

**Case 35 (November 16 2006):** [N Engl J Med 2006;355:2132-42](#)

**Demographic:** Male, Neonate, America North, General speciality

**Clinical features extracted from the case and entered into the query box:**

diffuse hypotonia  
highpitched cry  
mild jaundice  
decreased tone in abdominal wall muscles  
absent step and minimal Moro's reflexes  
marked head lag, arms and legs held in a flaccid extensor posture  
absent deep-tendon reflexes in the arms  
trace reflexes at the knees  
bilateral ankle clonus  
polymicrogyria  
elevated serum creatine kinase

**Synonyms used by Isabel for the above query:**

Highpitched cry

**STOP !**

**Before you read further you might want to construct your own:**

- Complete differential diagnosis
- Final diagnosis

**In the following section you will find:**

- The differential diagnosis constructed by the MGH panel
- The final diagnosis of the case
- Which of the MGH panel differential diagnoses did Isabel contain
- Did Isabel suggest the Final diagnosis

***Final Diagnoses of the case according to NEJM:***

Congenital muscular dystrophy

***Differential Diagnoses of the case as given by Isabel:***

Congenital muscular dystrophy (Muscular Dystrophies) – Isabel 1<sup>st</sup> page

***Was the final diagnosis given by Isabel:***

Yes, Isabel 1<sup>st</sup> page

***Entire presentation cut and pasted into the Isabel query box:***

None of the above

**Isabel differential of extracted features from entire case presentation:**

|   |   |
|---|---|
| <p><b>NEUROMUSCULAR DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Spinal Muscular Atrophies</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Muscular Dystrophies</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Congenital Myopathies</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Hereditary Motor-Sensory Neuropathies</a> <span style="float: right;">RD</span></li> </ul> | <p><b>NERVOUS SYSTEM DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Perinatal Asphyxia</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Brachial Plexus Injury</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Dystonia Disorders</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Neural Tube Defects</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Metachromatic Leukodystrophy</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Intracranial Hemorrhage</a> <span style="float: right;">RD</span></li> </ul> |
| <p><b>LIVER DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Kernicterus</a> <span style="float: right;">RD</span></li> </ul>   |   |
| <p><b>SOCIAL ISSUES</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Sexual Abuse</a> <span style="float: right;">RD</span></li> </ul>  |   |
| <p><b>METABOLIC DISEASES</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Hypoglycemia Disorders</a> <span style="float: right;">RD</span></li> </ul>   |   |
| <p><b>TRAUMA INJURIES</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Head Injury</a> <span style="float: right;">RD</span></li> </ul>   |   |
|   | <p><b>INFECTIOUS DISEASES</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Viral Meningoencephalitis</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Botulism</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Spirochetal Infections</a> <span style="float: right;">RD</span></li> </ul>   |
|   | <p><b>GASTROINTESTINAL DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Hiatus / Diaphragmatic Hernia</a> <span style="float: right;">RD</span></li> </ul>  |
|   | <p><b>ORTHOPEDIC DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Arthrogyposis Multiplex Congenita</a> <span style="float: right;">RD</span></li> </ul>  |
|   | <p><b>HUMAN GENETICS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Prader-Willi Syndrome</a> <span style="float: right;">RD</span></li> </ul>  |

## **Table 1: Differential Diagnosis of the Floppy Infant Syndrome**

### **Central nervous system disorders**

Congenital, nonprogressive encephalopathies  
Ischemic encephalopathies  
Infectious encephalopathies  
Metabolic encephalopathies  
Endocrine encephalopathies  
Developmental encephalopathies (e.g., Prader–Willi syndrome)  
Degenerative, progressive encephalopathies

### **Spinal cord disorders (anterior horn cell and peripheral nervous system)**

Infections (e.g., poliomyelitis)  
Motor neuron diseases (spinal muscular atrophy type 1)  
Neurogenic arthrogryposis  
Glycogen storage diseases (e.g., Pompe's disease)  
Lysosomal storage abnormalities  
Sensorimotor polyneuropathies  
Demyelinating disorders  
Axonal disorders

### **Disorders of the neuromuscular junction**

Presynaptic disorders  
Infantile botulism  
Congenital myasthenia  
Postsynaptic disorders  
Neonatal myasthenia gravis  
Congenital myasthenia

### **Muscle disorders**

Infantile myotonic dystrophy  
Congenital myopathies

**Isabel differential for floppy infant:**

|  |  |
|--|--|
| <p><b>NEUROMUSCULAR DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Congenital Myopathies</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Spinal Muscular Atrophies</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Muscular Dystrophies</a> <span style="float: right;">RD</span></li> </ul>   | <p><b>INFECTIOUS DISEASES</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Botulism</a> <span style="float: right;">RD</span></li> </ul>   |
| <p><b>LIVER DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Kernicterus</a> <span style="float: right;">RD</span></li> </ul>  | <p><b>DERMATOLOGY</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Ehlers-Danlos Syndrome</a> <span style="float: right;">RD</span></li> </ul>   |
| <p><b>NERVOUS SYSTEM DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Perinatal Asphyxia</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Metachromatic Leukodystrophy</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Mitochondrial Encephalomyopathies</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Spinal Cord Trauma</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Neural Tube Defects</a> <span style="float: right;">RD</span></li> </ul>  | <p><b>ENDOCRINE SYSTEM</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Smith-Lemli-Opitz Syndrome</a> <span style="float: right;">RD</span></li> </ul>  |
| <p><b>METABOLIC DISEASES</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Lysine Disorders</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Galactosialidosis / Sialidosis</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Zellweger Syndrome</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Glutamic Acid Disorders</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Methylmalonic Acidemia</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">β-Oxidation Cycle Defects</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Multiple Carboxylase Deficiency</a> <span style="float: right;">RD</span></li> </ul> | <p><b>NUTRITIONAL DISORDERS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Copper Deficiency</a> <span style="float: right;">RD</span></li> </ul>  |
|  | <p><b>HUMAN GENETICS</b> &lt;&lt; <a href="#">Click here</a></p> <ul style="list-style-type: none"> <li>↳ <a href="#">Down Syndrome / Trisomy 21</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Cri-du-chat Syndrome</a> <span style="float: right;">RD</span></li> <li>↳ <a href="#">Prader-Willi Syndrome</a> <span style="float: right;">RD</span></li> </ul> |

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|--|----|
| ↳ <u>Phenylalanine Disorders</u>         | RD |
| <u>Isovaleric Acidemia</u>               | RD |
| <u>Nonketotic Hyperglycinemia</u>        | RD |
| <u>Oxidative Phosphorylation Disease</u> | RD |
| <u>Lesch-Nyhan Syndrome</u>              | RD |
| <u>Propionic Acidemia</u>                | RD |
| <u>Congenital Glycosylation Disorder</u> | RD |
| <u>D-Bifunctional Protein Deficiency</u> | RD |