

The first patient with sporadic Huntington's disease due to a *de novo* (CAG)_n expansion in China

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TO THE EDITOR

Huntington's disease (HD) is an autosomal dominantly inherited neurodegenerative disorder, with abnormally expanded CAG repeat in the huntingtin (*IT15*) gene. The prevalence of new mutations for HD is extremely low, with only one sporadic HD case reported in non-Caucasians so far. We report the first sporadic HD patient due to *de novo* (CAG)_n repeats from 33 to 50 in China. This report showcases the need to consider HD for atypical patients without family history, but with choreatic movement.

A 30-year-old man, manifested as mild chorea and dystonia, was admitted to our hospital. Mild gait abnormalities have firstly complained in his 27, and chorea gradually existed in his face, upper and lower extremities from both sides. Magnetic resonance imaging (MRI) indicated atrophy of bilateral caudate nucleus and enlarged anterior horn of lateral ventricles (Figure 1). He has no family history of HD. The diagnosis was confirmed by the outcome of 13 and 50 CAG repeats in exon 1 of the *HTT* gene (Figure 2A). The gene test is based on polymerase chain reaction (PCR) using fluorescent-labeled primers, and the subsequent separation of the DNA fragments is conducted by automated capillary electrophoresis. No treatment has been initiated.

We examined his 60-year-old father and 56-year-old mother on movement, cognition, and psychiatric disturbance. There were no clinical abnormalities

observed. Family follow-up revealed an allele size of 13/17 in the mother and 17/33 in the father (Figure 2A). He is the second son of three children from a non-consanguineous marriage. No symptoms were observed in the two brothers. The genetic test did not proceed upon disagreement with the consensus. Paternity and maternity were confirmed through Huaxia™ Platinum PCR Amplification Kit. The pedigree is estimated in Figure 2B. Both the patient and his parents provided written informed consent.

To our knowledge, this is the first reported sporadic patient of HD in the Chinese population and the second one from non-Caucasians.^[1] *De novo* mutation is more common in Caucasians (about 10%), and the first sporadic case was reported in 1993.^[2,3] However, till date, we have only found one sporadic case in China. It could be due to a low mutation rate and misdiagnosis because of no family history. In this case, the clues have emerged from our thorough examination of the patient's MRI image. It has been reported that progressive regional brain atrophy and reduced diffusivity begin many years before the emergence of HD symptoms.^[4] So, for atypical patients, MRI examination could be an essential step that aids in HD diagnosis.

In this case, the *de novo* mutation is inherited from his father, which is consistent with other sporadic cases reported worldwide. However, two cases caused by maternal transmissions have been reported previously.^[5,6] It seems that

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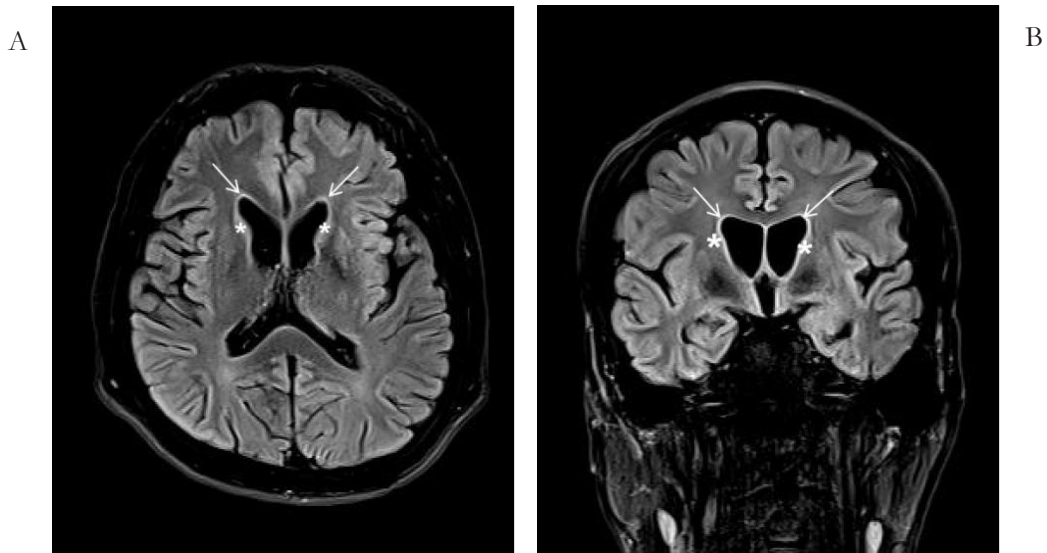


Figure 1: Coronal (A) and sagittal (B) T2 FLAIR-weighted magnetic resonance images. Symmetric atrophy of the caudate nuclei (asterisk) and enlarged anterior horn of lateral ventricles (arrow). FLAIR: fluid attenuated inversion recovery.

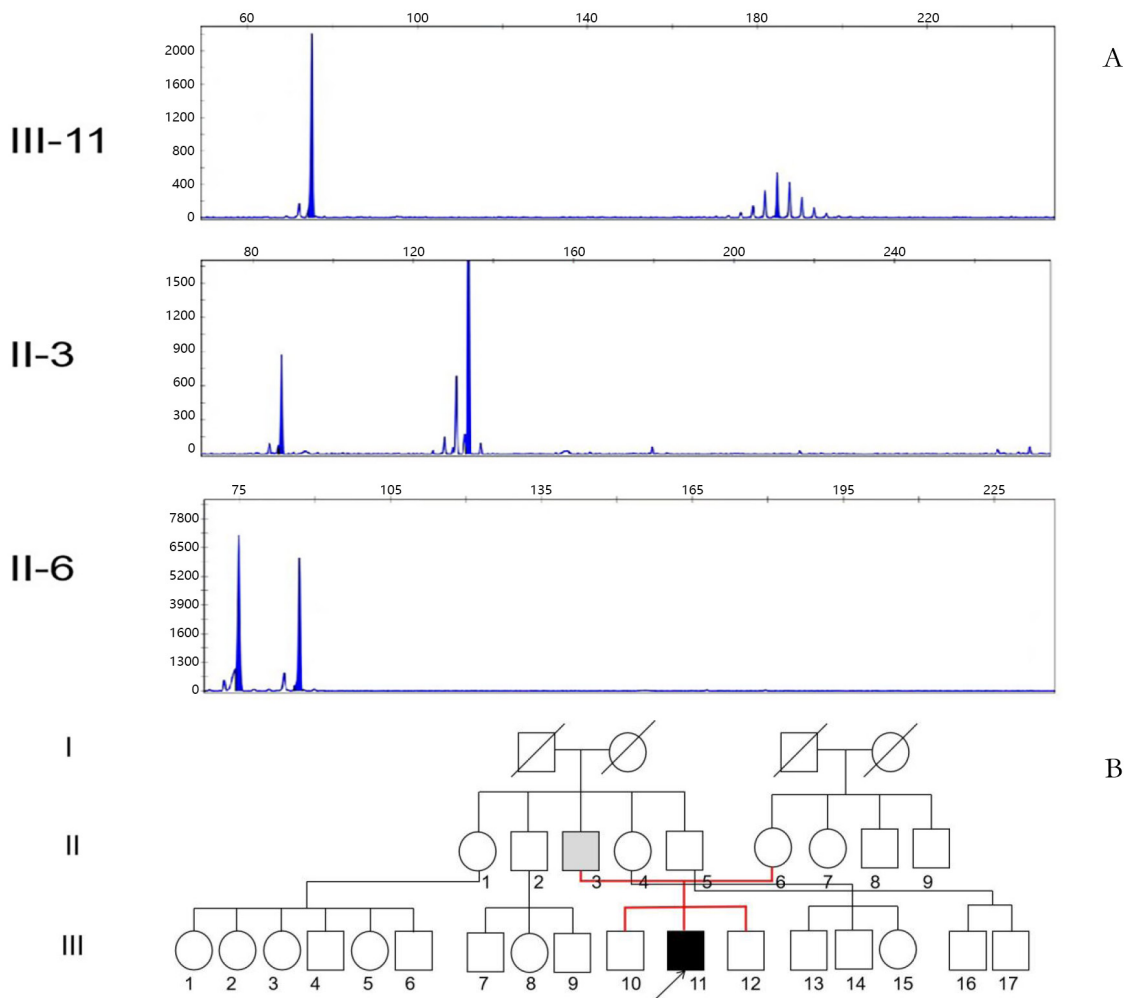


Figure 2: PCR results (A) and pedigree (B) of the family with the sporadic HD case. The proband (III 11) is indicated by a black square. His father, the carrier of the premutation allele, is represented by a gray square. HD: Huntington's disease; PCR: polymerase chain reaction.

the paternal intermediate allele is more likely to expand significantly to the allele of HD patients.

The present study has described a *de novo* (CAG)_n expansion in a Chinese HD patient. Although the incidence and carrier of the intermediate allele are markedly lower in Chinese populations than Caucasians, *de novo* mutation could significantly contribute to the maintenance of gene frequency.

Conflict of Interest

Authors state no conflict of interest.

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