Brain Metabolic Changes of Cervical Dystonia with Spinocerebellar Ataxia Type 1 after Botulinum Toxin Therapy

VII. 3. Brain Metabolic Changes of Cervical Dystonia with Spinocerebellar Ataxia Type 1 after Botulinum Toxin Therapy

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Cervical dystonia is characterized by involuntary abnormal movements and postures of the head and neck. We often experience long-term remission of cervical dystonia after several botulinum toxin treatments [1)]. To confirm whether botulinum toxin acts on the central level[2-5)] as well as neuromuscular junctions, we study the changes of brain metabolism in a cervical dystonia patient with spinocerebellar ataxia type 1 (SCA1) before and after botulinum toxin A (BTX-A) therapy using ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)[1)].

A 33-year-old man was hospitalized with severe fixed retrocollis, very mild cerebellar ataxia and pyramidal tract sign. Sensory trick, stereotype, and task specificity were observed. Brain MRI showed mild atrophy in the cerebellum and pons. Genetic analysis revealed expanded 49 CAG repeats in the SCA1 gene. An initial FDG-PET study was performed one month after the initial BTX-A treatment. His retrocollis exhibited dramatic and sustained improvement after several BTX-A treatments and was still improved 9 months after the last BTX-A treatment. A second FDG-PET study was then performed. The time difference between the first and second scans was 20 months. The types and doses of drugs were the same in the two FDG-PET studies.

We compared the FDG PET findings of this patient before or after BTX-A therapy to those of 18 age-matched normal controls. Two-sample t-tests were used for comparisons between the normal controls and the patient before and after BTX-A therapy using SPM5 software. The statistical threshold was set at family-wise error (FWE) $p<0.001$. The study protocol was approved by the Ethical Committee of Tohoku University Graduate School of

Medicine and a written informed consent was obtained from each subject after a complete description of the study. In the initial FDG-PET study, this patient showed hypermetabolism in the bilateral putamen and primary sensorimotor cortex compared to the 18 normal subjects. After the BTX-A therapy, most of the hypermetabolism in the bilateral putamen and primary sensorimotor cortex disappeared in this patient compared to in the normal group.

Because the frequency of dystonia in SCA1 patients is about 0 to 15%[6-8], cervical dystonia may be a presenting symptom in some patients with SCA1. Cervical dystonia showed a significant hypermetabolism in the lentiform nucleus[9] or the putamen[10] compared to normal controls using FDG PET. The cervical dystonia in this patient could be dramatically improved by the depression of hypermetabolism in the bilateral putamen and primary sensorimotor cortex after several BTX-A treatments. Therefore, the overactivities of bilateral putamen and primary sensorimotor cortex may be one of the most important factors for the pathogenesis of cervical dystonia with SCA1.

Cervical dystonia in this patient was improved in the long-term after several BTX-A treatments. BTX-A may act on the central nervous system (CNS) through afferent pathways from the injected site[2]. This patient is the first report to demonstrate that hypermetabolism in the bilateral putamen and primary sensorimotor cortex in cervical dystonia returns to normal after BTX-A therapy. We suggest that BTX-A has some effects on the CNS level to cause normalization in basal ganglia circuits and prolonged improvement[1].

References

1) Kikuchi A., Takeda A., Sugeno N., Miura E., Kato K., Hasegawa T., Baba T., Konno M., Oshima R., Watanuki S., Hiraoka K., Tashiro M. and Aoki M., Intern. Med. **55** (2016) 1919.
2) Giladi N., J. Neurol. Sci. **152** (1997) 132.
3) Kanovsky P., Streitova H., Dufek J., Znojil V., Daniel P. and Rektor I., Mov. Disord. **13** (1998) 108.
4) Ceballos-Baumann A.O., Sheean G., Passingham R.E., Marsden C.D. and Brooks D.J., Brain. **120** (1997) 571.
5) Etgen T., Muhlau M., Gaser C. and Sander D., J. Neurol. Neurosurg. Psychiatry. **77** (2006) 1017.
6) Lee W.Y., Jin D.K., Oh M.R., Lee J.E., Song S.M., Lee E.A., Kim G.M., Chung J.S. and Lee K.H., Arch. Neurol. **60** (2003) 858.
7) Pareyson D., Gellera C., Castellotti B., Antonelli A., Riggio M.C., Mazzucchelli F., Girotti F., Pietrini V., Mariotti C. and Di Donato S., J. Neurol. **246** (1999) 389.
8) Sasaki H., Fukazawa T., Yanagihara T., Hamada T., Shima K., Matsumoto A., Hashimoto K., Ito N., Wakisaka A. and Tashiro K., Acta. Neurol. Scand. **93** (1996) 64.
9) Magyar-Lehmann S., Antonini A., Roelcke U., Maguire R.P., Missimer J., Meyer M. and Leenders K.L., Mov. Disord. **12** (1997) 704.
10) Galardi G., Perani D., Grassi F., Bressi S., Amadio S., Antoni M., Comi G.C., Canal N. and Fazio F., Acta. Neurol. Scand. **94** (1996) 172.