1. FLOWCHART

Floppy neonate

Septic? Impaired responsiveness?

Septic screen

Central cause

Cranial US/MRI

Perinatal asphyxia/cerebral malformation

Screening for IEM consider:
- blood gas lactate ammonia
- plasma amino acids acylcarnitine profile very long chain fatty acids
- urine organic acids urine mucopolysaccharides

Maternal myotonia consider myotonic dystrophy

Maternal myasthenia consider transient myasthenia gravis

Genetic testing consider:
- array CGH
- karyotype
- fluorescence in situ hybridization (FISH)
- DNA methylation studies

AchR Ab and edrophonium test

High CK consider congenital muscular dystrophy

Normal CK

EMG/NCS

Myopathic

Congenital myopathies confirm by muscle biopsy

Neuropathic

NCS normal- SMA peripheral neuropathy confirm by nerve biopsy

Neuromuscular transmission defect

Transient myasthenia gravis congenital myasthenia syndromes

Normal CK

Genetic testing for SMA SMN1 gene deletion for SMA
1. AIM

1.1 To provide guidance on the management of hypotonic neonate

1.2 Congenital hypotonia is a relatively common diagnosis in the newborn period. It is defined as a subjective decrease of resistance to passive range of motion in a newborn and can be due to a defect at any level of the nervous system.

2. AETIOLOGY

Causes include (but are not limited to):

2.1 Central (most common)

- Sepsis
- Hypoxic ischaemic encephalopathy
- Intracranial haemorrhage
- Cerebral malformations
- Chromosomal abnormalities (e.g. Trisomy 21, Prader-Willi syndrome)
- Congenital infections (TORCH)
- Acquired infections
- Inborn errors of metabolism
- Endocrine: hypothyroidism
- Peroxisomal disorders
- Drug effects (e.g. benzodiazepines, magnesium toxicity)
- Benign congenital hypotonia

2.2 Spinal cord

- Birth trauma (especially breech delivery)
- Syringomyelia

2.3 Anterior Horn Cell

- Spinal muscular atrophy
- Pompe’s disease (acid maltase deficiency)
- Neurogenic atrogyrosis

2.4 Neuromuscular junction

- Myasthenia gravis (transient/congenital)
- Infantile botulism

2.5 Muscle

- Muscular dystrophies (inc. congenital myotonic dystrophy)
- Congenital myopathies (e.g. central core disease, nemaline rod myopathy, myotubular myopathy, congenital fiber type disproportion and multicore myopathy)
- Congenital muscular dystrophies (merosin deficient, Walker-Warburg disease, muscle-eye-brain disease, Fukuyama disease)

2.6 Peripheral nerves

- Hereditary motor and sensory neuropathies (Dejerine-Sottas disease)
- Congenital hypomyelinating neuropathy
- Hereditary sensory and autonomic neuropathy
2.7 Metabolic myopathies and multisystem disease

- Acid maltase deficiency
- Primary carnitine deficiency
- Cytochrome-c-oxidase deficiency
- Disease of glycogen metabolism
- Severe neonatal phosphofructokinase deficiency
- Severe neonatal phosphorylase deficiency
- Debrancher deficiency
- Peroxisomal disorder
- Neonatal adrenoleukodystrophy
- Cerebrohepatorenal syndrome (Zellweger's)
- Disease of creatine metabolism
- Mitochondrial myopathies

3. HISTORY

- Maternal history: systemic diseases
  - drug history
  - unrecognized myotonic dystrophy
- Family history: consanguinity
  - sudden infant deaths
- Pregnancy: foetal movement
  - drug exposure (e.g. AEDs)
  - polyhydramnios/oligohydramnios
  - abnormal presentation
- Delivery: Apgar score (muscle tone?)
  - resuscitation
  - cord gases
- Postnatal course: feeding
  - alertness
  - response to stimuli
  - spontaneous activity
  - respiratory effort
- Course of floppiness: deterioration over time?

4. PHYSICAL EXAMINATION

Key question:

Is the child ‘just’ floppy, or floppy and weak (e.g. in supine lying does the child have enough antigravity power to hold the limbs in the air?) Weakness implies a peripheral cause.

<table>
<thead>
<tr>
<th>Site of involvement</th>
<th>Clinical features</th>
<th>Differential diagnoses</th>
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<tbody>
<tr>
<td>Central:</td>
<td>normal strength</td>
<td>brain malformations</td>
</tr>
<tr>
<td></td>
<td>normal/ increased DTRs</td>
<td>perinatal asphyxia</td>
</tr>
<tr>
<td></td>
<td>+/- seizures</td>
<td>chromosomal disorder</td>
</tr>
<tr>
<td></td>
<td>+/- dysmorphic features</td>
<td>inborn errors of metabolism</td>
</tr>
<tr>
<td></td>
<td>+/- reduced alertness</td>
<td></td>
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Neonatal hypotonia clinical approach guidelines
Author: T Lucas Ginter Clinical Fellow in Paediatric Neurology
April 2017
Date of review April 2020

Site of involvement | Clinical features | Differential diagnoses
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• Anterior horn cell: | generalised weakness decreased/absent DTRs fasciculations often described as alert | spinomuscular atrophy

• Nerve | weakness distal>proximal decreased/absent DTRs +/- fasciculations | peripheral neuropathy

• Neuromuscular junction weakness, face /eyes /bulbar normal DTRs no fasciculations +/- arthrogryposis | myasthenia gravis botulism

• Muscle | weakness proximal>distal weakness face, EOM decreased DTRs +/- contractures | congenital muscular dystrophy congenital myotonic dystrophy congenital and metabolic myopathy

• Additional clues | hepatosplenomegaly- storage disorders, congenital infection renal cysts, high forehead, wide fontanelles- Zellweger’s hepatomegaly, retinitis pigmentosa- adrenoleukodystrophy congenital cataracts, glaucoma- Lowe syndrome abnormal odour - inborn error of metabolism hypopigmentation, undescended testes- Prader Willi

5. INVESTIGATIONS

The initial work-up of the floppy neonate depends upon the medical history and findings in the clinical evaluation

5.1 Sepsis screen if concerns over infection

5.2 Central hypotonia

• Congenital infection screen if clinical suspicion: toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, TORCH

• Screening for inborn errors of metabolism
glucose magnesium bone profile TFT blood gas lactate ammonia plasma amino acids acylcarnitine profile urine organic acids and urine mucopolysaccharides

• If dysmorphic features- array CGH, karyotype and fluorescence in situ hybridization (FISH) or DNA methylation studies ( e.g. Prader- Willi Syndrome)

• Consider CSF metabolic workup

• Neuroimaging for structural abnormalities and metabolic disease – cranial ultrasound scan and brain +/- spine MRI.
• EEG

5.3 Peripheral hypotonia

• Examination of parents- myotonia

• Creatine kinase – elevated in congenital muscular dystrophy, mildly in SMA and normal in many myopathies

• Specific genetic tests - DNA triplet (CTG) repeats for congenital myotonic dystrophy SMN1 gene deletion for SMA

• Electrophysiological studies- electromyography/ nerve conduction studies

• Muscle biopsy- myopathies, muscular dystrophy, metabolic disorders

• Trial of short acting acetylcholinesterase inhibitor if myasthenia is suspected

5.4 Consider discussion+/- referral to tertiary Paediatric Neurology

6. REFERENCES


Principles and Practice of Child Neurology in Infancy edited by Colin Kennedy 2012