Clinical Parkinsonism & Related Disorders 1 (2019) 72–73

Contents lists available at ScienceDirect

Clinical Parkinsonism & Related Disorders

journal homepage: www.elsevier.com/locate/prdoa

# A case report of a Chinese patient with 22q11.2 deletion accompanied with EOPD, severe dystonia and hypocalcemia

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ARTICLE INFO

*Keywords:*
22q11.2 deletion
Early-onset Parkinson's disease
Dystonia
Hypocalcemia

*Dear Editor,*

Chromosome 22q11.2 deletion is among the most common deletions found in humans and affects at least 1 in 4000 live births [1]. The prevalence of 22q11.2 deletion is higher in early-onset Parkinson's disease patients (EOPD, onset age <45 years). Mok et al. found that 0.49% EOPD patients had 22q11.2 deletions [1]. Majority of the previous studies on 22q11.2 deletions were conducted in samples of European ancestry. We reported a Chinese patient with 22q11.2 deletion combined with EOPD, severe dystonia and hypocalcemia. To the best of our knowledge, this is the first case report on 22q11.2 deletion combined with EOPD in the Chinese population.

The patient is a 49-year-old Han Chinese man with a ten-year history of involuntary tremor of limbs. He visited our hospital with complaints of severe twitching or muscle contraction caused by dystonia. This dystonia always originated from his right foot and ankle, and then spread to right leg, right arm, right neck, right face and finally to back muscle. It typically occurred 4–5 h after taking Benserazide-levodopa (mostly at 4 pm) and lasted 0.5–2 h. Muscular contraction was so intense that the patient cried. On admission, he had twitching of his right foot (Videos 1,2). He was taking Benserazide-levodopa (750 mg/day), pramipexole (1.5 mg/day), entacapone (600 mg/day), and selegiline (10 mg/day). There was no history of antipsychotic use.

His family had no history of parkinsonism or dystonia or parental consanguinity. According to his mother, the patient had learning difficulty from a child, and a surgery history because of congenital heart defect at age 18 years (details were not available), and anosphrasia in his 20s.

The first symptom that he was concerned about was “pill-rolling” movement of his right hand at 39 years of age. He saw a doctor for the first time at 41 years when he developed involuntary tremor and bradykinesia of his right arm and right leg. Diagnosed with Parkinson's disease (PD), he was given Benserazide-levodopa and pramipexole (doses were not available), after which the tremor and bradykinesia had greatly improved. At the age of 43, the tremor spread to his left side and jaw. At the age of 45, he developed repetitive involuntary muscle contraction in his right leg and right side of neck for which he was admitted to a hospital and diagnosed with hypocalcemia, although treatment with calcium did not obviously improve the muscle contraction.

The neurological examination on admission revealed the following: he had mask-like face, normal eye movements, slow and slurred speech, normal muscle strength of limbs, cogwheel rigidity in the limbs, stooped posture, and no pathological reflexes. Tendon reflex in the limbs showed minor decline. Chvostek and Trousseau signs were absent. A cognitive assessment using the mini-mental status examination scores were 8. The laboratory data on admission showed low serum calcium level (1.68 mmol/L, normal range 2.1–2.6 mmol/L), low intact parathyroid hormone (PTH) level (0.92 pmol/L, normal range 1.6–6.9 pmol/L), normal serum levels of phosphate and magnesium. Brain computed tomography (CT) demonstrated mild calcification of globus pallidus. Brain magnetic resonance imaging could not be conducted because of the patient's stooped posture.

Given the failed treatment with calcium, chromosome 22q11.2 deletion syndrome (22q11.2DS) was considered. We performed whole exome sequencing of genomic DNA, and no mutation was found in EOPD-causing genes. Based on a previous study [2], Weaver algorithm was used for the quantification and analysis of allele-specific copy numbers of structural variations. And then chromosomal microarray analysis was used to confirm the result of Weaver algorithm. A hemizygous deletion was found on chromosome 22, spanning approximately 3.15 Mb (chr22: 18648855–21800471) (Fig. 1). We tested his mother's DNA and no mutation was found. His father died of lung cancer 10 years ago.

We decreased the total dose of Benserazide-levodopa from 750 mg to 500 mg per day, and added 125 mg Carbidopa-levodopa at night and 1 mg clonazepam at noon. Calcium gluconate injection was also administered. Muscular contraction and pain were greatly improved. Severe dystonia was not detected, except for mild twitching of the right foot during hospitalization.

The family of patient was informed that data concerning the case would be submitted for publication, and they provided consent. Ethical approval was not required because it was a case report.

This patient had taken dopaminergic drugs for more than eight years from the time he was diagnosed as PD at the age of 41. Muscular contraction and twitching typically occurred 4–5 h after taking dopaminergic

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http://dx.doi.org/10.1016/j.prdoa.2019.07.002

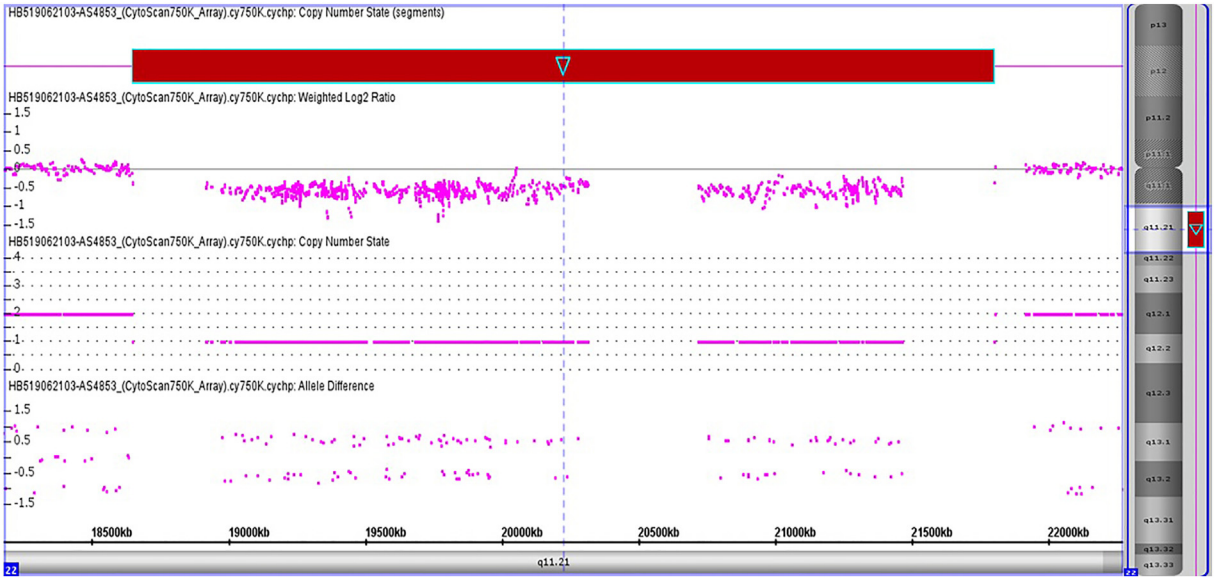


**Fig. 1.** By chromosomal microarray analysis, the patient was found to have 22q11.2 hemizygous deletion mutation (red represents the missing fragment).

drugs each time. These were consistent with the manifestations of levodopa-induced-dystonia. Idiopathic hypoparathyroidism was shown to induce parkinsonism and dystonia in a previous study, but showed good response to calcium supplementation [3].

Approximately 90% of deletions associated with 22q11.2DS spans about 3 Mb (around hg19 chromosome 22: 18.8–21.8 Mb) [1]. The deletion fragment spans about 3.15 Mb (chr22: 18648855–21800471) in our patient. It is similar to three cases (cases 2, 3, and 4) in a previous study [4]. All four patients had typical motor symptoms of PD, but the three patients (cases 2, 3, and 4) had no history of hypocalcemia or congenital heart defect, which were different from our patient. All four patients had similar deletion fragment between low copy repeat (LCR) A and LCR D. How similar deletions lead to variable phenotypes is not well understood. Mok et al. speculated that haploinsufficiency of one or more dose-sensitive genes within the deleted region played a potential role [1]. We considered that different breakpoints in LCRs A and D may play a role in the variable phenotypes.

There were few studies to evaluate the frequency of 22q11.2 deletion in the Chinese population. Foo et al. found that 0.13% of Chinese PD patients in Singapore carried 22q11.2 deletion [5]. Although the morbidity of 22q11.2DS is low, clinicians should consider the possibility of 22q11.2DS in patients with EOPD, severe dystonia, hypocalcemia and learning difficulty.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.prdoa.2019.07.002.

## Authors' contributions

Conception and organization of this study: Zheng-Xiang; Xiao-Dong. Writing of manuscript: Zheng-Xiang; Review and critique of manuscript: Xiao-Dong. Acquisition of data: Dan-Ning; Meng-Lu; Mei-Yuan. Gene testing: Qian-Ru; Shan-Shan.

All authors have approved the final article.

## Funding source

This work was supported by the Medical and Health Science and Technology Foundation of Zhejiang Province, China (2017KY126).

## Declaration of Competing Interest

There are no conflicts of interest.

## Acknowledgment

We thank the patient and his mother for their cooperation and permission to publish his clinical information.

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