

Spinocerebellar ataxia type 2 presenting with chorea: Korean cases

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Abstract

Spinocerebellar ataxia type 2 (SCA2) is an expanded CAG repeat disorder in ATXN2 gene with a wide range of clinical phenotypes. Chorea has been reported as one of extrapyramidal symptoms of SCA2 patients, but has not been reported in Korea. Here, we report two Korean cases of SCA2 presenting with chorea: one showed generalized chorea in young onset SCA2 with 57 CAG repeats, and the other showed mild chorea in the hands in adult onset SCA2 with 40 CAG repeats. This report documents the phenotype of chorea in Korean patients with SCA2.

Keywords: SCA2, Chorea, Korea

INTRODUCTION

Spinocerebellar ataxia type 2 (SCA2) is one of the polyglutamine-encoding CAG expansion disorders, which has dominant pattern of inheritance with genetic anticipation. The pathological repeat size of ATXN2 gene in SCA2 patients is over 33¹, and the repeat length correlates with disease severity and age of onset inversely as in Huntington's disease (HD).² Clinical phenotype of SCA2 is heterogeneous including progressive cerebellar ataxia, extrapyramidal symptoms, slow saccade, hyporeflexia, and dementia. The phenotype variability may relate to the number of polyglutamine repeats, CAA interruption in the middle of the CAG repeat expansions³, somatic mosaicism, genetic backgrounds, or environmental factors.²

Chorea in SCA2 patients has been reported with variable frequencies up to about 15%.⁴ However, no SCA2 cases with choreic manifestation have yet been reported in Korea. As SCA2 is the most common subtype in Korea⁵, it is expected to encounter this rare phenotypic variation in Korean SCA2 patients. Here, we describe two Korean SCA2 patients presenting with chorea: one is a case of generalized chorea in a 15-year-old boy with 57 CAG repeats, and the other is a case of focal chorea in 46-year-old man with 40 CAG repeats in ATXN2 gene.

CASE REPORTS

Case 1

A 15-year-old boy visited for second opinion, who had been diagnosed with SCA2 with 57 CAG repeats. At his age of 7, gait disturbance and cognitive impairment appeared and progressed. At age 10, neurologic examination revealed cognitive impairment, dysarthria, myoclonus, and ataxic gait. He showed neither parkinsonism nor dystonia. Levodopa was of no benefit. Other medications were tried including amantadine, procyclidine, baclofen, clonazepam, midodrine, buspirone, alprazolam, quetiapine, or fluvoxamine. Brain magnetic resonance (MR) image at 14 years old showed severe atrophy in the cerebellum and brain stem with mild, diffuse atrophy in the cerebrum.

His mother had trouble walking from her late 30s and developed slowly progressive dysarthria and imbalance. In her neurologic examination at age 37, she had ataxic gait and hypometric saccade with normal velocity. Gene test showed 39 CAG repeats in ATXN2. Follow-up examination showed slow saccade in her early 40s. The grandmother of the proband reportedly had gait problem in her old age.

At age 15, the patient became wheelchair-bound with severe cognitive impairment and hallucination. At this stage, severe generalized chorea with ataxia was his predominant symptoms. Choreic movements involved the whole body

including face, neck, trunk, and four extremities, which were exacerbated during speaking, outstretching the arms, or standing up.

Case 2

A 42-year-old man presented with clumsiness in the right arm and gait difficulty, which were slowly progressive. His mother had gait disturbance before she died at her age of 54, but she was not studied. Neurologic examination showed dysarthria, slow saccade, dysmetria, and ataxic gait. Brain MR showed moderate to severe atrophy in the cerebellum and pons. SCA2 was confirmed with 40 CAG repeats in the *ATXN2* gene. He had no other medical history and did not take any drugs during the 4 years of follow-up period. At age 46, he developed mild chorea in his right hand, which did not impair activities of daily living. Choreic movements were more prominent during walking and worse in the right hand than the left.

DISCUSSION

Spinocerebellar ataxias (SCAs) manifest ethnic and geographical differences in frequency, and clinical phenotypes, which may affect diagnosis and medical decisions. Understanding various phenotypes of genetic disorders is essential to diagnose early and prevent further transmission to the next generation.

Hamani *et al.* suggested pathophysiology of chorea as hypoactivity of subthalamic nucleus and increased neuronal activities of globus pallidum.⁶ Chorea in SCA2 patients could be explained by neuronal loss in basal ganglia-thalamocortical loop that were demonstrated in previous pathologic studies.¹ Clinical study with 163 SCA2 patients showed that the CAG repeat length was associated with chorea/dyskinesia in SCA2 patients.⁷ Supporting this, our young-onset patient with 57 CAG repeats showed severe generalized chorea whereas middle-aged-onset patient with 40 CAG repeats presented mild focal chorea. Different severity of chorea between two patients may result from different CAG repeat length.

While several studies reported frequency of choreic movement in SCA2 patients among large-scale western populations^{7,8}, few studies described chorea as a clinical feature of SCA2 in the Asian populations. For example, a study in Thailand reported that none showed chorea among unrelated 15 SCA2 patients.⁹ One of the Indian studies showed that 2 of 28 (7.1%) SCA2 patients presented chorea.¹⁰ Studies in Japanese SCA2

patients reported that choreiform movements were seen in 3 of 28 (11%) early-onset young patients in one study¹¹, and in 2 of 12 (17%) patients in the advanced stage in the other study.¹² Therefore, chorea has been reported with variable frequencies in small-scale Asian groups with SCA2.

In conclusion, we report two cases of SCA2 patients presenting generalized and focal chorea which supports a wide spectrum of phenotypes of SCA2 in Korea.

DISCLOSURE

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REFERENCES

1. Rüb U, Schöls L, Paulson H, *et al.* Clinical features, neurogenetics and neuropathology of the polyglutamine spinocerebellar ataxias type 1, 2, 3, 6 and 7. *Prog Neurobiol* 2013;104:38-66.
2. Geschwind DH, Perlman S, Figueroa CP, Treiman LJ, Pulst SM. The prevalence and wide clinical spectrum of the spinocerebellar ataxia type 2 trinucleotide repeat in patients with autosomal dominant cerebellar ataxia. *Am J Hum Genet* 1997;60:842-50.
3. Kim JM, Hong S, Gyoung PK, *et al.* Importance of low-range CAG expansion and CAA interruption in SCA2 parkinsonism. *Arch Neurol* 2007;64:1510-8.
4. Pedroso JL, Braga-Neto P, Escorcio-Bezerra ML, *et al.* Non-motor and Extracerebellar Features in Spinocerebellar Ataxia Type 2. *Cerebellum* 2017;16:34-9.
5. Kim HJ, Jeon BS, Lee WY, *et al.* SCA in Korea and its regional distribution: A multicenter analysis. *Parkinsonism Relat Disord* 2011;17:72-5.
6. Hamani C, Saint-Cyr JA, Fraser J, Kaplitt M, Lozano AM. The subthalamic nucleus in the context of movement disorders. *Brain* 2004;127:4-20.
7. Schmitz-Hübsch T, Coudert M, Bauer P, *et al.* Spinocerebellar ataxia types 1, 2, 3, and 6. *Neurology* 2008;71:982-9.
8. Rossi M, Perez-Lloret S, Cerquetti D, Merello M. Movement disorders in autosomal dominant cerebellar ataxias: A systematic review. *Mov Disord Clin Pract* 2014;1:154-60.
9. Boonkongchuen P, Pongpakdee S, Jindahra P, *et al.* Clinical analysis of adult-onset spinocerebellar ataxias in Thailand. *BMC Neurol* 2014;14:1-9.
10. Jhunjhunwala K, Netravathi M, Purushottam M, Jain S, Pal PK. Profile of extrapyramidal manifestations in 85 patients with spinocerebellar ataxia type 1, 2 and 3. *J Clin Neurosci* 2014;21:1002-6.
11. Sasaki H, Wakisaka A, Sanpei K, *et al.* Phenotype variation correlates with CAG repeat length in SCA2 - A study of 28 Japanese patients. *J Neurol Sci* 1998;159:202-8.
12. Sasaki H, Fukazawa T, Wakisaka A, *et al.* Central phenotype and related varieties of spinocerebellar ataxia 2 (SCA2): a clinical and genetic study with a pedigree in the Japanese. *J Neurol Sci* 1996;144:176-81.