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Case Report

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Remission Induction of Spinocerebellar Ataxia 6 with Medicinal Herbs

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Abstract

The spinocerebellar ataxias (SCAs) are clinically and genetically a heterogeneous group of neurodegenerative disorders. At present, we have no effective therapeutic tools. Previous studies have shown for the first time, the successful treatment of spinocerebellar ataxia by medicinal herbs [1,2]. Here we report the herbal therapy for another case of spinocerebellar ataxia 6 with typical symptoms. A 71-year-old female suffered from ataxia of gait and stance, limb ataxia and dysarthria. Genetic tests revealed an expanded allele of 22 CAG repeats at the spinocerebellar ataxia type 6 locus. She was diagnosed as spinocerebellar ataxia 6. A mixture of 21 medicinal herbs (a modification of Zhengan Xifeng Tang) was given according to the differential diagnosis based on the guideline of traditional Chinese medicine. Most of the symptoms were remarkably improved after 60 days of the herbal treatment. Ataxia of gait and stance disappeared, and her total ataxia score was improved from 26 to 12 on a 100-point semi-quantitative International Cooperative Ataxia Rating Scale (ICARS). Together with the previous report, the results imply therapeutic potential of the medicinal herbs for spinocerebellar ataxia 6.

Introduction

The spinocerebellar ataxias (SCAs) are clinically and genetically a heterogeneous group of neurodegenerative disorders. Although transient improvement of the ataxia with thyrotropin-releasing hormone, branched-chain amino acid, or zolpidem have been reported [3-5], we have no effective therapeutic tools against the degenerative diseases. Previous studies for the first time, have demonstrated the successful treatment of two cases of spinocerebellar ataxia 6 by systems therapy with medicinal herbs [1,2]. The remedy used for these cases consists of different types of herbs such as sedative, anticonvulsive, neuroprotective, neuroregulatory and DNA binding herbs. Most of the symptoms were remarkably improved after 60 days of the initial herbal treatment. Even after the first or the second relapse, the neurological symptoms were markedly improved with the herbal therapy within 60 days [1]. In order to see whether the herbal therapy could be effective against the other cases of SCA6, medicinal herbs (a modification of Zhengan Xifeng Tang) [1,2] were given for another patient with SCA6. We report here another successful treatment of SCA6 with the medicinal herbs.

Case Report

A 71-year-old female suffered from titubation, loss of balance and dysarthria was diagnosed as spinocerebellar ataxia. Dysarthria and loss of balance had gradually progressed until she could not walk well for these three years. Tendon reflexes were not increased. Considerably slow and dysarthric speech and definite slurring were observed. Mild ataxia was found on the lower extremities but not on the upper extremities. There were slight abnormalities of ocular saccadic pursuit. Autonomic disorders were not found. To identify various subtypes of spinocerebellar ataxias(SCAs), SCA1, SCA2, DRPLA (Dentatorubral-pallidoluysian atrophy), SCA3/MJD (Machado-Joseph disease), SCA6, SCA7, SCA8, SCA10 and SCA17 loci were assessed for expansion of trinucleotide repeats. Analysis of the SCA6 CAG tri nucleotide repeat at the CACNA1A gene in the patient's DNA demonstrated an expanded allele of 22 CAG repeat units [6,7]. The results of all other testing of DNA repeat expansion mutations associated with 9 different ataxias were within normal ranges. She was diagnosed as SCA6. For the systems therapy with medicinal herbs, the differential diagnosis by traditional herbal medicine was made according to the guideline [8]. A mixture of 21 medicinal herbs (Uchida Wakanyaku Co. Ltd, Tokyo, Japan) (a modification of Zhengan Xifeng Tang) was boiled and the supernatant was administered three times a day for 60 days (Table 1), which was expected to stabilize central nervous system and usually used against tremor, vertigo, or ataxia in traditional Chinese medicine [2]. Most of the symptoms including gait ataxia

and titubation were remarkably improved after 60 days of the treatment. Dysarthric speech and slurring was slightly improved but not completely recovered to normal. Total ataxia score was improved from 26 to 12 on a one-hundred-point semi-quantitative International Cooperative Ataxia Rating Scale (ICARS) [9]. Score for postural and a gait disturbance (Test No. 1-7) was reduced from initial score of 9/34 to 0/34 (Figure 1). Limb ataxia score (Test No. 8-14) was decreased from 12/52 to 7/52. However, disarthria score (Test No.15,16) was not apparently improved after the herbal treatment (5/8). To consolidate the effect of the medicinal herbs, the same remedy was given for another 60 days. No adverse effects were observed.

S. No	Ingredients of Modified Zhengan Xifeng Tang (G)
1	*Achyranthes bidentatae* Blume root (6)
2	*Plasrum testudinis* (smashed)(6)
3	*Fossilia ossis mastodi* (smashed) (6)
4	*Concha ostreae* (smashed) (6)
5	*Gasrodia elata* Bl root (4)
6	*Uncaria rhynchophylla* Jacks stem with hooks (4)
7	*Paeonia lactiflora* Pall root (8)
8	*Asparagus cochinchinensis* Merr root (3)
9	*Ophiopogon japonics* Ker-Gawl root (3)
10	*Scrophularia ningpoensis* Hemsl root (4)
11	*Rhemannia glutinosa* Libousch root (4)
12	*Melia toosendan* Sieb et Zucc fruit (3)
13	*Paeonia suffruticosa* Andr bark (6)
14	*Angelica sinensis* Diels root (4)
15	*Coptis chinensis* Franch root (3)
16	*Salvia miltiorrhiza* Bge root (3)
17	*Fritillaria thnbergii* Miq root (4)
18	*Magnolia officinalis* Rehd et Wils bark (3)
19	*Chaenomeles lagenaria* Koidz fruit (3)
20	*Platycodon grandiflorum* A.DC root (3)
21	*Glycyrrhiza uralensis* Fisch root (2)
21 ingredients were boiled in 800 ml of water for 30 min. The supernatant was Given three times a day between meals and before sleep.	

Table 1: Ingredients of Modified Zhengan Xifeng Tang (g).

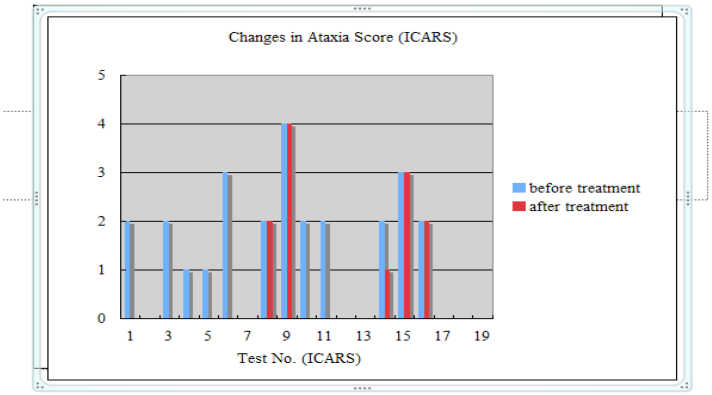

Figure 1: Changes in ataxia score before and after herbal treatment. ICARS are consists of 19 items with 4 subscales (Posture and Gait Disturbance, Kinetic Function, Speech Disorder, Oculomotor Disorders) which are popular tests for assessment of ataxia described in [9].

Discussion

A case of SCA6 was successfully treated with a mixture of 22 medicinal herbs (a modification of Zhengan Xifeng Tang). Most of the symptoms dramatically improved after 60 days of the treatment. Most of the ingredients included in the recipe were common to those used for the first case of SCA6 in our previous report [1,2].

The remedy used for this case consists of several different ingredients, which have well-established histories of use for treatment of vertigo, tremor, and ataxia in Asian countries and are expected to exert their specific effects [2]. The ingredients include sedative, anticonvulsive, neuroprotective, neuroregulatory and DNA binding herbs. The formula is chemically quite complex with hundreds of constituents. While the exact chemical nature and interaction of all these constituents are not well known, the following bioactivities have been demonstrated in the ingredients of this formula. An anticonvulsive herb, *Gastrodia elata*, a component of our modified Zhengan Xifeng Tang has been shown to protect against kainic acid-induced neuronal damages in the mouse hippocampus [10]. *Uncaria rhynchophylla* Jacks when combined with *Gastrodia elata* exhibited greater anticonvulsive effect in kainic acid treated rats [11]. The methanol exract of *Fossilia Matoidi* OSSIS showed anxiolysis, and anticonvulsive activity in mice [12]. The ethanol extracts of *Paeonia lactiflora* root, another component of the modified Zhengan Xifeng Tang and its active constituents, gallic acid and methyl gallate, exhibited a significant free radical scavenging effect against 1,1-diphenyl-

2-picryl hydrazine radical generation and had an inhibitory effect on lipid peroxidation. In addition, they strongly inhibited the hydrogen peroxide-induced DNA damage in mammalian cells [13]. Recently, paeoniflorin, a major active constituent of *Paeonia lactiflora* has been shown to attenuate neuroinflammation and doperminergic neurodegeneration by activation of adenosine A1 receptor [14]. Berberine, a major alkaloid component contained in *Coptis chinensis* Franch had neuroprotective actions against in vitro ischemia-induced neuronal cell damage in organotypic hippocampal slice cultures [15]. Alkaloid fraction of *Uncaria rhynchophylla* was shown to have a protective property against N-Methyl-D-aspartate (NMDA)-induced cytotoxicity by suppressing the NMDA-induced apoptosis in rat hippocampal slices [16]. In addition, Polygalae radix extracts have been shown to inhibit NMDA-induced neuronal cell death in rat cerebellar granule neurons [17]. Together with these observations, it is possible to consider that some herbs in this modified Zhengan Xifeng Tang exert their therapeutic effects through their anticonvulsive and neuroprotective activities against neuronal degeneration in cerebellum. Recently, SCA6 has been demonstrated to be an autosomal dominant cerebellar ataxia associated with small polyglutamine-dependent expansions in the alpha 1A-voltage calcium channel [6]. Berberine, palmatine and jatrorrhizine, major constituents of *Coptis chinensis* Franch have been shown to bind calf thymus DNA [18]. Berberine binds to human telomeric DNA as G-quadruplex stabilizing ligand [19]. Further extensive investigations are required to clarify the mechanisms by which the remission induction of this genetic disease of CAG repeat expansion mutation, has been attained with the medicinal herbs. Anyway, together with our previous reports [1,2], the findings of the present case imply the therapeutic potential of herbal medicine for this hereditary neurodegenerative disorder.

Conflict of Interest Statement: None Declared

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