Anticholinergic activity disappears soon after the prescription of cholinesterase inhibitor

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Abstract

In this article we present the 80 years of woman patient who showed delusion, hallucination and excitement at night, those were thought to be related with the toxicity of anticholinergic activity (AA). These symptoms were resolved soon after by the prescription of Aricept® which is cholinomimetic agent. Because the disappearance of AA is relatively short time, we speculated that the disappearance of AA was related rather directory with upregulation of acetylcholine (ACh) not with antagonizing with AA by upregulation of ACh. From these speculation we are more convinced of the existence of our hypothesis, i.e., an ‘endogenous anticholinergic cascade’.

Abbreviations: AA: anticholinergic activity; ACh: acetylcholine; AD: Alzheimer’s disease; ChEI: cholinesterase inhibitor; LBD: Lewy body disease; SAA: serum anticholinergic activity

Introduction

We previously proposed the hypotheses of “endogenous appearance of Anticholinergic activity (AA) in Alzheimer’s disease (AD) [1,2] and in Lewy body disease (LBD) [3]. However, these hypotheses are merely “hypotheses”. Therefore it is needed to prove these hypotheses. Recently, Yilmaz et al. [4] presented the case of a 19-year-old male who was brought to the emergency room for initial complaints of restlessness who was later diagnosed with intoxication of anticholinergic toxicity by herb medicine. Two milligrams of physostigmine were administered, which caused sudden recovery from the symptoms. From this case report, we are convinced of the existence of an ‘endogenous anticholinergic cascade [1,2,5]’ (Figure 1; courtesy of Hori et al. [5]). We also experienced the 80 years of woman patient whose clinical symptoms, those were thought to be related with AA, were resolved soon after by the prescription of Aricept® which is also cholinomimetic agent. In this article we present the case because we are more convinced of the existence of our hypothesis, i.e., an ‘endogenous anticholinergic cascade [1,2,5]’. The patient and her proxy have provided written consent authorizing publication of this report.

Case presentation

Patients was 80 years old woman when she visited our hospital at first time (X years and Y months). At X-20 years she felt digital numbness and anxiety after cerebral hemorrhage. Therefore, she was prescribed 2mg of etizolam. At X-3 years she also felt apathetic for cleaning her room. At X-2 years she was token mischief by neighborhood for some time. She has been delirious about her neighborhood. This delusion had been continued, therefore, at X years and Y months, she has been visited our hospital. We advised her to stop etizolam, but she could not stop because of her anxiety. She was also prescribed famotidine, however, true reason for this was not unknown. Even after visiting our hospital, she called for police because of mischief by neighborhood. Due to not ameliorating her symptoms, she was admitted to our hospital at X years and Y+1 months. We aimed to provide feeling of safety by separating her form her neighborhood and to adjust her medicines. We stopped her etizolam suddenly and prescribed 25 mg of quetiapine because etizolam poses anticholinergic property. However, her delusions had continued and she had exited, spoke loudly and was aggressive against the other patients and had been need to be restrained at night. In spite of this excitement at night, she had been relatively calm at daytime. She had seen her son who didn’t visit the hospital. We started to prescribe 3 mg of Aricept® at X years, Y+1 months and 14 days and increased Aricept® 5mg after 2 weeks. Next day of the prescription of Aricept® 3mg, she said “I mistook to think my neighborhood mischief and my son to come to the hospital”. Her symptoms of delusion, hallucination and excitement at night were disappeared since then. The score of mini-mental state examination (MMSE) [6,7] was 23 at study entry and the examination of cardiac 123-I-metaiodobenzylguanidine uptake and the examination of cardiac 123-I-metaiodobenzylguanidine uptake and

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Key words: acetylcholine (ACh), anticholinergic activity (AA), endogenous anticholinergic activity

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behavioral and psychological symptoms of dementia, NMDA: N-methyl-D-aspartate, AA: anticholinergic activity, cholinergic system. We call this vicious cycle an “endogenous AA cascade.”

AA was induced by other AA insert based on the base of downregulation of ACh. AA was reported that medication [16], physical illness [17] or mental stress [18] causes AA. However, we speculated that when the ACh system is intact and not depressed or overloaded, upregulation of ACh is possible even if another AA insert is present. Consequently, the inflammatory system is not upregulated, and AA does not appear [1]. Medicine with AA caused AA toxicity in patient of Yilmaz et al. and mental stress we speculated caused AA toxicity in our patient of course based on the not full intact ACh system. Thirdly Our patient was also suddenly ameliorated by the prescription of Aricept® because on the next day of first prescription of Aricept® clinical symptom related with AA in our patient disappeared, which is also similar with the patient in Yilmaz et al. Because the disappearance of AA is relatively short time in the patient of Yilmaz et al. and our patient, we speculated that the disappearance of AA was related rather directory with upregulation of ACh not with antagonizing with AA by upregulation of ACh. If the disappearance of AA had been related with antagonizing with AA by upregulation ACh, repetitive and relative long term of the prescription of cholinesterase inhibitors were needed. From these speculations we are more convinced of the existence of our hypothesis, i.e., an ‘endogenous anticholinergic cascade [1,2,5]’.

Our study had main two limitations. Firstly we didn’t measure SAA in this patient. Therefore the toxicity of AA was not definitely done in our patient. Secondary from the clinical features and MIBG findings that showed mild dysfunction of autonomic nervous system, we diagnosed her LBD. However, AD and stress response were not finally denied. Based on the diagnosis of LBD, we prescribed her Aricept®. In Japan only Aricept® (original medicine of donepezil) is permitted for LBD. The generic medicines of donepezil are not permitted for LBD. Nevertheless, our patient is precious case that suggested ‘endogenous anticholinergic cascade’ as with the patient of Yilmaz et al.

Conflict of interest

Koji Hori received lecture fees from Eisai Co. Ltd., Pfizer Japan Inc., Novartis Pharma KK, Daiichi Sankyo Inc., Ono Pharmaceutical Co. Ltd., Janssen Pharmaceutical KK, Yoshitomi Yakuhin Co. Meiji Seika Pharma Co. Ltd., and Mitsubishi Tanabe Pharma Co. Mitsugu Hachisu received lecture fees from Meiji Seika Pharma Co. Ltd. and Mitsubishi Tanabe Pharma Co. However, the sponsors had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Disclosure statement

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Author contributions

Taishi Koganemaru was chief doctor for this patient. Koji Hori mainly coordinates the study regarding to anticholinergic activity. Misa Hosoi, Kimiko Konishi, Mitsugu Hachisu, Hiroi Tomioka, Masayuki Tani, Yuka Kitajima all members in Showa University Dementia Study Group and checked this manuscript. Hiroi Tomika advised and orgernized the clinical practice of this patient. Kimiko Konishi, Mitsugu Hachisu, Hiroi Tomioka, Masayuki Tani, and Yuka Kitajima wrote articles related with AA before. Atsuko Inamoto is chief professor in Showa University Northern Yokohama Hospital Department of Psychiatry also advised and orgernized the clinical practice of this patient and checked this manuscript.
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