青木 正志（あおき まさし）
所　　属：東北大学大学院医学系研究科　神経内科学
研 究 協 力 者：加藤 昌昭 1)、竪山 真規 1)、割田　仁 1)、井泉 瑠美子 1)、鈴木 直輝 1)、島倉 奈緒子 1)、安藤 里紗 1)、北嶋 康雄 1)、高橋 俊明 2)、西野 一三 3)、森 まどか 4)、日下 博文 5)、樋口 逸郎 6)、村田 顕也 7)、山下　賢 8)、梶　龍兒 9)
研究協力者所属：1) 東北大学　神経内科
2) 国立西多賀病院
3) 国立精神・神経医療研究センター神経研究所　疾病研究第一部
4) 国立精神・神経医療研究センター病院　神経内科
5) 関西医科大学　神経内科
6) 鹿児島大学医学部・歯学部附属病院　神経内科
7) 和歌山県立医科大学　神経内科
8) 熊本大学　神経内科
9) 徳島大学　神経内科

2. 自己貪食空胞性ミオパチー患者の全国実態調査（13:25～13:45）

研 究 分 担 者：○杉江和馬（すぎえ　かずま）1) 2)
所　　属：奈良県立医科大学　神経内科
研 究 協 力 者：西野一三 2)
研究協力者所属：1) 奈良県立医科大学　神経内科
2) 国立精神・神経医療研究センター　神経研究所　疾病研究第一部

＊＊＊＊＊＊＊＊　　休憩　　13:45　～　13:55　　＊＊＊＊＊＊＊＊

Session II 13:55～14:55　　座　長　　林由起子

3. 先天性ミオパチーにおける骨格筋画像データベースの作成（13:55～14:15）

研 究 分 担 者：小牧 宏文
所　　属：国立精神・神経医療研究センター病院　小児神経科
研 究 協 力 者：○ 石山 昭彦（いしやま あきひこ）
研究協力者所属：　国立精神・神経医療研究センター病院　小児神経科

4. 先天性ミオパチーの病型頻度ならびに本邦ネマリンミオパチーの臨床遺伝学的特徴（14:15～14:35）

研究分担者：○林　由起子（はやし ゆきこ）1),2),3)
所　　属：東京医科大学神経生理学
研究協力者：宮武聡子 4)、輿水江里子 4)、松本直通 4)、埜中征哉 2）、西野一三 2),3)
研究協力者所属：1）東京医科大学神経生理学
2）国立精神・神経医療研究センター神経研究所疾病研究第一部
3）同トランスレーショナルメディカルセンター臨床開発部
4）横浜市立大学大学院医学研究科遺伝学

5. ウルリッヒ型先天性筋ジストロフィーの自然歴研究（14:35～14:55）

研究分担者：西野一三　1),3)
所　　属：独立行政法人国立精神・神経医療研究センター神経研究所　疾病研究第一部
研究協力者：○米川貴博 1)（よねかわたかひろ）、小牧宏文 2)、林由起子 1),3),4)、埜中征哉 1),2)
研究協力者所属：1）独立行政法人国立精神・神経医療研究センター神経研究所　疾病研究第一部
2）独立行政法人国立精神・神経医療研究センター病院
3）独立行政法人国立精神・神経医療研究センタートランスレーショナルメディカルセンター　臨床開発部
4）東京医科大学医学部医学科　神経生理学講座

＊＊＊＊＊＊＊＊　休憩　14:55 ～ 15:05　＊＊＊＊＊＊＊＊

Session III　14:55～15:55　座　長　大野欽司

6. 周期性四肢麻痺の遺伝子診断と新規遺伝子探索（14：55～15：15）

研究分担者：高橋　正紀
所　　属：大阪大学大学院　医学系研究科　神経内科学
研究協力者：○古田 充（ふるた　みつる）1)、中田 智彦 2)、穀内 洋介 1)、坂田 宗平 3)、木村 紘美 4)、伊藤 英樹 4)、相庭武司 5)、吉永正夫 6)、中森 雅之 1)、久保田智哉 1)、進藤 克郎 7)、清水渉 8)、堀江 稔 4)、岡村 康司 3)、望月 秀樹 1)、大野 欽司 2)
研究協力者所属：1）大阪大学大学院　医学系研究科　神経内科学
2）名古屋大学大学院　医学系研究科　神経遺伝情報学
3）大阪大学大学院　医学系研究科　統合生理学
4）滋賀医科大学　呼吸循環器内科学

5）国立循環器病医療研究センター　不整脈科
6）国立病院機構　鹿児島医療センター　小児科
7）倉敷中央病院　神経内科
8）日本医科大学　循環器内科

7. パールカン機能部分欠損疾患 Schwartz- Jampel 症候群の研究（15：15〜15：35）

研 究 分 担 者：○平澤恵理（ひらさわえり）
所　　属：順天堂大学老人性疾患病態・治療センター
研 究 協 力 者：野中理紗 1)、大野欽司 2)
研究協力者所属：1）順天堂大学老人性疾患病態・治療センター
2）名古屋大学大学院　医学系研究科　神経遺伝情報学

8．本邦における終板アセチルコリンエステラーゼ欠損症の分子病態（15：35〜15：55）

研 究 分 担 者：○大野欽司（おおのきんじ）
所　　属：名古屋大学大学院医学系研究科・神経遺伝情報学
研 究 協 力 者：中田智彦 1)、伊藤美佳子 1)、東慶輝 1)、大塚健司 1)、小牧宏文 2)、奥村彰久 3)、白石一浩 4)
研究協力者所属：1）名古屋大学大学院医学系研究科・神経遺伝情報学
2）国立精神・神経医療研究センター病院・小児神経科
3）順天堂大学医学部小児科
4）国立病院機構宇多野病院小児神経科

閉会挨拶　　15:55〜16:00　　研究代表者　　青木 正志