Clinical Characteristics, Radiological Features and Gene Mutation in 10 Chinese Families with Spinocerebellar Ataxias

Jian-Wen Chen[1], Li Zhao[1], Feng Zhang[1], Lan Li[2], Yu-Hang Gu[1], Jing-Yuan Zhou[1], Hui Zhang[1], Ming Meng[1], Kai-Hua Zhang[1], Wei-Dong Le[1,3], Chun-Bo Dong[1]

[1]Department of Neurology, The First Affiliated Hospital of Dalian Medical University, Dalian 116011, China
[2]Department of Neurology, The Second Affiliated Hospital of Dalian Medical University, Dalian 116023, China
[3]Center for Translational Research of Neurology Diseases, 1st Affiliated Hospital of Dalian Medical University, Dalian 116021, China

Abstract

Background: Spinocerebellar ataxias (SCAs) are a group of neurodegenerative disorders that primarily cause the degeneration in the cerebellum, spinal cord, and brainstem. We study the clinical characteristics, radiological features and gene mutation in Chinese families with SCAs.
Methods: In this study, we investigated 10 SCAs Chinese families with SCA1, SCA3/Machado–Joseph disease (MJD), SCA7, SCA8. There were 27 people who were genetically diagnosed as SCA, of which 21 people showed clinical symptoms, and 6 people had no clinical phenotype that we called them presymptomatic patients. In addition, 3 people with cerebellar ataxia and cataracts were diagnosed according to the Harding diagnostic criteria but failed to be recognized as SCAs on genetic testing. Clinical characteristic analyses of each type of SCAs and radiological examinations were performed.
Results: We found that SCA3/MJD was the most common subtype in Han population in China, and the ratio of the pontine tegmentum and the posterior fossa area was negatively correlated with the number of cytosine-adenine-guanine (CAG) repeats; the disease duration was positively correlated with the International Cooperative Ataxia Rating Scale score; and the CAG repeats number of abnormal alleles was negatively correlated with the age of onset.
Conclusions: Collectively our study is a systematic research on SCAs in China, which may help for the clinical diagnosis and prenatal screening of this disease, and it may also aid toward better understanding of this disease.

Key words: Genetic Testing; Radiological Features; Spinocerebellar Ataxias; Trinucleotide Repeat Expansion

Introduction

Spinocerebellar ataxias (SCAs) are a group of neurodegenerative disorders that primarily damage the cerebellum, spinal cord and brainstem and are genetically defined as autosomal dominant cerebellar ataxias (ADCAs). According to the predominant neurologic symptoms, there are 4 clinical categories in Harding classification. (1) The typical clinical manifestation of ADCA type I is cerebellar ataxia with ophthalmoplegia, dementia, extrapyramidal and pyramidal signs. It includes SCA1, SCA3/Machado–Joseph disease (MJD), etc. (2) The primary clinical manifestations of ADCA type II are cerebellar ataxia and pigmentary retinal degeneration, along with ophthalmoplegia, dementia and extrapyramidal features. This category includes SCA7. (3) ADCA type III only presents late onset of cerebellar ataxia. This category includes SCA8. (4) ADCA type IV presents cerebellar ataxia, myoclonus and hearing loss.[1-4] Although these clinical classifications provide clues for SCAs detection, the diagnosis and typing depend on genetic testing. More than 40 genetic subtypes have been reported, and the molecular etiologies include cytosine-adenine-guanine (CAG) coding polyglutamine repeat expansions, noncoding repeat expansions, ion-channel dysfunction and disorders of signal transduction.[5,6] SCA1, SCA2, SCA3/MJD, SCA6, SCA7, SCA12, SCA17 and dentatorubral-pallidoluysian atrophy (DRPLA) share the most prevalent form of unstable CAG repeats.[7] However, clinical manifestation and distribution of each SCA subtype differ across regions and ethnicities.[2,8,9] To study the clinical characteristics and different SCA subtypes in China, we investigated 10 families diagnosed with SCAs and analyzed the trinucleotide repeats of SCA1, SCA2, SCA3/MJD, SCA6, SCA7, SCA8, SCA12, and SCA17 and DRPLA, for a total of 9 subtypes.

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Methods

The present study was performed at the First Affiliated Hospital of Dalian Medical University, and all 10 index cases were hospitalized patients in the Department of Neurology.

Address for correspondence: Prof. Chun-Bo Dong, Department of Neurology, The First Affiliated Hospital of Dalian Medical University, Dalian 116011, China
E-Mail: dcb101@sina.com

We collected 50 members of the 10 SCA families, of whom 24 were diagnosed with SCAs clinically (10 males and 14 females, mean age of 45.5 years, range from 12 to 77, and disease duration from 2 to 40 years) and met the Harding diagnostic criteria.[1] The 50 family members underwent neurologic examination, ataxia assessment by International Cooperative Ataxia Rating Scale (ICARS),[10] cognitive testing by Mini-mental State Examination (MMSE)[11] and genetic testing.

After obtaining informed consent, we collected the natural history and peripheral blood samples from the 24 patients, whose inherited ataxia types were not genetically defined, and their relatives. DNA was extracted from the blood samples using the phenol chloroform extracting method. The repeat-containing regions of the genes causing SCA1, SCA2, SCA3/MJD, SCA6, SCA7, SCA8, SCA12, SCA17 and DRPLA were amplified using appropriate primer pairs with polymerase chain reaction (PCR) [Table 1]. Then, 1.5% agarose gel electrophoresis was applied to separate the PCR products, and fragment analysis based on capillary electrophoresis was performed using a CEQ8000 sequencer (Beckman Coulter, Inc., Fullerton, CA, USA).

Statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA), and the Spearman's rank

Table 1: PCR amplification primer sequences for SCA subtypes

SCA subtypes	Locus	Normal repeats	Primer sequences	
			Forward 5'-3'	Reverse 5'-3'
SCA1	6p23	6–44 times (CAG)	5'-AACTGGAAATGTGGACGTAC-3'	5'-CAACATGGGCAGTCTGAG-3'
SCA2	12q24	15–32 times (CAG)	5'-GGGCCCCTCACCATGTCG-3'	5'-CGGGCTTGCGGACATTGG-3'
SCA3	14q32.1	12–44 times (CAG)	5'-CCAGTGACTACTTTGATTCG-3'	5'-TGGCCTTTCACATGGATGTGAA-3'
SCA6	19p13	8–14 times (CAG)	5'-CAGGTGTCCTATTCCCCTGTGATCC-3'	5'-TGGGTACCTCCGAGGGCCGCTGGTG-3'
SCA7	3p14	7–18 times (CAG)	5'-TGTTACATTGTAGGAGCGGAA-3'	5'-CACGACTGTCCCAGCATCACTT-3'
SCA8	13q21	16–37 times (CTA/CTG)	5'-TTTGAGAAAGGCTTGTGAGGACTGAGAATG-3'	5'-GGTCCTTCATGTTAGAAAACCTGGCT-3'
SCA12	5q32	66–78 times (CAG)	5'-TGCTGGGAAAGAGTCGTG-3'	5'-GCCAGCGCACTCACCCTC-3'
SCA17	6q27	29–42 times (CAG)	5'-CCTTATGGCACTGGACTGAC-3'	5'-GTTCCCTGTGTTGCCTGCTG-3'
DRPLA	12p13.31	6–35 times (CAG)	5'-TCAGAGACCCCAGGGAGGGAGACAT-3'	5'-TAGCCAACAGCAATGCCCATCCAG-3'

PCR: Polymerase chain reaction; SCA: Spinocerebellar ataxia; DRPLA: Dentatorubral-pallidoluysian atrophy.

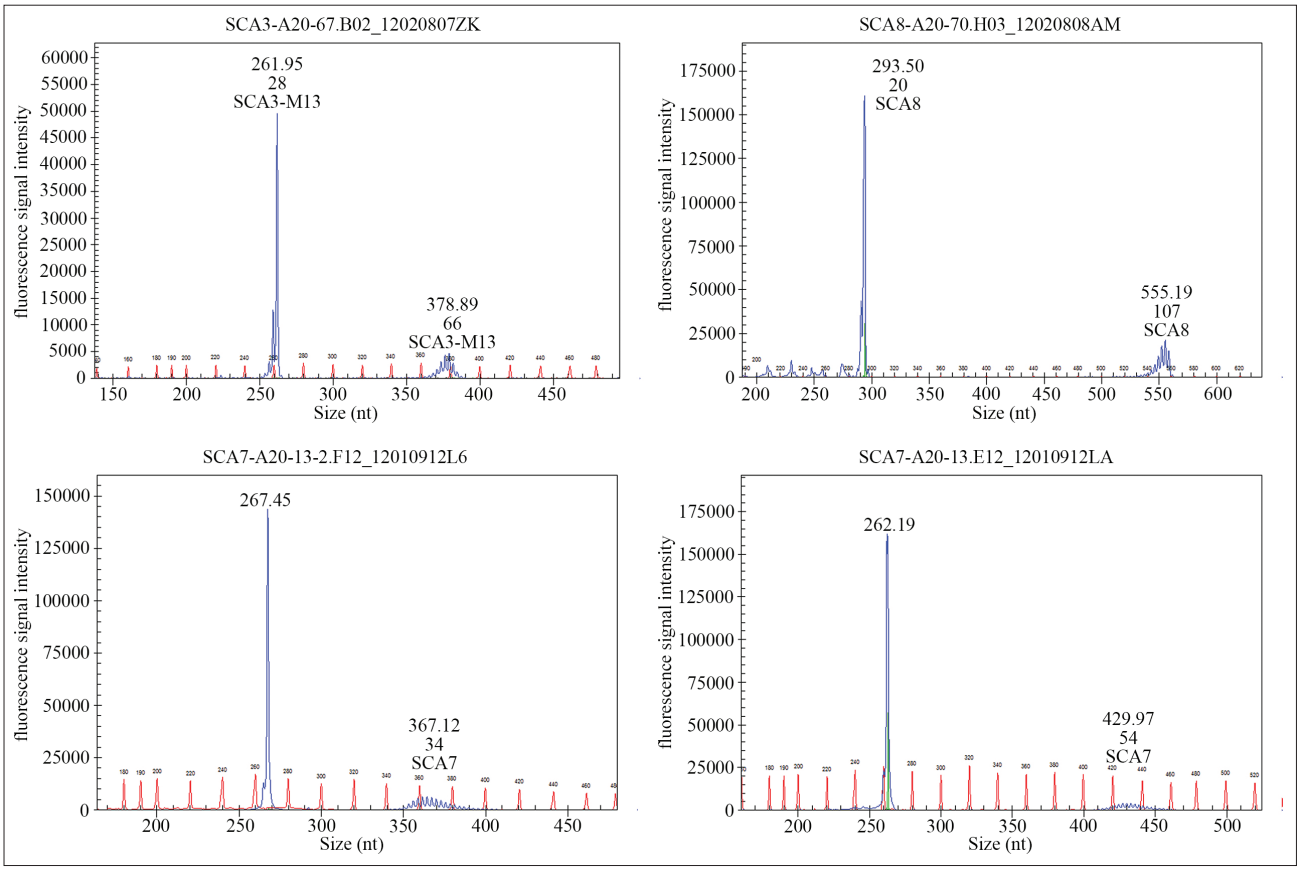

Figure 1: STR results of some spinocerebellar ataxias patients analyzed by fragment analysis of the CEQ8000 sequencer.

correlation (r_s) was used in correlation analyses. $P < 0.05$ was considered as statistically significant.

Results

From molecular genetic analysis, we found 1 SCA1, 6 SCA3/MJD, 1 SCA7, 1 SCA8 and 1 undefined families. Twenty-one people with clinical symptoms were genetically diagnosed as SCAs, and 6 people without clinical phenotype were recognized as presymptomatic patients. Three people with cerebellar ataxia and cataracts were diagnosed according to the Harding diagnostic criteria but failed to be recognized as SCAs on genetic testing. Clinical characteristic analyses of each type of SCAs, such as symptoms, neurological examination, ataxia assessment, cognitive testing and radiological features are described below. The STR results of some SCAs patients diagnosed by genetic testing are presented in Figure 1, which comes from fragment analysis of the CEQ8000 sequencer.

Spinocerebellar ataxia type 1 (Family A)

Family A was of the Han nationality. The pedigree of Family A is shown in Figure 2a, and their hereditary mode was in accord with autosomal dominant inheritance. Totally, 30 family members spanning 4 generations, including 7 people suspected with SCA, were investigated. The proband (III_{11}) was 31-year-old male who had SCA for 10 years. Initially, his symptoms were dysphagia and motion discordance, and then, unsteady gait, wide-based gait, and glossolalia developed. A neurologic examination of the proband indicated normal mental status, dysarthria, nystagmus, no gag reflex, finger-to-nose test (+), heel-knee-tibia test (+), adiadochokinesia, Romberg sign (−), without pyramidal or extrapyramidal signs and a normal sensory system. The patient's ICARS score was 25, and his MMSE score was 28. Cerebral magnetic resonance imaging (MRI) showed atrophy of the cerebellum and medulla oblongata [Figure 2b]. The proband was diagnosed as ADCA type I according to the Harding clinical classification system.[1] The polymorphic CAG repeats were expanded by 55 in the SCA1 gene.

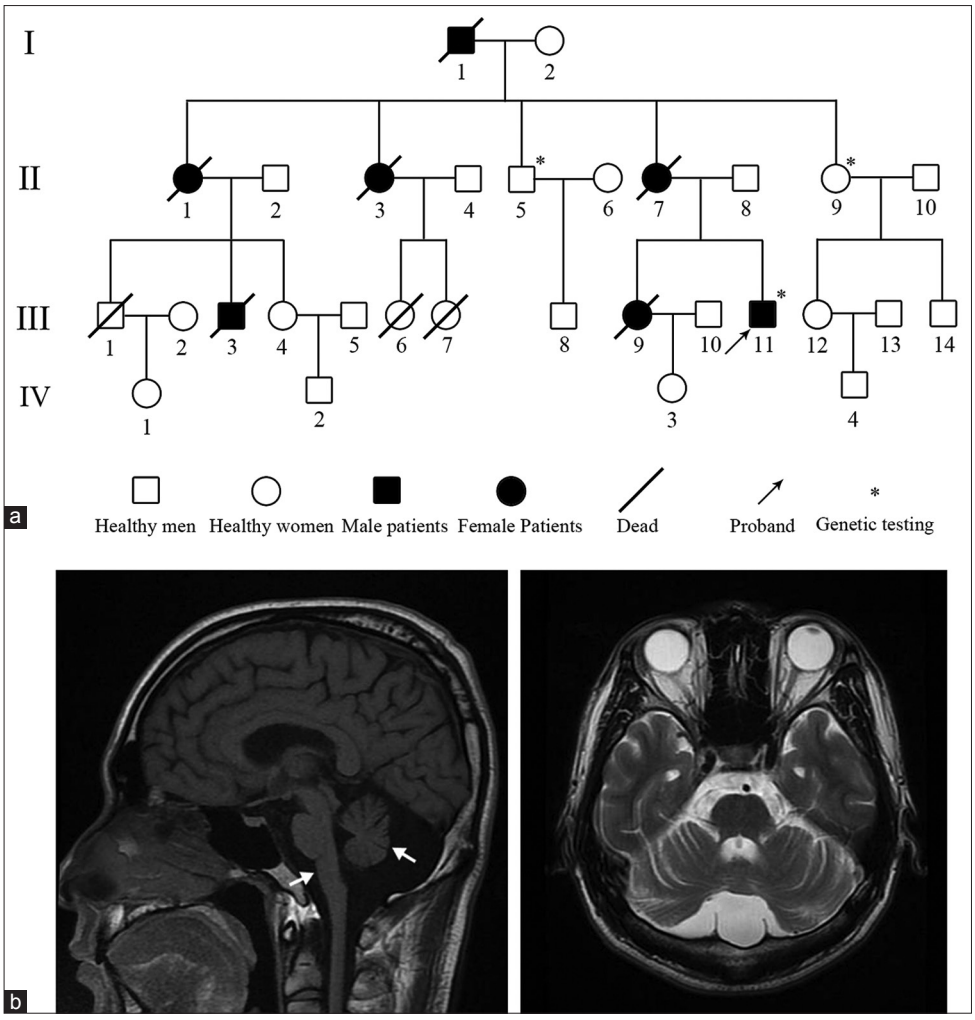

Figure 2: Pedigree and cerebral magnetic resonance imaging (MRI) of Family A. (a) Hereditary mode following autosomal dominant inheritance, 7 people suffered with spinocerebellar ataxia (SCA), and 1 people diagnosed as SCA1 genetically (III_{11}); (b) Cerebral MRI of III_{11} showing atrophy of the cerebellum and medulla oblongata.

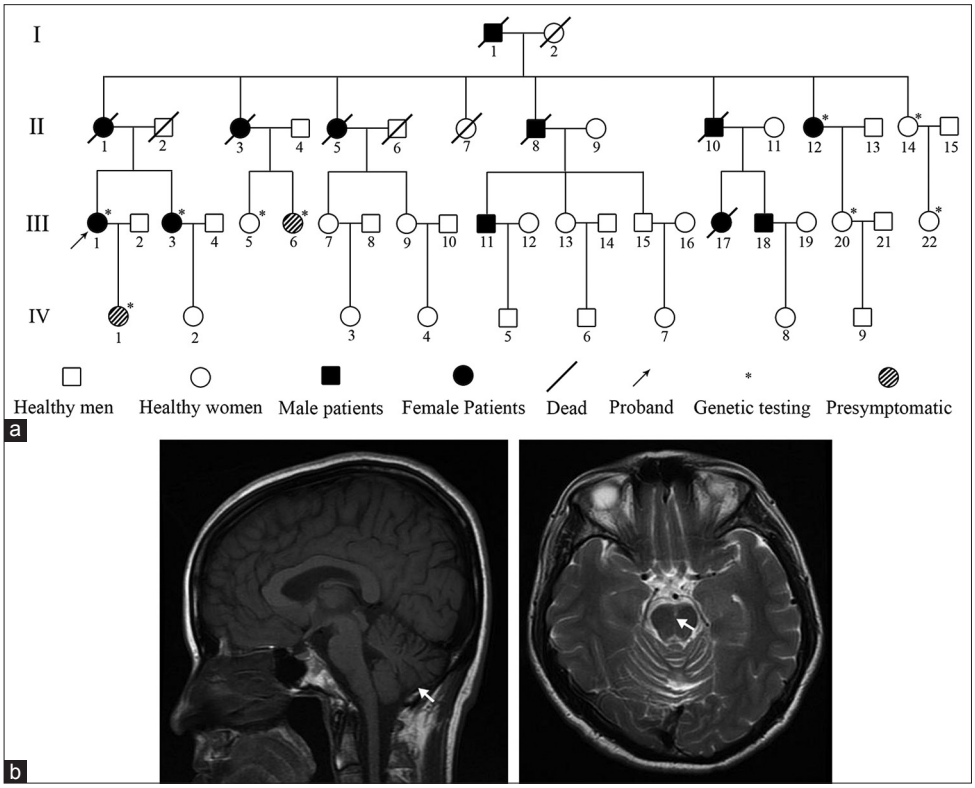

Figure 3: Pedigree and cerebral magnetic resonance imaging (MRI) of Family B. (a) Hereditary mode following autosomal dominant inheritance, 12 people suffered with spinocerebellar ataxia (SCA), and 3 people diagnosed as SCA3 genetically, 2 people without clinical phenotype recognized as presymptomatic patients genetically; (b) Cerebral MRI of III_1 showing cerebellum atrophy and a "vertical line" sign in pontine T2-weighted image signal change.

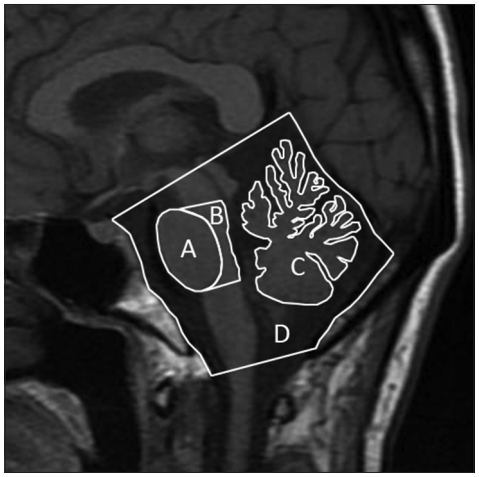

Figure 4: Areas of the pontine base, (A) the pontinetegmentum, (B) the cerebellar vermis (C) and the posterior fossa (D) were measured on midsagittal images from 7 spinocerebellar ataxia 3/Machado–Joseph disease patients. A low-intensity line demarcated the pontine base and tegmentum on magnetic resonance imaging. The ventral area to this line was identified as pontine base and the dorsal part as pontinetegmentum. The upper and lower margin of the pontinetegmentum was drawn perpendicularly to the longitudinal axis of the pons. The upper line was at the demarcation of midbrain and pontine base and the lower one at the pontomedullary junction. The total area of the posterior fossa was bounded by the tentorium cerebelli, the inner table of the skull, and the clivus.

Spinocerebellar ataxia type 3/Machado–Joseph disease (Families B-G)

The investigated Families B-G were of Han nationality (the pedigrees of Family B shown in Figure 3a), and their hereditary modes all were in accord with autosomal dominant inheritance. In total, 216 family members were investigated, including 40 individuals suspected with SCA. The common clinical manifestations of the affected individuals were cerebellar ataxia and pyramidal signs, along with extrapyramidal signs and brainstem or peripheral nerve damage. A cerebral MRI of some affected members showed cerebellum atrophy and a "vertical line" sign in pontine T2-weighted image (T2WI) signal change [Figure 3b]. A total of 17 family members had been diagnosed with SCA, which was classified as ADCA type I according to the Harding clinical classification.[1] The expansion of polymorphic CAG repeats in the SCA3/MJD gene ranged from 64 to 72. We found 5 presymptomatic individuals, and their glutamine-encoding CAG repeats were from 15/66 to 21/70 at SCA3/MJD gene loci. Disease duration was positively correlated with ICARS score ($r_s = 0.714$, $P < 0.05$). And the CAG repeats number of abnormal alleles was negatively correlated with the age of onset ($r_s = -0.826$, $P < 0.05$). No correlations with disease course were observed.

We measured the areas of the pontine base, the pontine tegmentum, the cerebellar vermis and the posterior

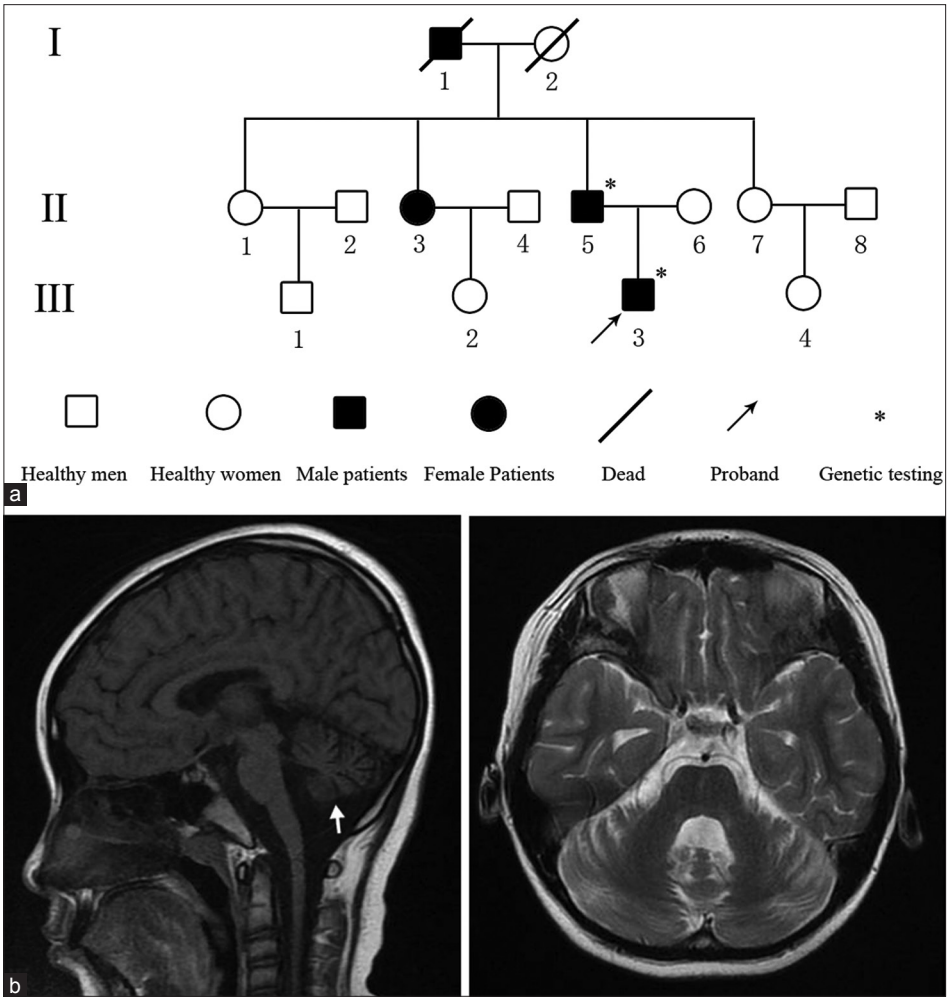

Figure 5: Pedigree and cerebral magnetic resonance imaging (MRI) of Family H. (a) Hereditary mode following autosomal dominant inheritance, 4 people suffered with spinocerebellar ataxia (SCA), and 2 people diagnosed as SCA7 genetically; (b) Cerebral MRI of III_3 showing cerebellum atrophy.

fossa [Figure 4] on midsagittal images demonstrating the cerebral aqueduct clearly from 7 SCA3/MJD patients. We found the ratio of B/D was negatively correlated with the number of CAG repeats ($r_s = -0.764$, $P < 0.05$). However, no obvious correlation was detected between the CAG trinucleotide repeats length with the ratio of A/D or C/D. Correlation analysis failed to reveal a significant association between the ratio of A/D, B/D, or C/D and disease course, ICARS score [Tables 2 and 3].

Spinocerebellar ataxia type 7 (Family H)

Family H was of Korean nationality. The pedigree of Family H is shown in Figure 5a, and their hereditary mode was in accord with autosomal dominant inheritance. Fourteen family members spanning 3 generations were investigated, including 4 individuals with suspected SCA. The proband (III_3) was 12-year-old male with a disease duration of 5 years. His initial symptom was progressive visual loss, followed gradually by unsteady gait, dysarthria, and dysphagia. The patient lost independent ambulation within the last year. A neurologic examination of the proband indicated normal mental status, dysarthria, visual acuity below light sense, dull gag reflex, finger-to-nose test (+), heel-knee-tibia test (+), Romberg sign (+), tendon reflex active, Babinski sign (+), no extrapyramidal signs, and an affected sensory system. His ICARS score was 63, and his MMSE score was 28. Cerebral MRI showed cerebellar atrophy [Figure 5b]. The fundus filming revealed bilateral macular degeneration. The visual evoked potential had longer P100 latency on both sides, and the brainstem auditory evoked potential exhibited auditory nerve damage. The proband was classified as ADCA type II according to the Harding clinical classification.[1] The expansion of polymorphic CAG repeats in the SCA7 gene was 54. The proband's father (II_5) experienced adult onset, with ataxia as the initial symptom, followed by visual loss at 9 years after onset, and was incapable of independent ambulation. His ICARS score was 65, and his MMSE score was 28. His fundus filming revealed bilateral pigmentary macular degeneration [Figure 6a]. Cerebral MRI showed olivopontocerebellar atrophy [Figure 6b]. Peripheral nerve conduction velocity was normal. The expansion of polymorphic CAG repeats in the SCA7 gene was 34.

Spinocerebellar ataxia type 8 (Family I)

Family I was of Korean nationality. The pedigree of Family I is shown in Figure 7a, and their hereditary mode was in

Table 2: Morphological measurement based on MRI and related clinical data of 7 SCA3/MJD patients

Pontine base area (A) (cm^2)	Pontine tegmentum area (B) (cm^2)	Cerebellar vermis (C) (cm^2)	Posterior fossa area (D) (cm^2)	CAG repeats	Disease course (years)	ICARS score
2.705	1.465	13.930	30.720	68	10	41
2.370	1.280	6.530	25.685	66	4	18
2.340	1.170	11.235	33.985	69	6	39
3.455	1.145	9.180	30.990	70	6	23
3.745	1.530	7.285	36.540	68	4	15
2.865	1.100	9.880	33.305	72	6	34
2.875	1.250	7.805	28.900	70	8	41

MRI: Magnetic resonance imaging; SCA: Spinocerebellar ataxia; MJD: Machado–Joseph disease; ICARS: International cooperative ataxia rating scale.

Table 3: Statistical analysis of morphological measurement based on MRI

Variables	A/D ratio	B/D ratio	C/D ratio
CAG repeats	−0.055	−0.764*	0.273
Disease course (years)	−0.225	0.019	0.730
ICARS score	−0.432	0.018	0.721

*P=0.046, correlation is significant at the 0.05 level. MRI: Magnetic resonance imaging; ICARS: International cooperative ataxia rating scale.

Table 4: Clinical features of different affected person from Family J

Variables	III_1	II_{11}	III_8
Age of onset (years)	30	30	25
Disease course (years)	8	18	5
Cerebellar ataxia	(+)	Initial symptom	Initial symptom
Visual loss	Initial symptom	(+)	(+)
Eye exam	Cataract	Cataract	Cataract
Dystonia	Hypomyotonia	Hypermyotonia	Hypomyotonia
Hyperreflexia	(+)	(+)	(−)
Babinski sign	(−)	(−)	(−)
Sensory neuropathy	(−)	Inexact	(−)
Amyotrophy	(−)	(−)	(−)
ICARS score	44	93	20
MMSE score	27 (elementary education)	5 (elementary education)	28 (secondary education)

ICARS: International cooperative ataxia rating scale; MMSE: Mini-mental state examination.

accord with autosomal dominant inheritance. Totally, 14 family members spanning 3 generations were investigated, and only the proband (II_5) was diagnosed as SCA. The proband was 49-year-old female and exhibited onset at 9 years of age. The typical syndrome of unsteady gait had progressed slowly over the previous 3 years, along with dysarthria and occasional falling. A neurologic examination of the proband indicated normal mental status, dysarthria, nystagmus, normal gag reflex, finger-to-nose test (+), heel-knee-tibia test (+), Romberg sign (+), no pyramidal or extrapyramidal signs, and an unaffected sensory system. Her ICARS score was 35, and her MMSE score was 30. Cerebral MRI showed cerebellar atrophy [Figure 7b]. The proband was diagnosed as ADCA type III according to the Harding clinical classification.[1] The expansion of polymorphic CTG

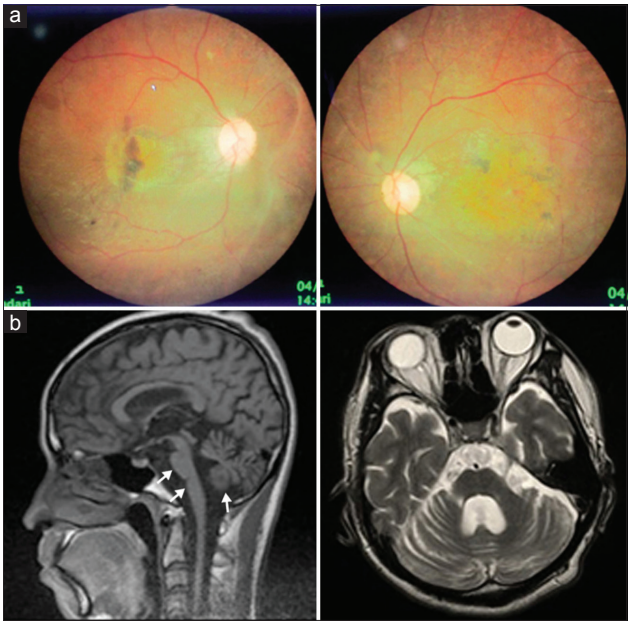

Figure 6: Cerebral magnetic resonance imaging (MRI) and fundus filming of II_5 (Family H). (a) Fundus examination showed bilateral pigmentary macular degeneration; (b) Cerebral MRI showed olivopontocerebellar atrophy.

repeats in the SCA8 gene was 107. The younger brother of the proband (II_7), who had no clinical manifestations of SCA, had an expansion of 101 CTG repeats in the noncoding region of the SCA8 gene. His cerebral MRI showed a nearly normal cerebellum and brainstem shape [Figure 7c].

Undefined family (Family J)

Family J was of Han nationality. The pedigree of Family J is shown in Figure 8a, and their hereditary mode was in accord with autosomal dominant inheritance. Twenty-eight family members spanning 4 generations were investigated, including 6 individuals with suspected SCA. In these 6 subjects, onset symptoms occurred between 21 and 30 years of age, and the natural disease duration of the deceased patients was 12–15 years. The maternal grandfather of the proband, (I_1) who do not suffer from SCA, was 80 years old. However, the maternal grandmother of the proband (I_2) who died from a gynecological surgery accident when she was 37-year-old, could not be excluded from the presymptomatic individual. The surviving patients primarily showed symptoms of cerebellar ataxia

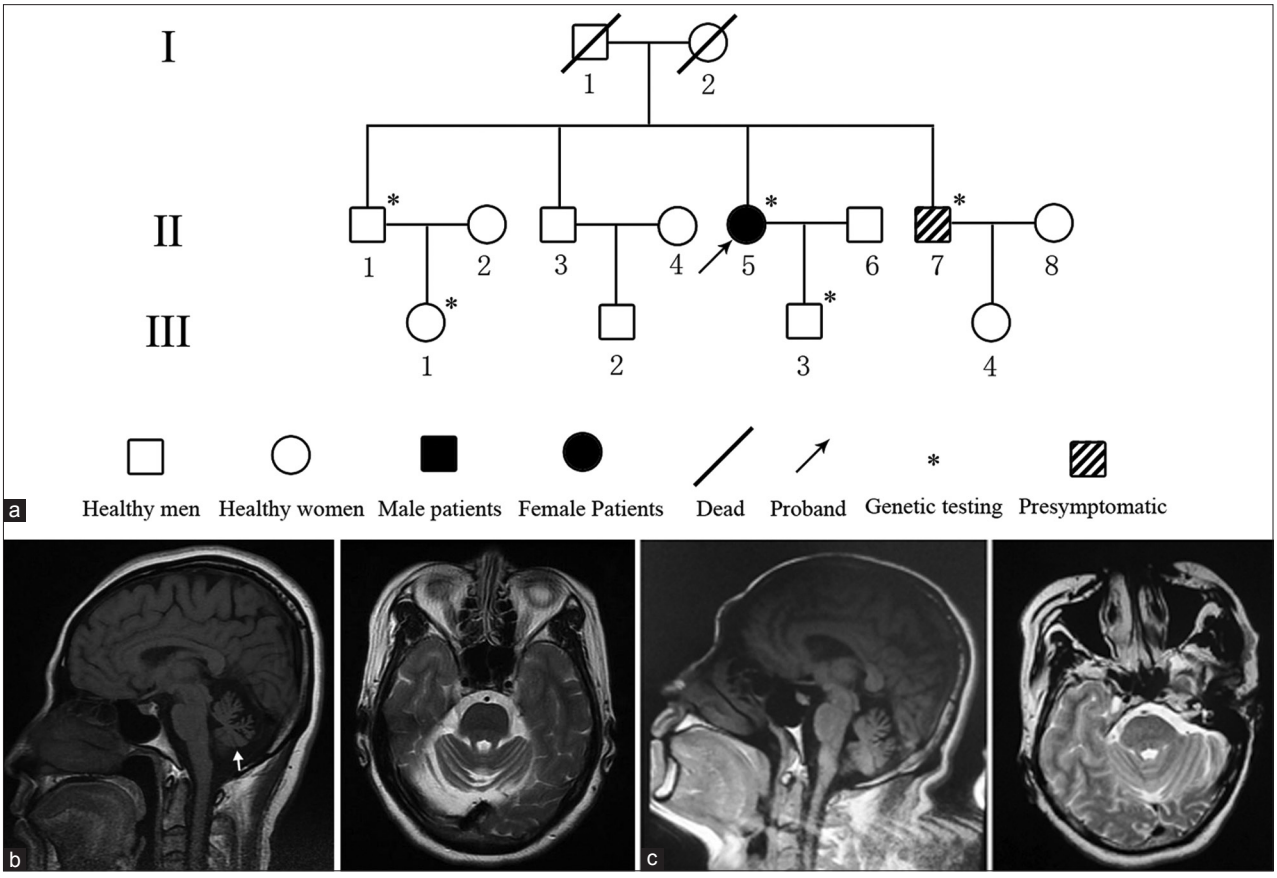

Figure 7: Pedigree and cerebral magnetic resonance imaging (MRI) of Family I. (a) The pedigree of Family I. Hereditary mode displayed autosomal dominant inheritance; only 1 people suffered with spinocerebellar ataxia (SCA) and diagnosed as SCA8 genetically (II_5), 1 people without clinical phenotype recognized as presymptomatic patient genetically (II_7); (b) Cerebral MRI of II_5 showed cerebellar atrophy; (c) Cerebral MRI of II_7 showed a nearly normal cerebellum and brainstem shape.

and bilateral cataracts, along with pyramidal signs and an affected brainstem. Intellectual deficiency and incontinence appeared at the late stage [Table 4]. Cerebral MRI showed atrophy of the cerebellum and brainstem, a vertical line in pontine T2WI with high signal change [Figure 8b and 8c]. The 3 surviving patients were diagnosed as ADCA type I according to the Harding clinical classification.[1] Genetic testing demonstrated that the trinucleotide repeat sequences of SCA1, SCA2, SCA3/MJD, SCA6, SCA7, SCA8, SCAl2, SCAl7 and DRPLA were normal.

Discussion

In our research, we performed a systematic study on 10 Chinese families with SCAs, among which 1 family was identified as SCA1, 6 families were SCA3/MJD, 1 family was SCA7, 1 family was SCA8 and 1 family was undefined. SCA3/MJD was the most common subtype in the Han population, whereas SCA7 and SCA8 were observed in the Korean population.

Spinocerebellar ataxia 1 is caused by the pathological amplification of CAG in the coding region on 6p23, which repeats 6–44 times in normal conditions and is separated by 1–4 CAT segments when repeated more than 20 times. When the repeat number reaches 39–82 without CAT segments separation, it is pathogenic.[2,12-14] Family A was formally diagnosed with SCA1 by genetic testing. However, the proband had disease duration of 10 years without ophthalmoplegia, pyramidal and mental damage, which was in contrast with previous studies and may indicate clinical variability.[2,8]

Spinocerebellar ataxia 3/MJD is caused by pathological amplification of CAG in the coding region on 14q32.1, which is repeated 12–44 times and become pathogenic at 51–86 repeats.[2,14-16] The 17 SCA3/MJD patients in our study displayed amplification in this range of repeats, with genetic characteristics as follows: (1) Delayed dominance: All patients exhibited adult-onset at 31–65 years of age; (2) clinical variability: SCA3/MJD-specific symptoms, such as exophthalmos caused by eyelid retraction, were not observed in our patients; and (3) genetic anticipation: The age of onset in generations I, II and III of Family D was 70, 59 and 44 years, respectively, and genetic anticipation was also observed in other families; and (4) disease duration was positively correlated with ICARS scores, whereas the CAG pathological repeat number of abnormal alleles was negatively correlated with age of onset. These genetic characteristics are consistent with previous studies.[2,8,9,17] Five presymptomatic patients require further follow-up.

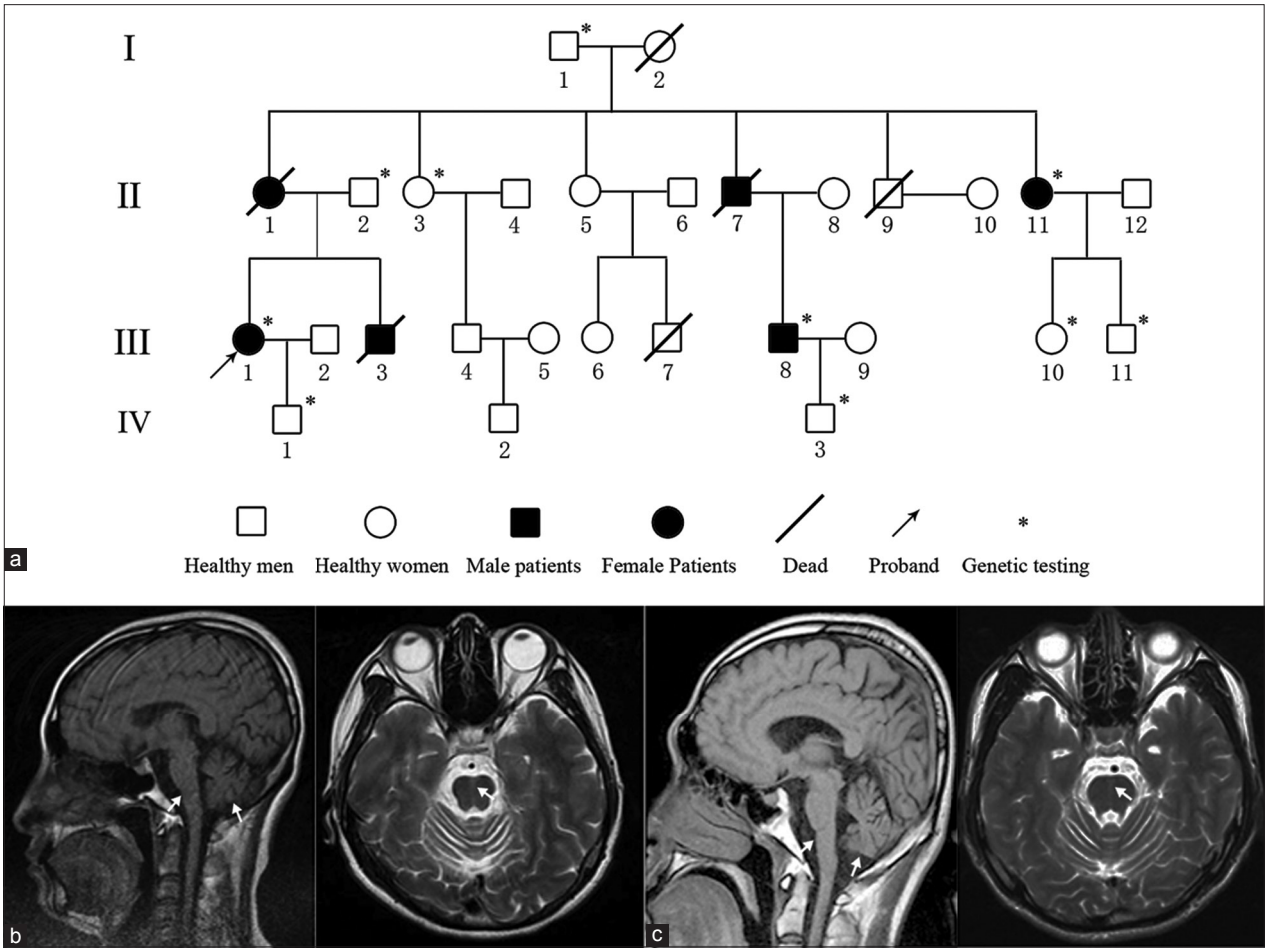

Figure 8: Pedigree and cerebral magnetic resonance imaging (MRI) of Family J. (a) Hereditary mode displayed autosomal dominant inheritance, 6 people suffered with spinocerebellar ataxia (SCA); (b) Cerebral MRI of III_1 showed atrophy of cerebellum and brainstem, a vertical line in pontine T2-weighted image with high signal change; (c) Cerebral MRI of III_8 showed the similar change as III_1.

The pathological SCA7 gene located on 3p14 is normally repeated 7–18 times and pathogenically repeated over 36 times; 28–33 repeats are considered intermediate alleles that will become pathogenic when the repeat number is expanded to pathological range in the passaging process and causes diseases in offspring.[12,14,18] In addition, alleles spanning 34–36 CAG repeats could present reduced penetrance, which could delay the age of onset and alleviate the disease progression.[19] Patient III_3 in Family H experienced juvenile onset, with progressive vision loss as the first symptom. Macular degeneration was observed in the fundus examination. 54 CAG segment repeats were observed in the coding region in this patient, who was diagnosed as SCA7. Patient II_5 experienced adult onset with cerebellar ataxia as the initial symptom. Vision loss occurred gradually, and pigmentary degeneration of the retina was observed in the fundus examination. CAG was repeated 34 times in this patient, which was considered as a reduced penetrance allele. As previously reported, age of onset decreased and disease progression increased as CAG segment amplification increased. Vision loss was most likely to be the first symptom as CAG pathological amplification increased,[12,20,21] which was verified in our study.

The SCA8 gene, which is located at 13q21, carries normal CTA/CTG repetitions of 16–37 in the noncoding region; however, approximately 1% of healthy persons exhibit over 100 CTA/CTG repeats. When the number of expanded allele repeats reaches 80–250, commonly with prior CTA trinucleotides, the carrier presents SCA8.[22-24] SCA8 mostly exhibits adult onset; however, child onset with slow progression and an unaffected life span has also been reported.[3,22,25] The II_5 of Family I reflects this observation. Due to incomplete penetrance in SCA8, II_7 of Family I requires long-term follow-up observation, despite exhibiting more than 101 CTG repeats.

In our study, the genetic testing of Family J, which presented clinically diagnosed SCA, was not in agreement with the known subtypes of SCA1, SCA2, SCA3/MJD, SCA6, SCA7, SCA8, SCA12, SCA17 and DRPLA. The clinical characteristics of this family were early onset and rapid disease progression, with main symptoms of cerebellar ataxia and cataracts. During the late stage, intellectual deficiency might also be observed. The previous studies showed that SCA7 accompanied cataracts,[26] but no SCA subtypes were primarily characterized by cataracts. Therefore, Family J

might be a new SCA subtype or a definite subtype with new concomitant symptom due to genetic heterogeneity.

Anatomically, SCAs are characterized by progressive atrophy of cerebellum, usually accompanying with brainstem, cerebral cortex, and medulla spinalis. However, different SCA genotype with variable clinical dysfunction shows unusual radiological features.[2,12] SCA1 shows remarkable atrophy of cerebral frontal lobe, caudate nucleus and putamen, and the atrophy in cerebellar hemispheres is more severe than in SCA3/MJD.[12,27] The characteristics of SCA3/MJD in MRI scan are atrophy of the frontal and temporal lobes and globus pallidus, along with the affected afferent and efferent cerebellar tracts.[28,29] The primary morphological characteristics of SCA7 involve the atrophy of brainstem rather than cerebellum, especially the pons.[12,30] SCA8 is usually characterized on MRI by different degrees of cerebellar atrophy without significant changes in any other brain region.[12,24]

One of the SCA3/MJD pathological features is the atrophy of pontine tegmentum and facial colliculus. In addition, the atrophic process is not parallel between the pontine base and tegmentum.[17,31,32] We found the ratio of the pontine tegmentum and the posterior fossa area was negatively correlated with the number of CAG repeats. In addition, it is worth noting that the common appearance of a vertical line with high signal change in the pons on T2WI in SCA3/MJD, indicating the atrophy of pons, plays an important role in pathological process. According to the previous literature, a cruciform hyperintensity in the pons on T2-weighted MRI was observed in 1.3% patients in SCA3/MJD.[33] In addition, the pontine midline linear hyperintensity on T2-weighted MRI is more prevalent due to mild olivopontocerebellar atrophy in SCA3/MJD.[29] The radiological features could be found out when the atrophy and gliosis occurred in the transverse part of the pontocerebellar fibers traveling to the middle cerebellar peduncles, the crossing part of the pontocerebellar fibers at the pontine base, and the middle part of the reticular formation.[34,35] However, more research should be done to improve the diagnosis value of imaging on SCAs.

Our study is a systematic study of SCAs in China, the result of which may help for diagnosis, prediction and prenatal screening of this disease, and it may also aid toward better understanding of this disease.

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