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A case of successful pregnancy managed in a patient living with Motor Neurone Disease for more than 3 years

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SUMMARY

A woman in her 20s presented with progressive weakness of her left arm and leg, slurred speech and swallowing difficulties. The clinical presentation and neurophysiological tests were consistent with motor neuron disease. She was referred to the regional ventilation unit for respiratory muscle function testing. This confirmed restrictive spirometry and borderline sniff nasal inspiratory pressure and cough peak expiratory flow. Three years later, she presented with an unplanned pregnancy and expressed the wish to continue the pregnancy to term. She was monitored throughout pregnancy with interval respiratory muscle testing and was reviewed in the high-risk pregnancy anaesthetic clinic. She was also closely monitored by the obstetrics and gynaecology team. A multidisciplinary team meeting between all stakeholders agreed on caesarean section delivery at 34 weeks. The pregnancy and the delivery were without complications; the baby was healthy and both mother and baby remain well to date.

BACKGROUND

Motor neuron disease (MND) is uncommon in patients less than 30 years of age. A large population-based study in the UK reported an incidence rate of 0.6 (CI 0.2, 1.3) in this age group.[1] There are only a few case reports of pregnancies in people living with MND (the majority of these cases were MND presenting for the first time during pregnancy). To our knowledge, this is the first case report of a successful pregnancy managed without any complication in a patient living with MND. We highlight the challenges faced throughout the pregnancy and how these were addressed using a multidisciplinary team (MDT) approach. This case report demonstrates the possibility of successful pregnancy in people living with MND and illustrates an approach which may help fellow clinicians support patients in their decision making. Finally, the case also illustrates other important complications of MND and interventions to manage them and that treatment is not always futile. Life events, therefore, need not to be denied to neuromuscular patients.

CASE PRESENTATION

Initial presentation and investigations

A fitness instructor woman in her 20s presented to the ventilation team with a weak cough and difficulty to expectorate thick and sticky phlegm. She was diagnosed with MND 3 months earlier following a review by the neurology team with left arm weakness, gradual left leg weakness and disarticulate speech. She also complained of food 'going down the wrong way' and choking spells when drinking liquids. This was followed by gradual exertional dyspnoea, cramps in hands, legs and feet as well as fasciculations. Her medical history was unremarkable and she was not on regular medications. There was no family history of MND.

Examination revealed 1 beat of clonus at both ankles, up-going plantar responses and symmetrical ankle jerks. Neurophysiological studies showed normal nerve conduction studies but widespread evidence of chronic neurogenic changes on needle electromyography. There was active denervation both distally and proximally in her left upper limb and distally in both lower limbs (see neurophysiological studies in table 1A–C). Her baseline investigations included normal CT of head, chest, abdomen and pelvis as well MRI of head and whole spine. She was commenced on riluzole with regular monitoring of biochemistry including liver function tests.

She was reviewed by the speech and language therapist (SALT) in regards to her swallow and was advised to add thickener to her fluids.

Sleep and ventilation team review

She was referred to the regional sleep and ventilation unit to assess her respiratory muscle function and to exclude sleep disordered breathing. She was managing to sleep well at night and felt refreshed in the mornings. She denied having any morning headaches and was able to lie flat without difficulty. Her investigations (as highlighted in her respiratory muscle testing in tables 2 and 3) revealed restrictive spirometry, borderline sniff nasal inspiratory pressure (SNIP) and cough peak flow with normal capillary blood gases. In this initial assessment, she was provided with information regarding the long-term feeding plan, including percutaneous endoscopic gastrostomy (PEG) insertion. She was referred for initiation of cough assist and an overnight pulse oximetry was arranged; this was found to be normal with no evidence of nocturnal desaturations.

She remained under regular review by the neurology, respiratory and SALT teams for worsening mobility, bulbar function and swallowing. She did not have sleep-related symptoms, although there has been gradual decline in her respiratory muscle testing. She mobilised short distances. She was admitted electively for PEG insertion 1 year following her diagnosis. This was complicated by

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Table 1 Neurophysiological studies

Upper limbs (NCS)							
A: Sensory nerve action potentials							
		Right		Left			
Nerve	**Digit**	**Conduction velocity (m/s)**	**Amplitude (µV)**	**Conduction velocity (m/s)**	**Amplitude (µV)**		
Median	III	56	33.9				
Upper limb surface EMG							
Muscle		**APB**	**ADM**	**APB**	**ADM**	**FDI**	
Side		R	R	L	L	L	
CMAP (mV)		7.8					
Terminal motor latency (ms)		3.5					
Conduction velocity (m/s)	Wrist-elbow	58					
	Ulnar groove	66					
	Elbow-axilla	63					
F-wave response (Ht 5 ft 6 in)	F-M (ms) (minimum)	24.9					
Lower Limbs (NCS)							
B: Sensory nerve action potentials							
		Right		Left			
Nerve	**CV (m/s)**	**Amplitude (µV)**		**CV (m/s)**	**Amplitude (µV)**		
Sural	43	14					
Lower limb surface EMG							
Muscle		**EDB**	**AH**	**EDB**	**AH**		
Side		**R**	**R**	**L**	**L**		
CMAP		8	8.7				
TML (ms)		4.8	4.1				
Conduction velocity (m/s)	Calf	49					
F wave response (Ht 5 ft 6 in)	F-M (ms) minimum	40.9	45.1				
C: Concentric needle EMG							
				Maximum effort			
Muscle	**Spontaneous activity**	**Motor units**		**Number**	**Max size (mV)**		
R.Biceps brachii	Fasciculations 3+	Long-duration polyphasic units		Reduced	2		
R.1ST Dorsal interosseous	FIBS 2+, fasciculations 3+	Long-duration polyphasic units		Discrete	2		
R.Rectus abdominis	Fasciculations 3+	Long-duration polyphasic units		Discrete	2		
R.Vastus lateralis	Fasciculations 2+	Long-duration polyphasic units		Reduced	2		
R.Tibialis anterior	Positive sharp waves 2+, FIBS 1+, fasciculations 1+	Long-duration polyphasic units		Discrete	3		
L.Tibialis anterior	Fasciculations 2+, positive sharp waves 3+, FIBS 3+	Long-duration polyphasic units		Discrete	3		
R.Medial gastrocnemius	FIBS 3+, Positive sharp waves 2+	Long-duration polyphasic units		Discrete	3		

CMAP, compound muscle action potential amplitude; EMG, electromyography; NCS, nerve conduction studies; TML, terminal motor latency.

post procedure pancreatic inflammation, treated by the surgical team with diagnostic laparoscopy, exploratory laparotomy and irrigation of peritoneal cavity. She recovered well from this episode and remained stable for the following 18 months.

TREATMENT

Pregnancy and MDT approach to management

Three years following her diagnosis of MND (May 2018), she confirmed a positive pregnancy test to the sleep and ventilation team. This was not a planned pregnancy; however, she wished to continue the pregnancy to term and optimise the chances of a successful outcome. She denied any symptoms of sleep-disordered breathing, was finding her sleep refreshing with no waking headache or any daytime somnolence. Respiratory muscle testing at this stage showed worsening restrictive defect in her spirometry with static SNIP and stable blood gases (investigation 2). Scarcity of evidence in the literature in regards to the safety of pregnancy in MND made it difficult to predict the course of the pregnancy. Nonetheless, the challenges ahead were extensively discussed during consultations and a personalised plan was drawn, including MDT approach to her further management (table 4). She was monitored closely with a monthly follow-up and regular respiratory muscle testing.

There was an appreciable decline in her motor function (especially upper limbs) and was using a wheelchair on regular basis. Her respiratory function, however, improved during pregnancy and remained stable throughout the pregnancy. Following parturition, both her spirometry and SNIP declined again to a new baseline. She was reviewed in the high-risk antenatal anaesthetic clinic given her known progressive MND, risk of diaphragmatic splinting and respiratory compromise with the advancing pregnancy.

Table 2 Serial pulmonary function tests before and during pregnancy

	At diagnosis	1 year before pregnancy	During pregnancy 1	During pregnancy 2	During pregnancy 3	During pregnancy 4	During pregnancy 5
FEV_1 (% predicted)	2.31 (70%)	1.79 (55%)	1.40 (44%)	1.70 (53%)	1.69 (53%)	1.71 (53%)	2.33 (73%)
FVC (% predicted)	2.46 (65)	1.84 (50%)	1.56 (42%)	1.79 (49%)	1.81 (49%)	1.88 (51%)	2.43 (66%)
Ratio	94	97	90	95	93	91	96
SNIP cmH_2O	−48	−30	−29	−36	−34	−35	−35
Cough peak flow L/min	160	Unobtainable	Unobtainable	Unobtainable	Unobtainable	Unobtainable	–
pH	7.44	7.41	7.45	7.48	7.50	7.47	7.50
P_{CO_2}	4.79	5.20	4.22	4.13	3.96	4.26	3.96
PO_2	10.60	11.40	12.80	12.40	13.90	12.90	12.10
HCO_3^-	23.80	24.10	21.80	22.60	22.80	23.20	22.90
Oxygen saturations	95.80	98.10	98.40	98.60	99.30	99	98.50

FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; SNIP, sniff nasal inspiratory pressure.

Perioperative care plan was then planned following an MDT meeting between the obstetric, anaesthetic and the respiratory consultants. Her detailed plan included:

- An elective caesarean section at 34 weeks: on balance, it was felt to be the safest time for both mother and baby and carried less risk of decompensation and need for invasive ventilation.
- Discussion with the intensive care unit and plan for invasive ventilation in the event of respiratory compromise.
- Management in the maternal high dependency unit (maternal HDU) in the first 24 hours post delivery, with support from ventilation nurse specialists, in case of non-invasive ventilation requirement post partum.
- Patient and partner were given a guided tour of the maternity unit to inform their expectation and to reduce anxiety.

At this stage, she was rarely mobilising except for limited occasions with support from her partner. She was able to transfer from bed to chair unaided.

Parturition and postpartum care

She was admitted in October 2018 for an elective caesarean section (C-section) at 34 weeks and 4 days gestation. An arterial line was inserted for blood gases monitoring and a spinal anaesthetic was used, achieving a block to T4. Although non-invasive ventilation was on standby, she did not require any assistance with ventilation and was stable from respiratory point of view throughout the procedure. Initially, her head was elevated to a 15-degree angle, raising to 30 degrees soon after C-section to ensure the local anaesthetic did not distribute caudally. Phenylephrine infusion was used throughout the delivery to prevent hypotension. The C-section was completed without complication. Following delivery she was monitored in the recovery unit and later transferred to the maternity HDU as planned. A healthy baby boy, weighing 2.76 kg was delivered and assessed by the paediatric team; his APGAR score (appearance, pulse, grimace, activity, respiration) was 9 at 1 min and 10 at 5 min. No abnormality was detected during examination. The baby was admitted to the transitional care unit for nasogastric feeding and remained stable throughout.

Her stay in maternity HDU was uneventful, and she was stepped down to the ward the following day. She received regular chest physiotherapy given her relatively weak cough. She struggled with mucus clearance 48 hours post partum; this was managed with regular chest physiotherapy, mucolytics (carbocisteine) and saline nebulisers. She did not tolerate a trial of manual insufflation exsufflation and her chest stabilised the following day. She was deemed medically optimised for discharge 5 days post partum but remained in hospital for further 2 days until baby was weaned from nasogastric feeding.

Table 3 Serial pulmonary function tests after pregnancy

	2 months post partum	4 months post partum	7 months post partum
FEV_1 (% predicted)	1.01 (32%)	1.09 (34%)	1.06 (33%
FVC (% predicted)	1.07 (29%)	1.21 (33%	1.09 (30%)
Ratio	94	90	98
SNIP cmH_2O	−27	−22	−20
Cough peak flow L/min	Unobtainable	Unobtainable	Unobtainable
pH	7.41	7.45	7.46
P_{CO_2}	5.24	4.55	4.18
PO_2	9.90	13	11.86
HCO_3^-	24.30	22.90	22
Oxygen saturations	96	98.10	97

Table 4 Multidisciplinary team approach

Team	Input
Sleep and ventilation	She was provided with a non-invasive ventilation in the event she required this in the latter stages of her pregnancy. A repeated overnight pulse oximetry was, again, normal. She was regularly reviewed throughout her pregnancy and her respiratory muscle testing improved to her baseline prior to pregnancy. She had no symptoms of sleep disordered breathing and remained stable from respiratory point of view throughout.
Obstetrics team	She was commenced on a prophylactic dose of low-molecular-weight heparin at 20 weeks gestation in view of her venous thromboembolism risk and this was continued for 6 weeks post partum. She was also consented to an elective caesarean section.
Anaesthetic team	Detailed perioperative care plan (discussed below).
Gastroenterology	PEG feeding was felt to be safe during pregnancy.
SALT and dieticians	She was assessed for PEG feeding due to the expected higher nutritional demand in the latter stages of pregnancy.
Neurology team	Regular review with the neurology consultant and MND nurse specialist.

MND, motor neuron disease; PEG, percutaneous endoscopic gastrostomy; SALT, speech and language therapist.

OUTCOME AND FOLLOW-UP

At the time of writing of this article, mother and baby (2 years and 8 months) remain well. The baby is meeting all his developmental milestones. The patient is under regular review for her MND by the various MDTs and has interval respiratory muscle function tests. She remains stable from respiratory point of view and is not on a ventilator (NIV). She enjoys regular family trips and leads as active a lifestyle as possible with support from her very supportive partner.

DISCUSSION

Pregnancy in women with MND is rare and presents a theoretical risk to both the mother and child. Previous reports have described women developing signs of the disease during pregnancy or early post partum. Our case is unique in that we describe a female patient with known MND conceiving and delivering a healthy baby 3 years after her diagnosis. Challenges for clinicians arose due to limited data in the literature regarding the effects of MND on the pregnancy, parturition and the newborn in addition to the effects of pregnancy on the course of disease. We are aware of only one previous case report of a planned pregnancy in known amyotrophic lateral sclerosis (ALS).[2] A case of a young woman with sporadic ALS who gave birth twice during the course of her disease. The first pregnancy occurred 1 month after diagnosis (conceived before diagnosis was made). This resulted in an uncomplicated delivery. Second pregnancy occurred 2 years after diagnosis, when she was confined to bed due to the severity of her MND. This pregnancy was complicated by progression of dysphagia and cachexia and at 21-week gestation; PEG tube was performed. Emergency C-section was needed at 34-week gestation. The baby girl suffered from intrapartal asphyxia; APGAR score was 7 and increased to 8 after 5 min. She required admission to neonatal ward for oxygen therapy. Two months after delivery, mother was tracheostomised and put on long-term invasive mechanical ventilation. She died 11 months after the second childbirth due to severe gastrointestinal haemorrhage. This case represents very rapid progression of symptoms during and after pregnancy, and the postpartum period was complicated for both mother and child. In contrast, our case's symptoms stabilised during the gravid period; the parturition was relatively uneventful, and the postpartum period was without any complications for both mother and child.

Our case demonstrated appreciable improvement in the spirometry and SNIP values during pregnancy. The forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) continued to show sustained improvement until parturition. Following childbirth, the FEV_1, FVC and SNIP declined to a new baseline which was sustained for few months post partum. Chemical/hormonal changes and the mechanical effects of the progressive uterine distension lead to changes in respiratory physiology during pregnancy.[3] Progesterone gradually increases during pregnancy from 25 ng/mL at 6 weeks gestation to a peak of 150 ng/mL at 37 weeks, and it is known to increase the sensitivity of the respiratory centre to carbon dioxide. Similarly, the oestrogen level increases during pregnancy and is responsible for higher number of progesterone receptors within the hypothalamus and medulla.[3] The progressive uterine distension leads to elevation of the diaphragm which can affect lung volume and chest wall/thoracic configuration.[4] In most cases, the FVC, FEV_1 and peak expiratory flow remain unchanged or modestly increase during pregnancy. This could explain the respiratory function test observed in our case.

These cases should remind clinicians looking after younger patients with MND of the importance of early family planning discussion. The patients should be informed of the limited evidence on pregnancy influencing disease progression. In the early stages of MND, there is no evidence in the limited literature of adverse events to mother and baby; however, in the latter stages when respiratory and dietary issues become evident, outcomes to both mother and baby can be catastrophic.

The most important aspect of care for a woman with respiratory muscle weakness secondary to neurological disorder is to carry out an early risk stratification and then to clearly discuss the risks and benefits of each treatment. This will allow the clinician to decide on appropriate and timely investigations (such as respiratory muscle function tests and blood gases) and liaise closely with other colleagues involved in patient's care. Any investigation and/or treatment needs to be individualised and tailored to the needs of the patient depending on the type of neurological condition and the degree of severity. As our case illustrates, it is also important to optimise the patient's nutritional demands, general physical health and to coordinate care between all the MDT caring for the patient. Regular monitoring throughout pregnancy, the timing of elective admission for C-section and carefully agreed postpartum care played a significant role in the success of pregnancy and stable postpartum period in our case.

Learning points

- Respiratory muscle assessment for people living with motor neuron disease (MND) and the importance of regular monitoring during pregnancy.
- A multidisciplinary team of physicians and healthcare professionals is essential in positive outcomes for mother and baby in MND pregnancies.
- MND does not have harmful consequences on fetal development, but respiratory function of the mother should be carefully monitored.
- In younger patients with new diagnosis of MND, family planning should be discussed early.
- Careful planning of interventions increases the chances of successful outcome.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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