Neurologia i Neurochirurgia Polska
Polish Journal of Neurology and Neurosurgery
2022, Volume 56, no. 2, pages: 191–192
DOI: 10.5603/PJNNS.a2022.0008

ISSN: 0028-3843, e-ISSN: 1897-4260

LRRK2 R1441C mutation causing Parkinson's Disease in an Egyptian family

Shan Ali, Zbigniew K. Wszolek

Department of Neurology, Mayo Clinic College of Medicine, Jacksonville, Florida, United States

Key words: Egyptian, leucine-rich repeat kinase 2 gene, Parkinson's Disease, R1441C mutation

(*Neurol Neurochir Pol 2022; 56 (2): 191–192*)

To the Editors

The most common cause of familial Parkinson's Disease (PD) involves mutations in the gene encoding leucine-rich repeat kinase 2 (LRRK2). The LRRK2 R1441C variant is the second most common, and has been implicated as a cause of PD [1]. A literature review revealed that this variant has been seen in kindreds originating from Europe and America, and more rarely from Asia and Africa [1]. It has never been reported in Egypt.

We here present the first Egyptian family with inherited PD due to R1441C mutation in LRRK2, as seen in Figure 1. Genetic testing confirmed that the proband was a carrier of the LRRK2 R1441C gene mutation. He was unaware of the medical history of his grandparents.

The proband was a 57-year-old male patient who came to our clinic for a second opinion regarding a diagnosis of PD. His symptomatic disease onset was at 49 years and he presented with left leg dragging, soon followed by a reduced mobility of his left hand. He was clinically diagnosed with PD at age 52. At age 57, he showed typical akinetic-rigid PD manifesting as bradykinesia and rigidity which were more pronounced on the left side. He exhibited hypomimia, hypophonia, a decreased rate of blinking, a reduced arm swing while walking, shuffling gait, and gait freezing. However, he had no resting tremor, extraocular impairment, dyskinesias, or cognitive deficits. On the pull test, he was able to recover on his own. The patient required minimal assistance in daily living activities and exhibited risky behaviour, excessive daytime sleepiness, nightmares and depression. He had an excellent response to carbidopa/levodopa therapy, and his depression was well controlled with escitalopram. Head magnetic resonance imaging studies done at ages 55 and 56 showed no brain abnormalities. Past medical history included gastric bypass surgery at age 54.

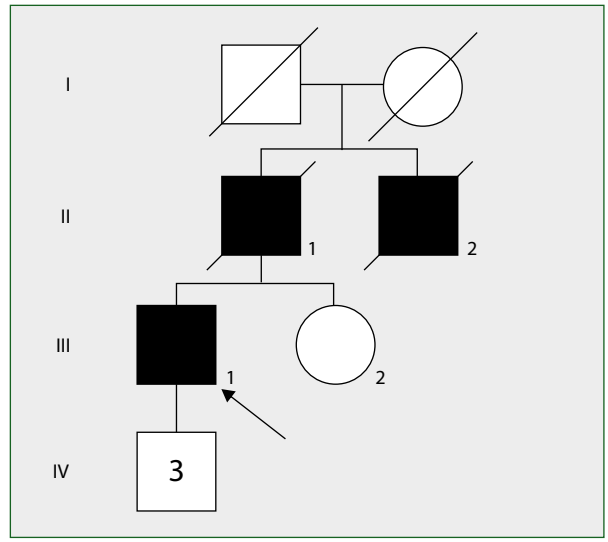

Figure 1. Pedigree of an Egyptian family with inherited *LRRK2* R1441C mutation causing Parkinson's Disease (PD). An arrow indicates the proband. Squares represent males and circles represent females. Black symbols represent individuals with PD. Diagonal lines through symbols represent decreased persons. A symbol with a number inside represents number of offspring

The clinical features of sporadic PD and inherited PD from LRRK2 R1441C mutation are similar, and this was the case with our patient as he showed typical akinetic rigid type parkinsonian motor symptoms and depression. The proband

Address for correspondence: Shan Ali, Department of Neurology, Mayo Clinic College of Medicine, 4500 San Pablo Rd, Jacksonville, FL 32224, USA; e-mail: ali.shan@mayo.edu

Received: 13.12.2021 Accepted: 20.12.2021 Early publication date: 14.01.2022

did not have cognitive impairment; this is consistent with the hypothesis that LRRK2 mutation carriers show slower cognitive decline [2].

A 2017 literature review of PD patients with R1441C mutation in LRRK2 found the mutation present in American (including western Nebraska), Italian, Irish, Belgian, German, Russian, Spanish, Singaporean, and Chinese populations [1]. This mutation has not been reported in the Polish population [3]. LRRK2 G2019S mutations are common in Egypt and North Africa (including Mauritania, Morocco, Algeria, Tunisia and Libya) [4]. However, we here present the first family of Egyptian origin with inherited PD due to the LRRK2 R1441C mutation. It would be beneficial to study the Egyptian population for LRRK2 gene mutations, particularly for the R1141C mutation. Understanding the geographical landscape of LRRK2 mutation globally is important, since medication trials and gene therapies specifically designed to treat LRKK2 mutation carriers are under development [5].

Ethical compliance statement: *We conducted all genetic analyses under approval of the institutional review board (IRB) of Mayo Clinic Florida. Written informed consent was obtained. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.*

Financial disclosure/conflict of interest: *ZKW is partially supported by the NIH/NIA and NIH/NINDS (1U19AG063911, FAIN: U19AG063911), Mayo Clinic Center for Regenerative Medicine, Mayo Clinic in Florida Focused Research Team Program, gifts from the Sol Goldman Charitable Trust, and the Donald G. and Jodi P. Heeringa Family, the Haworth Family Professorship in Neurodegenerative Diseases Fund, and the Albertson Parkinson's Research Foundation. He serves as PI or Co-PI on Biohaven Pharmaceuticals, Inc. (BHV4157-206 and BHV3241-301), Neuraly, Inc. (NLY01-PD-1), and Vigil Neuroscience, Inc. (VGL101-01.001) grants. He serves as Co-PI of the Mayo Clinic APDA Center for Advanced Research and as an external advisory board member for Vigil Neuroscience, Inc.; SA has nothing to disclose.*

Funding: *None.*

References

1. Peng F, Sun YM, Chen C, et al. The heterozygous R1441C mutation of leucine-rich repeat kinase 2 gene in a Chinese patient with Parkinson disease: a five-year follow-up and literatures review. J Neurol Sci. 2017; 373: 23–26, doi: 10.1016/j.jns.2016.12.009, indexed in Pubmed: 28131193.
2. Srivatsal S, Cholerton B, Leverenz JB, et al. Cognitive profile of LRRK2-related Parkinson's disease. Mov Disord. 2015; 30(5): 728–733, doi: 10.1002/mds.26161, indexed in Pubmed: 25650144.
3. Milanowski ŁM, Ross OA, Friedman A, et al. Genetics of Parkinson's disease in the Polish population. Neurol Neurochir Pol. 2021; 55(3): 241–252, doi: 10.5603/PJNNS.a2021.0013, indexed in Pubmed: 33539026.
4. Benamer HTS, de Silva R. LRRK2 G2019S in the North African population: a review. Eur Neurol. 2010; 63(6): 321–325, doi: 10.1159/000279653, indexed in Pubmed: 20413974.
5. Fiandaca MS, Lonser RR, Elder JB, et al. Advancing gene therapies, methods, and technologies for Parkinson's disease and other neurological disorders. Neurol Neurochir Pol. 2020; 54(3): 220–231, doi: 10.5603/PJNNS.a2020.0046, indexed in Pubmed: 32557526.