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CASE REPORT

A Clinical Approach to Juvenile Parkinsonism During Pregnancy

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Abstract

Juvenile parkinsonism is a rare disease affecting patients younger than the age of 21 years. When superimposed with pregnancy, most physicians fear its health complications and the role of the treatment and its safety for the fetus. This case presents a 37-year-old woman diagnosed with juvenile parkinsonism who was blessed with her second child, eight years after her first. Despite all the odds, concerns, and warnings from family and physicians, the patient was determined to conceive, avoiding all means of contraception. During pregnancy, the patient experienced multiple hypoglycemic attacks and was diagnosed with gestational diabetes mellitus, which was controlled accordingly. The patient also suffered from motor impairments that worsened with the progression of pregnancy. However, the patient regained previous motor function upon delivery. The expectation that pregnancy may permanently worsen the symptoms of Parkinson's disease is not explicit; some pregnancies are uncomplicated by Parkinsonism yet complicated by pregnancy-induced medical conditions. As demonstrated in this case, family support and care, alongside continuous maternofetal monitoring, aids in the success of pregnancy in patients with juvenile Parkinson's disease regardless of their risks.

Keywords: Female, Juvenile Parkinsonism, Pregnancy, Parkinson's disease, Therapeutic Safety

Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder involving the degeneration of the dopaminergic neurons of the basal ganglia. Its symptoms are subdivided into motor symptoms such as resting tremor, bradykinesia, and rigidity, and other non-motor involvements, including autonomic, sensory, sleep, and neuropsychiatric impairments.

The prevalence of PD is age-dependent, with a prevalence of about 5% in patients younger than 40 years of age. Hence, PD is commonly missed and under-diagnosed in this population. PD is more common in males than females, with a ratio of 3:2. However, the reasoning behind such gender predominance is still undetermined, yet some studies have indicated the protective role of estrogen, which reduces the rates of the disease in females.

Since the prevalence of PD in individuals aged less than 40 years is low, it justifies the low prevalence of the disease during pregnancy. Multiple concerns exist in patients with PD and pregnancy, mainly regarding the safety of both the

mother and the fetus during conception, gestation, and delivery. Since there is a low prevalence of patients with PD and pregnancy, there is no single established management plan and guidelines for such rare cases since the data from the available publications has numerous limitations. However, the cases with a positive and successful outcome were preponderant.[1]

Case Presentation

A 37-year-old woman, gravida 3, para 1, abortion 1, was admitted to the Bahrain Defense Force (BDF) hospital at 23 weeks of gestation. The patient was diagnosed with juvenile parkinsonism at the age of 18 years in Saudi Arabia through clinical evaluation and radiological confirmation. Initially, she suffered from bilateral upper limb paresthesia with upper limb postural tremors, which progressed to bilateral upper limb stiffness, and at the age of 28, the stiffness advanced to involve both upper and lower limbs. In 2011, the patient developed an unsteady shuffling gait and impaired short-term memory. As for the neuropsychiatric aspect of PD, the patient initially suffered from insomnia, then depression and generalized anxiety disorder. The patient also presented with postural hypotension and hyperhidrosis. The patient denied any history of dysphagia, urinary incontinence, or stool incontinence. The patient's symptoms were aggravated by stress and anxiety and were significantly relieved by levodopa. No history of any substance abuse was reported. The family history for PD and its sub-entities was negative. No genetic testing was conducted to confirm the genotypic mutation involved.

The patient was initially started on Levodopa/carbidopa (a decarboxylase inhibitor that increases dopamine in the central nervous system (CNS)) and Pramipexole (a dopamine agonist) at the age of 20, and subsequently developed peaked dose dyskinesia and wearing-off phenomena with episodes of sudden freezing while sitting, and hence amantadine, an antiviral associated with increasing dopamine in the CNS, was added. Escitalopram, a selective serotonin reuptake inhibitor, was used to alleviate neuropsychiatric symptoms. Multiple neurosurgical interventions were attempted, with her first deep brain stimulation (DBS) inserted in April 2014, but unfortunately, it was removed due to the complication of a hemorrhagic stroke, resulting in right-sided spastic hemiparesis. In 2016, another DBS was inserted successfully in Germany.

During the patient's first pregnancy in 2012, stiffness was exaggerated, and she suffered from fatigue and severe body aches. The patient was on the following medications then: Pramipexole 0.18 mg, and Levodopa/carbidopa. Eventually, in the 31st week of gestation, due to the severe exacerbation of symptoms, the patient delivered a baby girl by cesarean section with a birth weight of 1.7 kg. The baby was kept in the nursery for 2 months, and is currently, healthy. Following her first pregnancy, the patient desired to conceive although she had a first-trimester spontaneous miscarriage in 2019.

In 2020, the patient had a positive home pregnancy test and confirmed it at the health center and was not able to follow up with neurologists in Saudi Arabia and Germany due to the coronavirus disease of 2019 (COVID-19) pandemic, and hence tapered medications down by herself, consuming Pramipexole 0.52 mg and Stalevo 100 mg. No special tests or investigations were ordered by neurologists. Continuous follow-ups with obstetrician throughout the pregnancy, which were all insignificant until the second trimester, when the patient reported feeling dizzy and collapsing on multiple occasions, along with progressive motor impairments and occasional loss of consciousness, hence was admitted for further investigations.

Upon admission at 23 weeks of gestation, the patient was medically evaluated and was oriented to time, place, and person. No auditory or visual deficits and had good facial and constructive organization. The patient had adequate cognitive functioning for short-term cognitive screening. Mini-mental state was 27/30 with minor deficits in her calculation skills. Symptoms were more predominant on right side. She suffered from mild postural instability. An intact sensory examination was reported. The patient had no dysarthria, no facial or gaze paresis. Hyperkinesia of the left side and right-sided hemiparesis with no leg dropping nor pronation of the right arm. A corresponding disturbance of

fine motor skills in juvenile Parkinson's syndrome was reported. Due to the COVID-19 pandemic, the patient was not able to follow up on her DBS device in Germany, and this might have added to the worsening of motor functions.

Investigations were carried out and the patient was diagnosed with gestational diabetes and was discharged on metformin (a biguanide that increases insulin sensitivity) to obtain glycemic control. With regards to motor impairments and loss of consciousness, the patient was dependent on her husband, who took the time to provide care for her. The patient was re-admitted at 34th week of gestation for an elective cesarean section, with the outcome of a healthy baby girl weighing 2.5 kg and an Apgar score of 9 at 5 minutes. Further neonatal examination revealed no anomalies. Following discharge, the patient was competent to care for her two daughters with the help of her husband and family, regaining her prior motor function.

Discussion

PD is mostly known to affect the elderly. However, in less than 5% of the population, the disease is diagnosed before 40 years of age and is known as early-onset Parkinson's (EOPD), which is sub-classified into juvenile parkinsonism and young-onset Parkinson's disease (YOPD). Patients with juvenile parkinsonism have the onset of their symptoms before 21 years of age, while patients with YOPD have their symptoms appear between the ages of 21 and 40.[2] In this case, the patient's signs and symptoms first appeared at the age of 18 years.

A systematic analysis compared the prevalence and morbidity of PD from 1990 to 2016. This study showed that in 2016 there were 6.1 million patients with PD, whereas in 1990 the prevalence was only 2.5 million. This significant increase in the global burden of PD is due to a larger population, an increased life expectancy, and environmental and demographic factors.[3]

Even though no genetic confirmation was done in this case, as juvenile Parkinsonism is a rare entity in PD, it is important to identify the mutations involved in its pathogenesis. There has been successful identification of some of the genes that are linked with early-onset Parkinson's, including impairments in PRKN, PINK1, and DJ-1; numerous more mutations have yet to be identified. Multiple autosomal recessive variants of juvenile Parkinson's have been identified, some of which are associated with mutations in the DNAJC6 gene, which encodes for 970 proteins.[4] Another rare autosomal recessive variant of juvenile Parkinson's is Kufor-Rekab syndrome (KRS), which is linked to a mutation in the ATP13A2 gene[5], and other cases of autosomal recessive juvenile Parkinson's have been documented to involve a parkin gene mutation (ARJP/PARK2), which is associated with a marked response to levodopa and is associated with levodopa-induced dyskinesia.[6]

The diagnosis of PD is made clinically with the aid of history, examination, and responsiveness to levodopa. Magnetic resonance imaging (MRI) is used to exclude the differential diagnosis, while morphometric and functional MRI, along with transcranial Doppler ultrasound studies, are being used to differentiate idiopathic Parkinson's from other parkinsonian disorders. Radionuclide imaging such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT) can be used to assess dopamine metabolism and deficiency by using a dopamine transporter ligand, revealing an asymmetrical reduction in the uptake, mainly in the dorsal striatum. No biomarkers have been identified to be distinctly associated with PD. However, increased alpha-synuclein in the cerebrospinal fluid indicates possible cognitive impairments.[7]

The semiology of Parkinson's disease is not exclusive to it, coinciding with the clinical features of other diseases, including Wilson's disease, dopa-responsive dystonia, and drug-induced parkinsonism. The clinical manifestations of PD include motor and non-motor manifestations. The motor signs include resting tremor, cogwheel rigidity, and bradykinesia, along with impaired postural reflexes and unstable gait, mainly shuffling gait. There are similarities and differences when comparing early-onset and late-onset Parkinson's disease (LOPD); patients with EOPD have more prominent muscle stiffness and marked levodopa-induced side effects such as "wearing-

off phenomena," "on-off" dystonia, and peak-dose dyskinesia. Patients with juvenile Parkinson's specifically, have more prominent dystonia and akinetic rigidity. Patients with LOPD more often present with gait disturbances and postural instability. The non-motor manifestations of PD include cognitive and psychological impairments, including psychosis, confusion, and hallucinations. In EOPD, depression was more prominent, which might be linked to a longer duration of the disease and its morbidity. Paresthesia, restlessness, and hyperhidrosis were profound in patients with EOPD.[8] This study supports the current case report findings, as the patient experienced significant levodopa-induced side effects and depression, in addition to the general signs and symptoms of Parkinson's disease.

The incidence of pregnancy in patients with Parkinson's is rare. This study postulated that the clinical manifestation of juvenile Parkinson's might be hormonally linked since they noted that in their patients, symptomatic exacerbations occurred at estrogenic surges such as between ovulation and menstruation, antenatal, and late pregnancy. Estrogen functions in the regulation of dopaminergic neurotransmission in the basal ganglia and hence alters the symptoms of Parkinson's.

A survey conducted in the United Kingdom showed that 65% of women had worsened symptoms despite continuous treatment, speculating that this was associated with the altered serum drug concentrations due to the physiological increase in plasma volume and changes in gastrointestinal absorption and renal excretion during pregnancy. The study signified the continuation of treatment before and during pregnancy, and the importance of having a sufficient multidisciplinary team to monitor pregnant women with Parkinson's disease; however, there are no clear guidelines for an exact management plan. No data indicates increased fertility, maternofetal, or intrapartum complications in women with PD. This survey indicated that there is no contraindication to normal vaginal delivery in patients with PD and that a cesarean section should not be prompted for.[9] However, in this case, the patient had two cesarean sections, and this could be due to motor impairments.

Postpartum maternal acts might be affected by the level of motor deterioration per individual. Breastfeeding is an option despite the limited data about the harms of possible horizontal transmission of medications via breastmilk and the role of levodopa in suppressing lactation, though in this study, two women breastfed their infants comfortably.[9] However, even though the data suggests no harm is implied to infants from lactation, some mothers, like our patient, are still reluctant to breastfeed.

Conclusion

Despite the limited data on juvenile Parkinson's during pregnancy, there are successful uncomplicated cases, and some complications are transient, resolving upon delivery. In such cases, it is important to monitor for gestational-induced conditions not only for the symptoms of parkinsonism since they are also detrimental to maternofetal safety. As illustrated by previous studies, there is an important role for a multidisciplinary team to manage pregnant ladies with juvenile Parkinsonism. Despite the disease's high morbidity for patients and their lives, patients can function normally in social and familial settings.

Conflict of interest

The authors declare no conflicts among them for this publication.

References

1. Olivola S, Xodo S, Olivola E, *et al.* Parkinson's Disease in Pregnancy: A Case Report and Review of the Literature. *Frontiers in Neurology*. 2020;10.

2. Post B, van den Heuvel L, van Prooije T, van Ruissen X, van de Warrenburg B, Nonnekes J. Young Onset Parkinson's Disease: A Modern and Tailored Approach. *Journal of Parkinson's Disease*. 2020:1-8.

3. Dorsey E, Elbaz A, Nichols E, *et al*. Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet Neurology.* 2018;17(11):939-953.

4. Edvardson S, Cinnamon Y, Ta-Shma A, *et al*. A Deleterious Mutation in DNAJC6 Encoding

the Neuronal-Specific Clathrin-Uncoating Co-Chaperone Auxilin, Is Associated with Juvenile Parkinsonism. *PLoS ONE*. 2012;7(5):e36458.

5. Anwar A, Saleem S, Akhtar A, Ashraf S, Ahmed M. Juvenile Parkinson Disease. *Cureus*. 2019.
6. Serikawa T, Shimohata T, Akashi M A, *et al*. Successful twin pregnancy in a patient with parkin-associated autosomal recessive juvenile parkinsonism. *BMC Neurology*. 2011;11(1).
7. Rizek P, Kumar N, Jog M. An update on the diagnosis and treatment of Parkinson disease. *Canadian Medical Association Journal*. 2016;188(16):1157-1165.
8. Klepac N, Adamec, Margetic, *et al*. An update on the management of young-onset Parkinson's disease. *Degenerative Neurological and Neuromuscular Disease*. 2013:53.
9. Young C, Phillips R, Ebenezer L, *et al*. Management of Parkinson's Disease During Pregnancy: Literature Review and Multidisciplinary Input. *Movement Disorders Clinical Practice*. 2020;7(4):419-430.