A CASE WITH HYPOCRETIN(OREXIN) DEFICIENT NARCOLEPSY, PARKINSON'S DISEASE AND SEVERE PSYCHOSIS WAS SUCCESSFULLY TREATED BY MODIFIED ELECTRO-CONVULSIVE THERAPY

Yuya Takahashi[1)], Yuka Kikuchi[1)], Takashi Kanbayashi[1)], Akira Hanazono[2)], Shunichiro Abe[1)], Shinobu Iwaki[1)], Ko Tsutsui[1)], Hideka Suda[1)], Fumi Maruyama[3)] and Tetsuo Shimizu[1)]

(received 31 May 2011, accepted 8 August 2011)

[1)]*Department of Psychiatry, Akita University Graduate School of Medicine, Akita 010-8543, Japan*
[2)]*Department of Neurology, Akita University Graduate School of Medicine, Akita 010-8543, Japan*
[3)]*Department of Psychiatry, Suwa Red Cross Hospital, Japan*

Abstract
We report the case of a 60-year-old male who exhibited severe psychosis two years after beginning treatment with methylphenidate for hypocretin deficient narcolepsy. He also suffered from Parkinson's disease (PD) and was treated by several medications. The psychotic episode persisted several weeks after medication cessation and required management with modified electro-convulsion therapy. Physicians should be aware that psycho-stimulants and anti-PD medications commonly prescribed for treatment of narcolepsy and PD may precipitate psychosis in those patients.

Introduction

Previously, we reported a case with Parkinson's disease (PD) comorbid with hypocretin (orexin) deficient narcolepsy[1)]. This case has subsequently affected severe psychosis and has been treated by modified electro-convulsive therapy (mECT) with good outcome.

Case report

A 58-year-old man with mild PD for 15 years was admitted to a hospital due to sleep attacks in 2004. In high school, he suffered from excessive daytime sleepiness (EDS). However, he had not been diagnosed nor treated at that time. He never had cataplexy. At age 43, he had tremors in his left fingers and was diagnosed with PD at age 45. He got hit by a motor vehicle due to EDS at age 55. He frequently experienced hypnagogic hallucinations with abnormal limb movements. He had Hoehn-Yahr stage 2 parkinsonism and scored 14 in the unified PD rating scale part III. Epworth sleepiness scale was 19/24 (normal range <11/24). In multiple sleep latency test (MSLT), the sleep latency was two minutes (normal range >8 min) and sleep onset REM periods were present in all four naps. REMs were frequently observed without atonia even in the early stages of nocturnal sleep. Tonic and phasic REM sleep occupied 62% of sleep time (Table 1, Fig. 1). HLA was positive for DR15[2)] as seen in typical idiopathic narcolepsy. CSF hypocretin concentration was very low (86 pg/ml, normal range >200 pg/ml). We had started methyl-

Correspondence : Takashi Kanbayashi, M.D.
Department of Neuropsychiatry, Akita University Graduate School of Medicine, 1-1-1 Hondo, Akita 010-8543, Japan
Tel : 81-18-884-6122
Fax : 81-18-884-6445
E-mail : takashik@psy.med.akita-u.ac.jp

Table 1. Sleep parameters of polysomnography.

Time in bed	8 : 02 : 00
Sleep period time	7 : 54 : 30
Total sleep time	6 : 29 : 30
Sleep efficiency	80.8%
Number of awakening	34
Wake after sleep onset	81 : 00
Sleep latency	0 : 02 : 30
REM latency	0 : 03 : 00
	(%SPT)
Wake	17.1%
Stage 1-REM	50.4%
Stage 2-REM	11.7%
Stage 1	14.2%
Stage 2	5.6%
Stage 3-4	0%
Movement Time	0.8%
Apnea-Hypopnea Index	0.0
Arousal index	7.8
Periodic Leg Movement Index	11.1
PLM arousal index	0.2

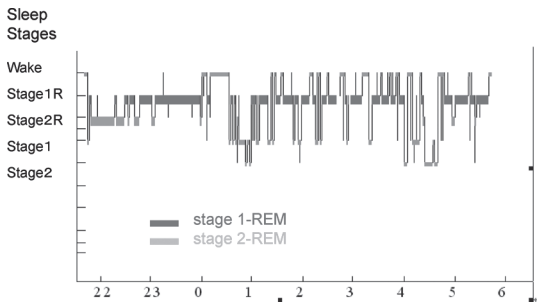

Fig. 1. Hypnogram of the patient at the diagnosis of narcolpesy.
The polysomnography showed no slow wave sleep (delta waves). REM without atonia appeared in all sleep stages, even when spindles showed. On the video monitor, sleep talking and arm movements were observed at REM sleep. These phenomena were seen in REM sleep behavior disorders.

phenidate (MPH) for EDS in addition to medications for PD. During the next two years, the condition was good. Thereafter, he became delusional and suffered from auditory hallucinations. We stopped MPH and some other medications for PD and used anti-psychotics. However, the serious psychotic symptoms persisted. Finally he was treated by mECT in addition to anti-psychotics with good outcome. He is now continuously treated with anti-psychotics and maintenance mECT every month.

Discussion

In recent studies[2-5], CSF hypocretin levels were reported as normal in PD with EDS. In contrast to these results, our case presented a low CSF hypocretin level (maeda). This was the first reported case of hypocretin deficient narcolepsy accompanied with PD (maeda). Thereafter, this case has developed psychiatric symptoms.

Several reports say symptoms of psychosis and narcolepsy occur in the same individual[6-9]. Psychosis in patients with narcolepsy can occur in three ways ; (a) as the psychotic form of narcolepsy with hypnagogic and hypnopompic hallucinations ; (b) as a result of psycho-stimulant use in a patient with narcolepsy ; and (c) as the concurrent psychosis of schizophrenia in a patient with narcolepsy[6-9]. This case had serious psychotic symptoms rather than REM sleep related symptoms (hypnogogic and hypnopompic hallucinations) or side effects of psycho-stimulants (persistent hallucinations and delusions without sleep relation). We are wondering if his diagnosis is late onset schizophrenia or not. Since we could not use enough anti-psychosis due to his PD, mECT was selected for controlling his psychosis which resulted in good outcome. There have been several reports of mECT for patients with PD and psychosis[10-13]. Since there have been no reports of narcolepsy cases treated with mECT, this patient is thought to be the first case. His mental and parkinsonian symptoms have been stable for several years. Physicians should be aware that psycho-stimulants and anti-PD medications commonly prescribed for treatment of narcolepsy and PD may precipitate psychosis in those patients.

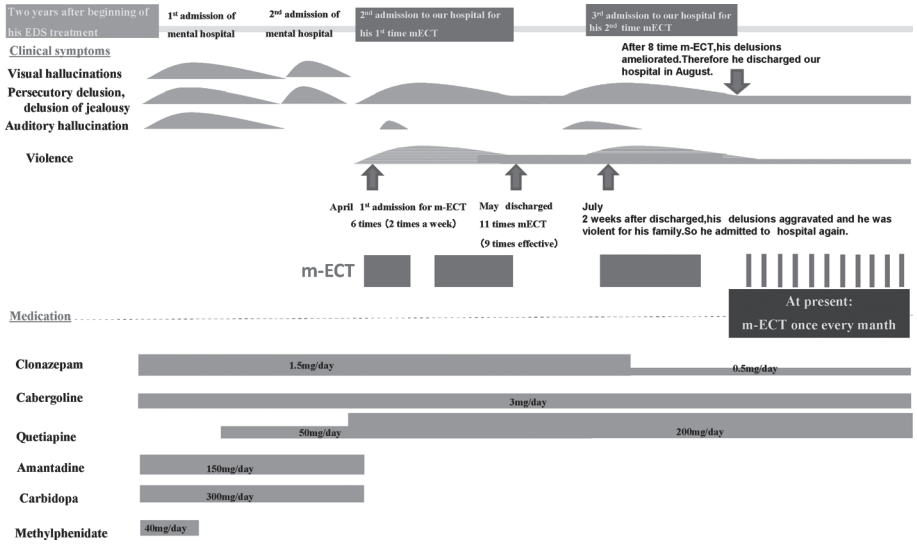

Fig. 2(a). Clinical course of this case. Two years after beginning his EDS treatment.
He developed psychiatric symptoms two years after stimulant medication. He experienced visual and auditory hallucinations, and persecutory and jealousy delusions occurred. He was admitted to state mental hospital for several times. Methylphenidate (MPH) was stopped and anti-psychotics were started. Although his symptoms disappered during his stay in the hospital, those symptoms reoccurred after discharge.
Fig. 2(b). 2nd admission to our hospital for initial mECT.
After discharge from state mental hospital, persecutory and jealousy delusions reoccurred. Violence against his family also appeared. He was referred to university hospital for considering mECT. He was treated using mECT 17 times with good outcome. He was discharged after two months admission.
Fig. 2(c). Subsequently 2nd admission and maintenance mECT.
Soon after his discharge, his delusions aggravated and he became violent against his family. Therefore, he was admitted to hospital again. His delusions ameliorated by treating him with mECT 8 times. He is continuously treated by mECT every month with anti-psychoties. His mental and parkinsonian symptoms have been stable for several years.

References

1) Maeda, T., Nagata, K., Kondo, H. and Kanbayashi, T. (2006) Parkinson's disease comorbid with narcolepsy presenting low CSF hypocretin/orexin level. *Sleep Med*., **7**(8), 662.
2) Ripley, B., Overeem, S., Fujiki, N., *et al*. (2001) CSF hypocretin/orexin levels in narcolepsy and other neurological conditions. *Neurology,* **57**, 2253-2258.
3) Yasui, K., Inoue, Y., Kanbayashi, T., Nomura, T., Kusumi, M. and Nakashima, K. (2006) CSF orexin levels of Parkinson's disease, dementia with Lewy bodies, progressive supranuclear palsy and corticobasal degeneration. *J. Neurol. Sci.,* **250**(1-2), 120-123.
4) Fronczek, R., Overeem, S., Lee, S.Y., Hegeman, I.M., van Pelt, J., van Duinen, S.G., Lammers, G.J. and Swaab, D.F. (2007) Hypocretin (orexin) loss in Parkinson's disease. *Brain*, **130**(Pt 6), 1577-1585.
5) Asai, H., Hirano, M., Furiya, Y., Udaka, F., Morikawa, M., Kanbayashi, T., Shimizu, T. and Ueno, S. (2009) Cerebrospinal fluid-orexin levels and sleep attacks in four patients with Parkinson's disease. *Clin. Neurol. Neurosurg.,* **111**(4), 341-344.
6) Bhat, S.K. and Galang, R. (2002) Narcolepsy presenting as schizophrenia. *Am. J. Psychiatry*, **159**(7), 1245.
7) Kishi, Y., Konishi, S., Koizumi, S., Kudo, Y., Kurosawa, H. and Kathol, R.G. (2004) Schizophrenia and narcolepsy : a review with a case report. *Psychiatry*

Clin. Neurosci., **58**(2), 117–124.

8) Kondziella, D. and Arlien-Soborg, P. (2006) Diagnostic and therapeutic challenges in narcolepsy-related psychosis. *J. Clin. Psychiatry,* **67**(11), 1817–1819.

9) Fortuyn, H.A., Lappenschaar, G.A., Nienhuis, F.J., Furer, J.W., Hodiamont, P.P., Rijnders, C.A., Lammers, G.J., Renier, W.O., Buitelaar, J.K. and Overeem, S. (2009) Psychotic symptoms in narcolepsy : phenomenology and a comparison with schizophrenia. *Gen. Hosp. Psychiatry*, **1**(2), 146–154.

10) Zahodne, L.B. and Fernandez, H.H. (2008) Pathophysiology and treatment of psychosis in Parkinson's disease : a review. *Drugs Aging*., **25**(8), 665–682.

11) Fregni, F., Simon, D.K., Wu, A. and Pascual-Leone, A. (2005) Non-invasive brain stimulation for Parkinson's disease : a systematic review and meta-analysis of the literature. *J. Neurol. Neurosurg. Psychiatry*, **76**(12), 1614–1623. Review.

12) Höflich, G., Burghof, K.W., Kasper, S. and Möller, H.J. (1994) Electroconvulsive therapy in comorbidity of treatment refractory paranoid hallucinatory psychoses with Parkinson disease. *Nervenarzt*, **65**(3), 202–205.

13) Asnis, G. (1977) Parkinson's disease, depression, and ECT : a review and case study. *Am. J. Psychiatry*, **134**(2), 191–195.