Case 10. Mom Knows Best: No So Transient

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History

The patient was a baby boy born by 32-years-old mother Gravida 2 Para 0 at full term by normal spontaneous vaginal delivery with birth weight of 3390 g with Apgar 7 at 1 min and 8 at 5 min. He had weak cry and hypotonia at birth. Mom was a known case of autoimmune myasthenia gravis (MG) with antibodies against acetylcholine receptor (AChR). She had recent exacerbation of her MG requiring treatment with Intravenous Immunoglobulin only. No systemic steroids were given. She was on pyridostigmine 30 mg three times a day and thyroxine during labor. Due to hypotonia and ptosis noted at birth with a maternal history of MG, he was diagnosed with transient neonatal myasthenia gravis (TNMG). Because of severity of clinical symptoms, his blood was tested for antibodies against AChR which confirmed the diagnosis. He was treated with neostigmine and pyridostigmine which he did not tolerate, developing bradycardia. He required respiratory support in the form of nasal continuous positive airway pressure (CPAP) and oxygen by nasal cannula during the neonatal period and required nasogastric feeding. He was sent home on modified breast and bottle feeding after prolonged stay for 35 days. No polysomnogram (PSG) was done during his stay in neonatal intensive care (NICU). Mom monitored his pulse oxygen and noted frequent desaturation during sleep and hence referred to the sleep specialist.

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Examination

At first exam at age of 3 months, mom came with few videos recording of episodes in sleep which showed fast eye movements consistent with REM stage of sleep, snoring and desaturation in the upper 80s, thus confirming clinical impression of significant obstructive sleep apnea (OSA) during REM sleep. He was getting tired during feeding and hence getting small amount (60 mL instead of 120 mL) of frequent feedings (every 2 h instead of 4 h) including in sleep. He choked when he tried to take more volume. Hence, mom was strict with feeding volume and precaution. During office visit, he got tired with 5–6 sucks and started retraction and portable carbon dioxide (CO_2) monitoring went up from 30 to 38. He recovered quickly on stopping feeding. He did not have head control (expected by 2 months) and had drooping of eye lids. At 6.5 months, there was no drooping of eyelids, improved head control and he tried to seat with support. Also, choking was less frequent than before. His pulse oxygen was normal when he slept in prone position. But in supine position, it decreased to 91–94%. His other mental developmental milestones were good. He was gaining weight at a normal pace.

Investigations

Swallow study done at age of 7 days
Findings:

- First swallow: Thin liquid by level 1 nipple, recumbent position. Severe oral delay and mild swallow trigger delay.
- Second swallow: Thin liquid by level 1 nipple, upright position. Moderate oral delay and mild swallow trigger delay. Nasopharyngeal regurgitation.
- Third swallow: Thin liquid by level 2 nipple, upright position. Moderate oral delay and mild swallow trigger delay. Nasopharyngeal regurgitation.

Impression:

1. No aspiration observed.
2. Moderate to severe oral delay and mild swallow trigger delay as described.
3. Nasopharyngeal regurgitation.

Lab results for AChR antibodies are shown in Table 10.1.

ECHO: done at age of 10 weeks: normal.

PSGs done at age of 4 and 7.5 months are shown in Table 10.2.

Table 10.1 Acetylcholine receptor antibodies over time

Name of test	Test date 03/2021	Test date 01/2022	Interpretation Negative	Interpretation Indeterminate	Interpretation Positive
ACh receptor Blocking Ab	74%	0%	0–26%	27–41%	≥42%
ACh receptor Binding Ab	24.9 nmol/L	0.04 nmol/L	0.0–0.4 nmol/L		≥0.5 nmol/L
ACh Modulating Ab	89%	1%	0–45		≥46%
Muscle Specific Tyrosine Kinase		0	0–0.3 nmol/L		≥0.04 nmol/L

Ach = acetylcholine; Ab = antibodies

Table 10.2 Polysomnography data over time

Polysomnogram	4 months	7.5 months
AHI-total	15.9	4.6
AHI: REM sleep	20 (all supine)	9.2 (supine 10.1/h)
AHI: Non-REM sleep	12.2	2.5
Pulse oxygen: 92–96%	1.2%	0.9%
Pulse oxygen: <92%	0.5%	0.1%
REM sleep %	47.7%	31.3%
PLMS	6.8%	0
CO_2 > 50 mmHg	0%	0%

AHI = apnea-hypopnea index; PLMS = periodic limb movements of sleep; CO_2 = carbon dioxide

Diagnosis

Transient neonatal myasthenia gravis with OSA, improving with time.

Discussion

Transient neonatal myasthenia gravis (TNMG) is a neuromuscular junction disorder secondary to trans-placental transfer of maternal IgG antibodies again AChR [1]. Normally, such antibodies get degraded and disappear from the body fast, around 4 months [1]. Most important issue for TNMG is risk for aspiration/choking during feeding. Hence extreme precaution is required during feeding. As managed in this case, small frequent feeding is advised [2]. In some cases, the infant may need gastric tube feeding. Other major issue is difficulty in breathing/respiratory distress. Normally, it is managed by supportive care like nasal CPAP or supplemental oxygen as needed [2]. Medications like neostigmine and pyridostigmine are

reserved for the severe cases such as this one in order to help in feeding and breathing [2]. The medications are known to produce significant side effects, more severe being cardiac side effects such as bradycardia and cardiac arrhythmias [2]. Hence, usually conservative approach is done especially if the child cannot tolerate the pharmacological treatment. As hypotonia is primary problem, it gets worst in REM sleep due to its associated muscle atonia. The obstruction of airway is caused by tongue falling backward, blocking the oropharynx along with atonia of upper airway muscles. Often, caregiver learns and tries to keep babies in prone or side position during sleep. This position prevents obstruction of upper airway. The recovery period depends on the original titer of those three antibodies [1] as shown in Table 10.1. This condition affects skeletal muscles only [2] and the brain function is not affected. Thus, such patients' response to desaturation is appropriate and fast, making frank apnea rare. Also, for the same reason, the severity of desaturation is not bad as shown in the Table 10.2. Always, question arises if to treat such patients with PAP therapy or not. As most of infants fight with PAP therapies and cry, thus exhaust their muscles, often conservative approach is the best approach. It avoids midfacial hypoplasia secondary to compression of bridge of nose from use of PAP therapy. Prone and side position is an alternative approach worth considering especially if family is reliable. Caregivers prefer this approach though most physicians are not in favor of prone positioning due to risk for sudden infant death syndrome (SIDS)/apparent life threatening episode (ALTE)/brief resolved unexplained episode (BRUE). In such situation, family should be provided with pulse oximetry to monitor the condition. It must be used during all sleep time including naps.

Family must be provided with list of medications to be avoided, for example, aminoglycosides, macrolides (like azithromycin), fluoroquinolones, beta blockers, procainamide, quinidine, neuromuscular blocking agents and magnesium [2].

It is also important to inform the mom that her subsequent babies are at higher risk of developing TNMG [1].

References

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