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Dr. Srijamya
Department of Neurology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

Dr. Sri Anjali Gorle
Faculty of Medicine, Andhra Medical College, Andhra Pradesh, India

Faiza Bahadur Khan
Faculty of Medicine, University of Georgia, Tbilisi, Georgia

Lalitha Lavanya Shree S
Faculty of Medicine, Georgian National University SEU, Tbilisi, Georgia

Dr. Sarika Mutyala
Faculty of Medicine, Gandhi Medical College, Hyderabad, India

Dr. Muhammad Yousuf Siddiq
Neurologist and sleep specialist, Rush Copley Medical Center and Ascension Mercy Hospital, Chicago, USA

Corresponding Author:
Dr. Srijamya
Department of Neurology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

The trifecta challenge: Lacunar stroke associated with Parkinson's disease, and ehlers-danlos syndrome: A challenging case study

Srijamya, Sri Anjali Gorle, Faiza Bahadur Khan, Lalitha Lavanya Shree S, Sarika Mutyala and Muhammad Yousuf Siddiq

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Abstract
A 40-year-old man presented with left sided droopy face and hemiparesis, diagnosed with lacunar stroke. The patient had medical history with complex interaction of PD, DVT, stage 4 CKD and EDS. Since treatments aimed at one disease may make the others worse, their divergent symptoms provide a serious therapeutic dilemma. Tremors, cogwheel rigidity and cognitive decline were among the patient's symptoms that clinically pointed to PD. The PD diagnosis was confirmed DaT scan, which were performed due to the patient's younger age, medical history of EDS diagnosed at age 12 with rare positive PLA2G6 gene mutation, and absence of a family history of Parkinson's disease. This case presented a therapeutic challenge and demanded the multispecialty involvement for the patient treatment plan.

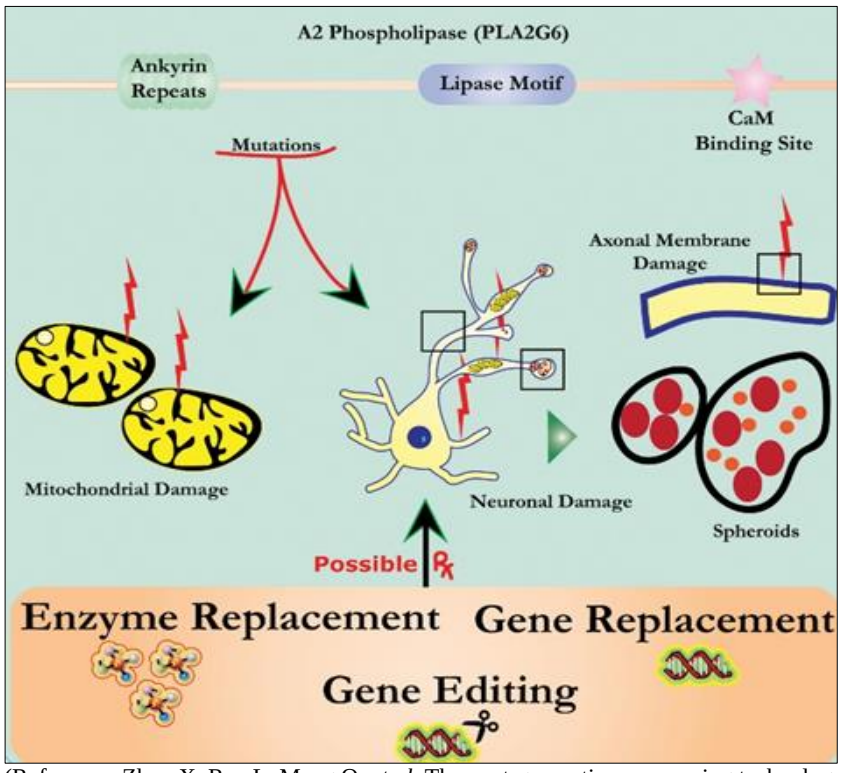
Keywords: Lacunar stroke, hemiparesis, facial droop, parkinson's disease (PD), cognitive decline

Introduction
Parkinson's disease (PD) is a neuromuscular degenerative disorder with the prevalence of 8.5 million worldwide. PD compasses the major symptoms of difficulty in coordination and movement, tremors, stiffness, dementia etc. The major cause of mortality in PD patients is pneumonia.

Ehlers-Danlos Syndrome (EDS) is a genetic disorder characterized by joint hypermobility and fragile connective tissue, leading to an increased risk of bleeding due to impaired collagen production [1].

The PLA2G6 gene encodes a calcium-independent phospholipase A2 enzyme essential for lipid metabolism and inflammatory responses. Mutations in PLA2G6 can disrupt enzyme activity, causing dysregulated lipid metabolism and inflammation, which are associated with an elevated risk of thrombosis. Certain variants of PLA2G6 are also linked to abnormal platelet function, potentially contributing to thrombotic events [2].

In the realm of genetic research on Parkinsonism, there is growing interest in the role of zinc metabolism and its implications for neurological disorders. Mutations in zinc transporters, including those encoded by PLA2G6, are known to underlie various inherited diseases with diverse clinical manifestations. These findings highlight the genetic influence on zinc homeostasis and its potential impact on neurological conditions such as Parkinsonism [3]. Specifically, biallelic mutations in PLA2G6 are associated with early-onset parkinsonism, characterized by symptoms such as dystonia, pyramidal and cerebellar signs, myoclonus, cognitive impairment, as well as early psychiatric manifestations and bladder overactivity [4]. Furthermore, the presence of peripheral neuropathy in complex inherited diseases emphasizes the genetic basis of neurological symptoms observed in EDS. Genes such as PLA2G6 and C19orf12 have been implicated in parkinsonism, providing valuable insights into the genetic mechanisms underlying these conditions and enhancing our understanding of how EDS-related manifestations are influenced by genetic factors [5].



(Reference: Zhou X, Ren L, Meng Q, *et al*. The next-generation sequencing technology for eukaryotic microbial transcriptomics. Front Genet. 2018;9:597. doi:10.3389/fgene.2018.00597.

Fig 1: PLA2G6 mutation

The presented case involves the complexity of a lacunar stroke, single instance of thrombosis, parkinsonism, and EDS, all of which are related to the PLA2G6 gene. All opposing intricacies amplifying the difficulty for treatment options.

Patient Information: A 40-year-old patient presented to the emergency clinic with symptoms of a drooped left-sided face, slurred speech and left sided hemiparesis for over 6 hours in the morning. The family member informed that patient was doing well at night before sleep. Emergency diagnostic protocols confirmed the patient had experienced a lacunar stroke and acute stroke protocol was initiated under which patient was administered IV Heparin that was well tolerated by the patient. Blood pressure recorded for the patient was 156/98 mm Hg and therefore the patient was administered Labetalol 20 mg with slow infusion. The patient became stable after 2 hours of treatment initiation. The patient remained in Intensive Care Unit and was discharged on the 10th day in the stable condition.

The patient's medical history is notable for a diagnosis of EDS, including symptoms of joint hypermobility and skin fragility, and early-onset Parkinsonian symptoms. Clinical evaluation revealed the co-existence of EDS and PD, highlighting the complex interaction between these conditions. EDS primarily presents with connective tissue laxity, whereas PD is marked by rigidity, presenting a unique challenge to conventional understanding and treatment. There was no family history of PD. Managing this patient's conditions required a tailored, interdisciplinary approach to address the conflicting nature of the symptoms effectively. Considerations for treatment also considered the patient's current medications, lifestyle factors, and any relevant family history to ensure comprehensive care.

Table 1: Timeline of patient treatment and response

Date/Time	Event
[At the age of 12]	Patient was diagnosed with EDS.
[Day 1]	Patient presented to the ER with left-sided facial droopiness, slurred speech, left hemiparesis.
[Day 1]	Acute stroke protocol was initiated.
[Day 1]	Stroke was confirmed after CT and MRI
[Day 1]	IV Heparin and IV Labetalol was initiated and further investigation continued. The patient became stable after 2 hours of treatment.
[Day 1]	Neurological examination revealed resting tremors, slow speech, and cog-wheel rigidity.
[Day 2]	Suspected diagnosis of Parkinson's disease based on clinical findings.
[Day 3]	DaT scan conducted. Findings: decreased uptake of the tracer in the striatum area of the brain
[Day 3]	Diagnosis of Parkinson's disease was confirmed based on clinical examination and imaging results

Diagnostic Assessment

The patient underwent acute stroke protocol and the diffusion weighted MRI confirmed lacunar stroke due to infarction in right thalamic region.

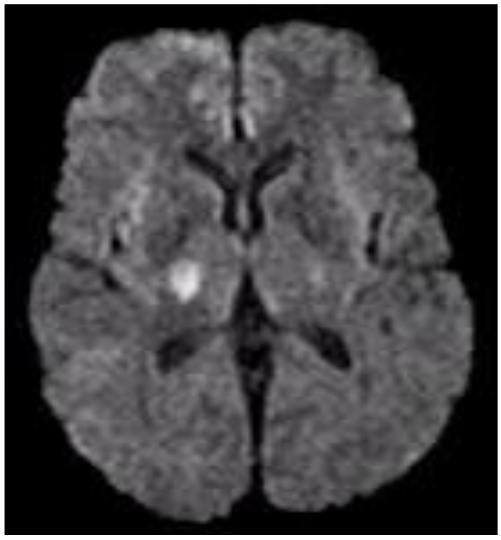


Fig 2: MRI confirming the lacunar stroke in right thalamic region

PD was confirmed via DaT scan and clinical symptoms. EDS was earlier diagnosed clinically with positive gene mutation PLA2G6. Reported complications in the patient were stage 4 chronic kidney disease (CKD) for which he was on dialysis every week, and a previous Deep venous thrombosis (DVT) for which he was treated in the past and takes baby aspirin for prophylaxis.

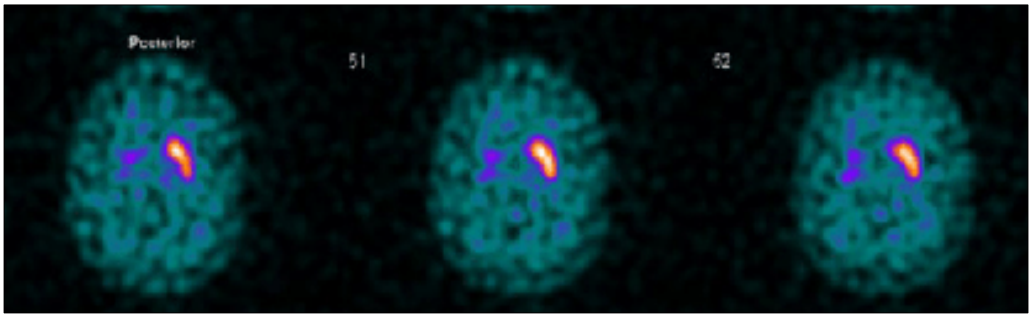


Fig 3: DaT Scan: The image shows the absence of radioligand intake in right caudate and putamen

Therapeutic Intervention: This patient was diagnosed with lacunar stroke and PD. The current diagnosed pathology and the past medical history of EDS, DVT, and stage 4 CKD was a challenge for the treatment option and required close monitoring for each condition. He was started on Selegiline 5mg, as other Parkinsonism drugs were not recommended for patients with impaired renal function. Selegiline showed improvement in his motor symptoms with minimal side effects. The patient also began physical therapy focused on improving mobility, reducing rigidity, and preventing falls, with exercises tailored to accommodate the joint hyper flexibility associated with EDS. To reduce the risk of DVT recurrence, he was advised to avoid prolonged sitting and long flights. Additionally, the patient is on regular dialysis to manage stage 4 CKD, with his renal function tests closely monitored by a nephrologist. The patient's general physician was also kept in loop to keep a follow up on his blood pressure, lipid profile, and blood sugar reports.

Table 2: Patient's disease and interventions done

Disease	Proposed Intervention for the patient
Lacunar Stroke	IV Heparin + IV Labetalol Aspirin 81 mg was continued with discharge Physical therapy Blood pressure and cholesterol level follow up under general physician
Parkinsons disease	Selegiline 5 mg Exercise tailoring to minimize fall risks
Stage 4 CKD	Dialysis per week and follow up with nephrologist
Ehlers Danlos Syndrome	Physical therapy and counseling for the risk of bleeding

Follow-up and Outcomes

The patient experienced improved motor symptoms with selegiline and reported minimal side effects and good tolerability. Regular serum creatinine, Glomerular filtration rate (GFR), electrolytes, lipid profile and blood pressure monitoring showed stable renal function despite ongoing dialysis. Follow-ups with a hematologist have revealed no new DVT episodes, indicating that preventive measures have been effective. The patient's adherence to treatment, including selegiline and physical therapy, was monitored through self-reports and session progress reports, showing active participation and improved mobility and rigidity.

Dialysis sessions were consistently attended without any reported complications. Overall, no adverse events related to treatments have contributed to the patient's stable and manageable condition.

Discussion

A rare mutation in the PLA2G6 gene, associated with dystonia-parkinsonism, could potentially be found in patients with EDS. These individuals typically experience the symptoms of PD early and have shortened life expectancies. However, the variability and severity of the gene mutation may lead to a less prevalent manifestation of this condition, concerning its implications for effective patient management.

The presented case is one of its kind showing the complexity and the challenge of the treatment protocol. The patient presented with stroke which could be due to vascular malformation or compromised artery walls resulting from EDS. The past medical history of CKD and DVT also possess a challenging situation for drug prescription and demands meticulous follow up.

Results

This case is a presentation of complicated and challenging diseases including stroke, PD, EDS, Stage 4 CKD in a single patient with treatment dilemma which involved multiple specialty follow up. The rare case of PLA2G6 gene mutation possessed multiple oppositional symptoms in a patient demanding multiple treatment modality approach with a personalized treatment plan in this case. The patient was treated for each disease starting with chief complaint of face droopiness and left hemiparesis due to right sided thalamic lacunar stroke followed by diagnosing of PD with clinical symptoms and DaT scan. The dialysis for stage 4 CKD was a challenge while prescribing drugs to the patient but with the close follow up patient showed the good response of the treatment along with physiotherapy aligned for PD, stroke, and EDS.

Conclusion

The rare mutation of PLA2G6 gene mutation brought a rare and challenging case of a 40 year old patient with lacunar stroke and past medical history EDS, DVT, Stage 4 CKD. Left sided facial droop and hemiparesis were prominent symptoms. Additionally neurological assessment showed tremors and cogwheel rigidity which was indicative of PD and was confirmed with DaT scan. This led to a treatment dilemma although the collaboration of the multispecialty team facilitated patient recovery.

References

1. Wilson GN, Tonk VS. Clinical-genomic analysis of 1261 patients with Ehlers–Danlos syndrome outlines an articulo-autonomic gene network (Entome). Curr Issues Mol Biol [Internet]. 2024;46(3):2620-2643. Available from: http://dx.doi.org/10.3390/cimb46030166
2. Cardinal RN, Bullmore ET. The diagnosis of psychosis. Cambridge, England: Cambridge University Press; c2011.
3. Hogstrand C, Maret W. Genetics of human zinc deficiencies [Internet]. Encyclopedia of Life Sciences. Wiley; c2016 p. 1-8. [cited 2024 Jul 17]. Available from: https://www.semanticscholar.org/paper/c151e282d937483a93cd4da09cb201f2069be731
4. Magrinelli F, Mehta S, Di Lazzaro G, Latorre A, Edwards MJ, Balint B, *et al.* Dissecting the phenotype and genotype of PLA2G6-related parkinsonism. Mov Disord [Internet]. 2022;37(1):148-161. Available from: http://dx.doi.org/10.1002/mds.28807
5. Rossor AM, Carr AS, Devine H, Chandrashekar H, Pelayo-Negro AL, Pareyson D, *et al.* Peripheral neuropathy in complex inherited diseases: An approach to diagnosis. Neurosurgery & Psychiatry. 2017;88(10):846-863.