

A Successful Pregnancy in a Woman with Segawa Disease

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Case Report

The patient was born in Hong Kong and her perinatal development was normal. At the age of 3 years, the patient had ptosis of her eyes and after investigation, a diagnosis of ocular myasthenia gravis was made. Her anti-acetylcholine receptor antibody was positive. Her symptoms improved with pyridostigmine bromide (Mestinon; JDH, Singapore). Thymectomy was also performed at the age of 10 years. At the age of 8 years, she had progressive dystonia. The dystonia was diurnal and progressive during the day and was worst at evening. After extensive investigations, a diagnosis of Segawa disease was made and her symptoms of dystonia improved with the use of Madopar (levodopa and benserazide) [Madopar Roche, Basel, Switzerland]. At the age of 19 years, thyrotoxicosis was also found of which treatment was given for 1 year. It was subsequently stopped when she was euthyroid.

The patient married at the age of 31 years and spontaneously conceived the next year in 2003. At the booking visit of 15 weeks' gestation, physical examination was uneventful. In view of her complicated medical history, joint medical and obstetrical care was arranged with our neurologists. Her symptoms (myasthenia and dystonia) were stable on the drug regimen (Mestinon 20 mg thrice daily and Madopar 62.5 mg thrice daily) and there was no deterioration in her muscle power and tone. The tendon reflexes and cranial nerve were all normal. She complained of some difficulty in breathing in the latest part of pregnancy, and the symptom was attributed to the splinting of the diaphragm. At 39 weeks' gestation, she had spontaneous

onset of labour and the first stage lasted for 10 hours. Ventouse extraction was performed for poor maternal effort (second stage, 48 minutes). A baby girl weighing 3.4 kg was born with good Apgar score. Although we have alerted our intensive care unit team for possible post-delivery ventilation, there was no deterioration in her respiratory effort or muscles tone. The mother was discharged well on the third day. The baby was observed in the special care baby unit because of maternal history of Segawa disease, myasthenia gravis, and maternal fever. The baby was normal on examination without any features of congenital myasthenia gravis, dystonia, thyrotoxicosis, or congenital abnormalities. Blood for anti-acetylcholine receptor was negative. Clinical geneticist was consulted and commented that Segawa disease is autosomal dominant with low penetrance, however, usually due to mutations. So far there were not many mutations reported and the mutational study was not available in Hong Kong. As the symptoms can be late in onset, observation for a longer duration was advised. Up to 5 years of follow-up, there was no evidence of Segawa disease of the child.

The patient became pregnant again in 2004 and the antenatal course was uneventful. As we had taken care of the same patient in her first pregnancy, we were less concerned about the effect of Segawa disease on the course of her second pregnancy. There was no deterioration in her dystonia or muscle tone during

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the second pregnancy and delivery. A healthy baby girl weighing 3.32 kg was born normally at term. The perinatal course was similar. There was no evidence of Segawa disease or other dystonia in 4 years' follow-up.

Discussion

The first report of Segawa disease was on two girls, cousins of each other, with dystonic posture, under the title of "Hereditary progressive basal ganglia disorder" in 1971¹. After accumulation of such cases in adults, Segawa¹ confirmed this disease does not transform to Parkinson's disease in adulthood and published with a nomenclature of "Hereditary progressive dystonia with marked diurnal fluctuation" in 1976. It was also called dopamine-responsive dystonia. The incidence is very low (estimated to be 0.5 per million) and pregnancy associated with Segawa disease is even rarer. Extensive literature search only identified a case report of three pregnancies in one patient with Segawa disease². According to that case report in 1997, which described a normal pregnancy outcome in a third pregnancy of a woman with Segawa disease, the patient was treated throughout gestation with 500 mg per day of levodopa alone. A male infant weighed 2350 g at birth and was developing normally at the time of report. The woman had two other pregnancies but both ended up into first trimester miscarriage. Investigation failed to find any cause for the miscarriages.

We reported on a patient with Segawa disease and there was no adverse maternal or neonatal outcome, which was probably the second reported case in the world literature.

The difficulty in prenatal diagnosis and postnatal confirmation of the Segawa disease in the two infants are presented, as the disease may be late-onset and has variable penetrance. Guanosine triphosphate cyclohydrolase I (GCH-I) deficiency caused by mutation of the *GCH-I* gene located on 14q22.1-q22.2 was recently found in the Segawa disease patients³. With the improvement in the molecular diagnosis of Segawa disease, more precise prediction of the antenatal and / or postnatal diagnosis can be made in the future.

Although levodopa, either alone or in combination with carbidopa, has caused visceral and skeletal malformation in rabbits⁴, similar effect in human was not observed based on the small number of reported cases⁵. It seems that there is no firm reason to withhold l-dopa during pregnancy.

In conclusion, Segawa disease-complicating pregnancy is rare. We estimate that the effects of the Segawa disease and its associated drug treatment on maternal and perinatal outcomes are minimal. However, long-term follow-up of the offspring is required.

References

1. Segawa M. Segawa disease [in Japanese]. *Brain Nerve* 2008; 60:5-11.
2. Nomoto M, Kaseda S, Iwata S, Osame M, Fukuda T. Levodopa in pregnancy. *Mov Disord* 1997; 12:261.
3. Segawa M, Nomura Y, Nishiyama N. Autosomal dominant guanosine triphosphate cyclohydrolase I deficiency (Segawa disease). *Ann Neurol* 2003; 54(Suppl 6):S32-45.
4. Product information. Sinemet. *DuPoint Pharmaceuticals*, 1997.
5. von Graeventiz KS, Shulman LM, Revell SP. Levodopa in pregnancy. *Mov Disord* 1996; 11:115-6.