Rare disease

Management of DYT1 dystonia throughout pregnancy

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A 30-year-old woman with generalised DYT1 dystonia, controlled with medication, presented at 9 weeks gestation with an unplanned pregnancy. A number of learning points were highlighted in management of the patient's dystonia alongside pregnancy including avoidance of excessive medication exposure to the fetus, while maintaining symptom control to a level acceptable and safe for the patient and prenatal diagnostic testing. In our case there was no overt ill effect to the newborn. This is a common worry among pregnant women with dystonia and as such the authors felt it important to report.

BACKGROUND

Dystonia is a rare neurological movement disorder characterised by abnormal postures of affected body parts. As a result, many working outside the field of neurology will be unfamiliar with it. Yet, due to its lifelong course, dystonia and its medical management can complicate relatively common life events, such as pregnancy. We highlight areas which clinicians faced with a similar situation should consider early in the clinical course. Also included is a review of the literature surrounding the relevant medications used to manage dystonia, with focus on their use during pregnancy.

CASE PRESENTATION

A 30-year-old Caucasian, primigravida, with a 23-year history of DYT1 dystonia, was admitted to hospital at 40 weeks for induction of labour in order to minimise further foetal exposure to her dystonia medication. The patient's dystonia began in her right leg at the age of 7 and generalised to involve all four limbs and her trunk over several years. She had previously declined deep brain stimulation surgery and was therefore managed with medication. (figure 1).

At 9 weeks gestation she was taking the following medications: baclofen 10 mgs three times daily, clonazepam 2.5 mgs three times daily, pimizide 2 mgs three times daily and trihexyphenidyl 25 mgs three times daily. She was also taking 400 mcg of folic acid. On examination, she walked with one crutch, had bilateral leg stiffness, an internally rotated right leg that worsened on walking and tremor of her outstretched hands.

She was instructed at week 12 to gradually reduce pimizide over 2 weeks (week 14) and then baclofen in a similar manner (week 16). Stopping pimizide had no effect on her dystonia. However baclofen reduction resulted in spasms of stronger intensity and frequency than in the last 10 years, stopping her from driving and working.

At neurological review during week 23 she was now only taking clonazepam 2.5 mgs three times daily and

trihexyphenidyl 25 mgs three times daily. Examination revealed marked mobile dystonia in both feet, worse on the right, and a mild tremor of her right hand. Walking was difficult due to spasm of her right trunk and leg. She was monitored closely with the aim of stopping clonazepam and trihexyphenidyl by 36 weeks. Trihexyphenidyl was stopped completely with a slight increase in dystonia, however the patient was still able to walk. Clonazepam was continued at 0.5 mgs three times daily throughout pregnancy.

OUTCOME AND FOLLOW-UP

Labour was uneventful, although siting an epidural proved difficult due to the patient's lumbar scoliosis. A healthy baby was born, weighing 3400 g, with Appearance, Pulse, Grimace, Activity, Respiration 9/1 min and 9/5 min. Paediatric review noted good tone, no dysmorphism or talipes. Both mother and baby had normal postnatal observations. One month after delivery, the patient had increased her clonazepam (2.5 mgs three times daily) and restarted baclofen (10 mgs three times daily) and trihexyphenidyl (25 mgs three times daily) at prepregnancy doses, with reasonable control of her dystonia. Pimizide was not restarted as symptom severity did not change when it was stopped during pregnancy.

DISCUSSION

DYT1 dystonia typically begins during childhood and persists throughout life thus having the potential to cause difficulty during pregnancy.¹ As there is currently no curative treatment, most patients are managed with lifelong medication and few by deep brain stimulation. Our case provides an example of how these medications and the effects of generalised dystonia may be managed in pregnant women.

In most pregnancies, the general rule with respect to medication is 'less is better' and, if possible, none whatsoever. However in patients with dystonia, as exemplified by our case, a compromise must be reached between

Figure 1 A timeline showing the clinical course of our patient.

reduction in medication and the unacceptable increase in dystonia symptoms. At the time of conception, most patients will have been on stable dose combinations for many years. Yet in a report of ten patients with dystonia with planned pregnancy, none could be tapered off their medications prior to conception, due to worsening of symptoms.² Furthermore pregnancies which are unplanned do not allow time for adjustment of medication, as was the case in our patient.

The medications commonly used, and evidence for their use during pregnancy, are as follows;

- ▶ Baclofen is used to treat spasticity; however its exact mechanism of action is not clear. It is thought to act via effect on GABA-B receptors. One case reported convulsions 7 days after birth in a neonate exposed to baclofen in utero.³ Rodent studies have suggested an increased incidence of spina bifida with baclofen use.⁴ Our patient stopped taking baclofen by 16 weeks gestation and noticed a significant increase in dystonia symptoms. Gradual reduction is advised as withdrawal symptoms, including seizures, may arise on those taking baclofen for long periods. If a withdrawal syndrome occurs, baclofen should be restarted.
- ▶ Trihexyphenidyl is an anticholinergic. A large prospective study assessing anticholinergic effects in the first trimester found them to be associated with minor foetal abnormalities. However, only nine of these patients took trihexyphenidyl.⁴ The current recommendation in the British National Formulary (BNF) is to only use the drug if the benefits outweigh the risks.

As anticholinergics are a commonly used class of drugs in dystonia and other movement disorders, we felt it important to stress that they have been associated with the induction of eclamptic seizures.⁵ Our patient was able to stop her trihexyphenidyl slowly with only a partial increase in symptoms.

- ▶ Clonazepam, a benzodiazepine, is known to cause neonatal withdrawal symptoms, respiratory depression and hypotonia.⁴ Studies suggest that major neonatal malformation is not a feature of clonazepam use in pregnancy; however larger cohorts are needed.⁶ Our patient remained on a low dose throughout pregnancy. As with baclofen, withdrawal seizures have been reported and patients should be appropriately counselled.
- ▶ Pimoide is classed as an antipsychotic. It acts by blocking a number of central receptors including dopamine and acetylcholine. There is only a single case report of its use (for Gilles de la Tourette syndrome) during pregnancy. In this case no ill effect to the child was seen.⁷
- ▶ Botulinum toxin is another medication used to manage dystonia. It acts by preventing presynaptic acetylcholine release at the neuromuscular junction. The BNF advises it should only be used if essential, with toxicity being demonstrated in animal studies. Safe use has been reported in the literature.^{8,9}
- ▶ Pethidine is a commonly used opioid analgesic during labour, was contraindicated due to its respiratory depressive effect, when combined with clonazepam, on the neonate. Clinicians should be aware that pain during delivery is likely to cause severe dystonic movements.

Appropriate counselling before conception, on the effects of patients' medication on their pregnancy allows a regime conducive to uncomplicated foetal development to be instituted.

DYT1 is an autosomal dominant condition with 30–40% penetrance of clinical symptoms and genetic counselling is offered, but our patient declined. Her decision was based on her apprehension of the spontaneous abortion risk associated with amniocentesis and the high chance of the fetus not manifesting symptoms even if the abnormal gene was inherited. A novel, non-invasive, method of prenatal diagnosis, using maternal plasma, has been used to diagnose DYT1 in two patients.¹⁰ This may be an option for genetic testing during pregnancy in the future.

Although other reports of generalised dystonia in pregnancy are documented, patients' symptoms were not controlled with regular medication alone. One woman with DYT1 dystonia controlled with deep brain stimulators (DBS), after failing many of the medications our patient was taking, gave birth to a healthy baby.¹¹ As DYT1 dystonia has shown the best response to DBS, its increasing use is likely. Thus it may feature more in cases involving pregnant women with dystonia.

Our case illustrates the need for a multi-disciplinary approach to pregnancy management in dystonia. Prepregnancy counselling is important to prepare the patient for increase in symptoms. A consultant obstetrician and neurologist are essential. The patient should be educated on the risks to the fetus both due to being affected by DYT1 and of continuing medication during pregnancy. An accommodating and effective therapeutic regimen should be reached before conception. We recommend family planning discussions early in patients with dystonia to allow flexibility in planning antenatal care. Regular review is crucial, as is a thorough history and neurological examination to identify potential antenatal problems. Urgent general practitioner referral to a neurologist is crucial in unplanned pregnancy.

In closing, management of dystonia is a specialist area and the interactions of the illness and its treatments to the natural process of pregnancy are not well understood. We have described the experiences of one patient who was treated solely with medication and resulted in an uneventful labour and birth.

Learning points

- Early multi-disciplinary communication between general practitioner, neurologist and obstetric team is required for best outcome.
- Pregnancy and its possible effects on dystonia should be discussed and a plan drawn up with the patient to manage medication reduction and warn of the likely increase in symptoms during this period.
- Taper doses gradually to prevent withdrawal symptoms and stop as many medications as possible. Balance this with increase in dystonia symptoms and loss in quality of life.
- Further studies are needed on the use of these medications in pregnancy.
- Antiemetic medications commonly used during pregnancy can precipitate dystonia. Use in patients with dystonia should be guarded, if at all.

Competing interests None.

Patient consent Obtained.

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