Everyday Neurologic Problems at Your Hospital

What Will You Do?

2nd Annual Jason French Pediatric Hospital Medicine Symposium
October 7, 2022

Paul Graham Fisher, M.D., F.A.A.P.
Professor, Neurology and Pediatrics,
and by courtesy, Neurosurgery, Epidemiology, and Human Biology
The Beirne Family Professor of Pediatric Neuro-Oncology
The Dunlevie Family University Fellow in Undergraduate Education
Chief, Division of Child Neurology | Senior Vice Chair, Department of Neurology
Stanford University and Lucile Packard Children's Hospital
Palo Alto, CA 94304-1517
(650) 736-0885
pfisher@stanford.edu

1

I have the following financial relationships to disclose

- Johnson & Johnson – stocks/bonds (please note: personal holdings <$5,000)
- Elsevier – employee (please note: Associate Editor, *The Journal of Pediatrics*)
- NIH/National Human Genome Research Institute – research grant (please note: U grant for Undiagnosed Diseases Network)
- NIH/National Cancer Institute – research grant (please note: U grant for Pediatric Brain Tumor Consortium)
- American Academy of Pediatrics – prior CME speaker (<$5,000)
- Neurocrine Biosciences – data and safety monitoring committee (<$5,000)

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

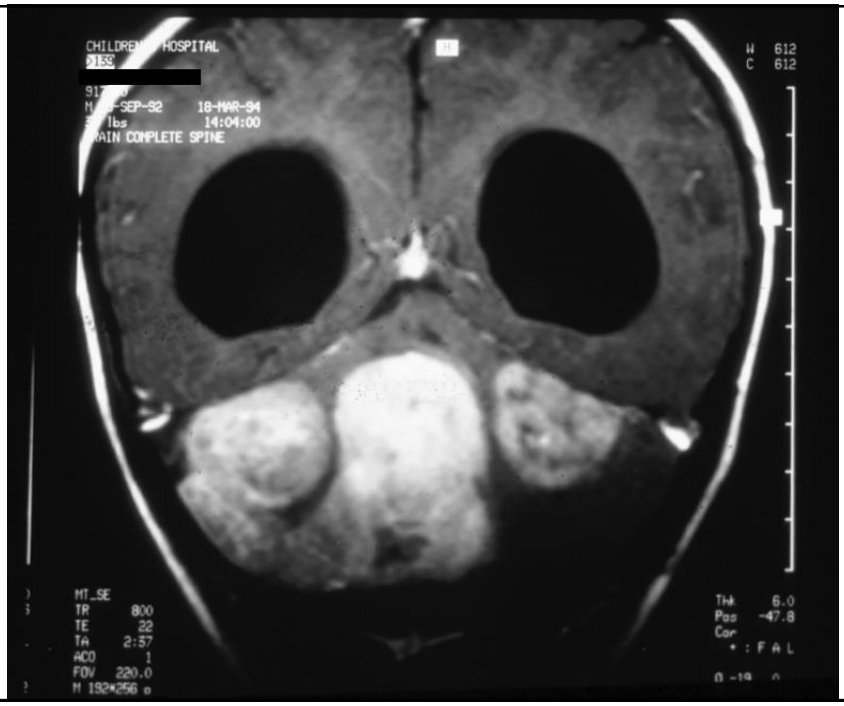
2

As a result of attending this session, I encourage you to incorporate these changes in your practice

- **MOST IMPORTANT: To be able to manage increased intracranial pressure, acute weakness, status epilepticus, and spine trauma.**
- Distinguish acute weakness from acute ataxia
- Formulate management plans for status epilepticus, acute cord syndromes, and encephalopathy

CASE 1

An 18-month-old with longstanding macrocephaly--head circumference 54.0 cm (>95%)--and strabismus presents to his pediatrician with a delay in walking. He was then referred to a neurologist, and the infant is diagnosed with "cerebral palsy." The parents are told to obtain a brain MRI at their convenience. You (of course) get paged about his MRI.



5

OCCIPITOFRONTAL CIRCUMFERENCE

Term gestational babies on average have OFC 35 cm ♂, 34 cm ♀…

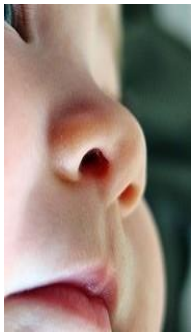
3rd trimester	-3 cm/month (mo)
Months 1-3	2 cm/mo
Months 4-6	1 cm/mo
Months 7-12	½ cm/mo

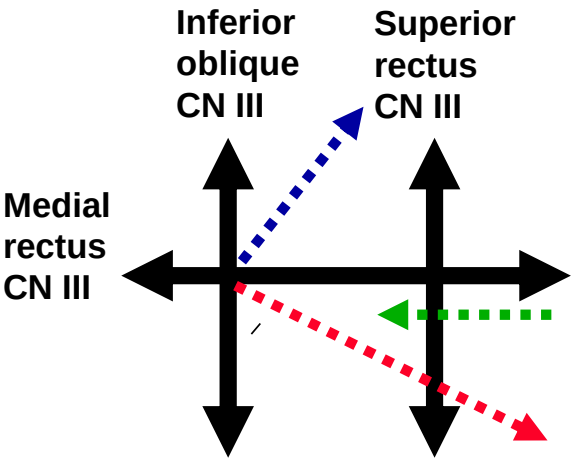
Or…

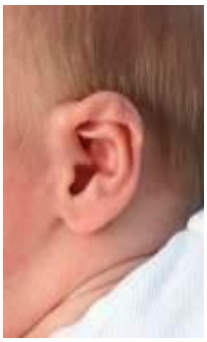
0 (birth)	35 cm
3 months	40 cm
9 months	45 cm
3 years	50 cm
Adult	55 cm

6

EXTRAOCULAR MOVEMENTS







CN III palsy
CN IV palsy
CN VI palsy

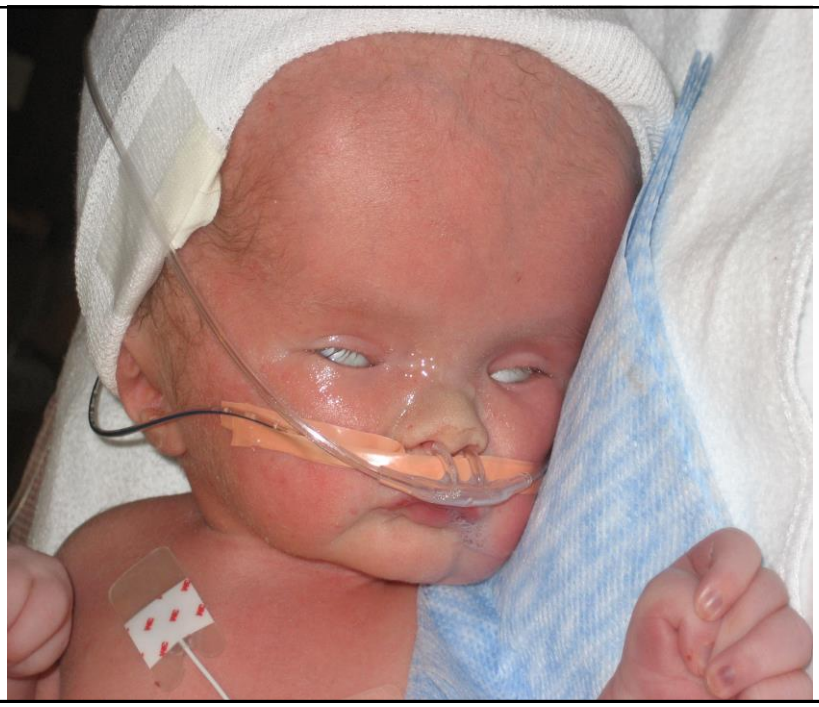
7

INCREASED INTRACRANIAL PRESSURE

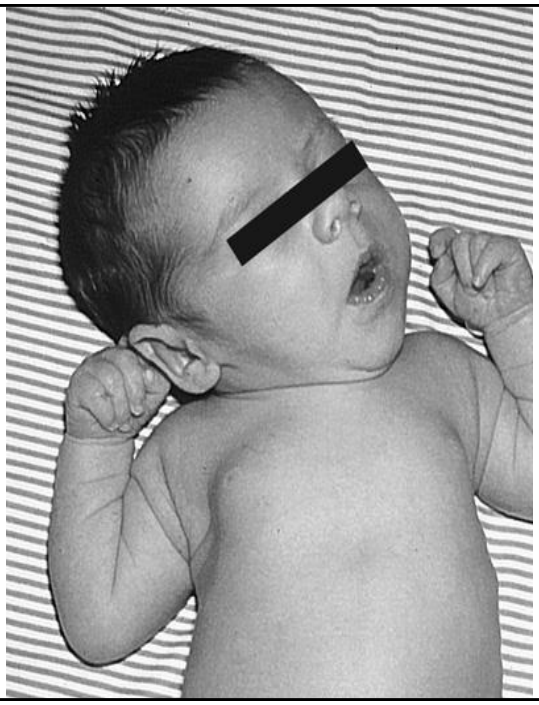
Presentation

- Irritability, lethargy, shrill cry
- Vomiting
- Bulging fontanelle
- Separation of cranial sutures, macrocephaly
- Papilledema (with loss of venous pulsations)
- “Setting sun sign” (Parinaud syndrome)
- Anisocoria
- Horizontal diplopia
- Ataxia
- Head tilt

8



9



10

HEAD TILT
Differential Diagnosis

- Posterior fossa mass
- Cranial nerve IV, or III or VI deficit
- Dystonia
- Syringomyelia
- Hearing loss
- Gastroesophageal reflux (Sandifer syndrome)
- Epiglottitis
- Retropharyngeal abscess
- Hemivertebrae
- Paroxysmal torticollis
- Spasmus nutans
- Torticollis

INCREASED INTRACRANIAL PRESSURE
Differential Diagnosis

- Hemorrhage
- Tumor
- Hydrocephalus
- Abscess
- Meningitis
- Encephalitis
- Pseudotumor cerebri
- Diffuse cerebral edema (head trauma, hypoxia)

Too much solid and or liquid in a fixed “box”

INCREASED INTRACRANIAL PRESSURE
Urgent Management

- Head elevation 30-45^{0}
- Fluid restriction to no more than maintenance; watch for SIADH
- Oxygenation
- Gentle blood pressure control, e.g., labetalol
- Furosemide 1 mg/kg
- Dexamethasone 1-2 mg/kg for vasogenic edema (e.g., tumor)

INCREASED INTRACRANIAL PRESSURE
Emergent Management

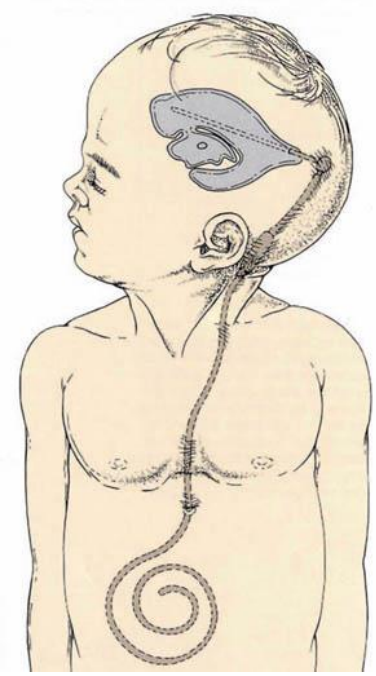
- Sedation may be required
- Hypertonic saline – 5-10 ml/kg 3% saline
- Mannitol 0.5-1 g/kg - effect starts after 20 minutes, lasts 3-4 hours
- Hyperventilation - 5-10 mm Hg decrease in CO_2 lowers ICP 25-30% within minutes, lasts for hours
- Neuromuscular blockade; consider continuous EEG
- CSF drainage - consider in first 24 hours, particularly when GCS $\leq$8
- ?High-dose barbiturate therapy, mild hypothermia, decompressive craniectomy?

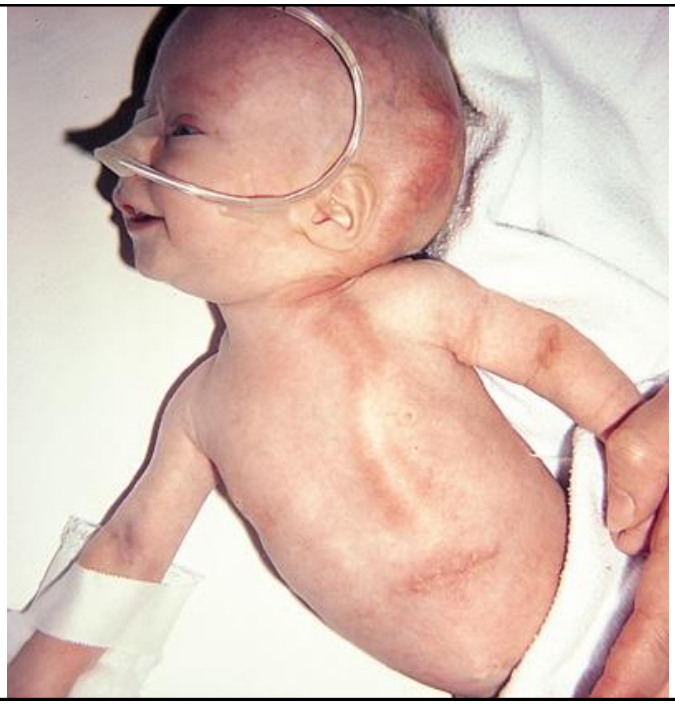
SHUNT OR THIRD VENTRICULOSTOMY MALFUNCTION
Presentation

- “Anything that goes wrong with a patient with shunted hydrocephalus is due to a shunt malfunction until proved otherwise”
- Most infections --typically *Staphylococcus*--occur within 2-3 months of placement
- Symptoms and signs of malfunction include lethargy, irritability, poor feeding, headache, vomiting, excessive head growth, bulging fontanelle, photophobia, papilledema, diplopia (typically abducens paresis), or “setting sun” sign (Parinaud syndrome)

SHUNT MALFUNCTION
Management

- Non-contrast head CT
- Shunt series x-rays
- Notify neurosurgeon and consider shunt tap



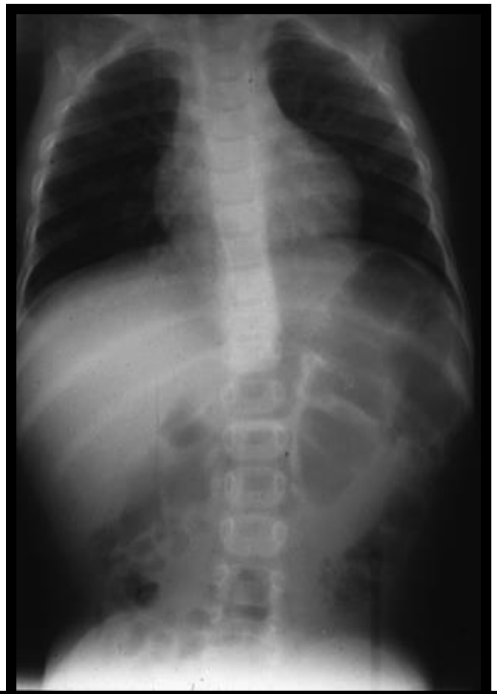


17

CASE 2

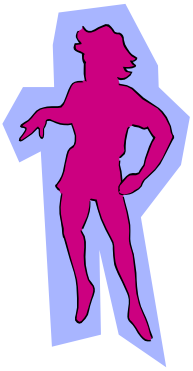
A 20-month-old with Turner syndrome presents with a 10-day history of low-grade fevers, irritability, jerking of extremities, abnormal eye movements, and a limp. Exam reveals opsoclonus, myoclonus, and impressive ataxia. Head circumference is 46.0 cm (10%). You're thinking all sorts of things in your differential diagnosis, but then go back to basics about ataxia.

18



19

ACUTE ATAXIA
Differential Diagnosis



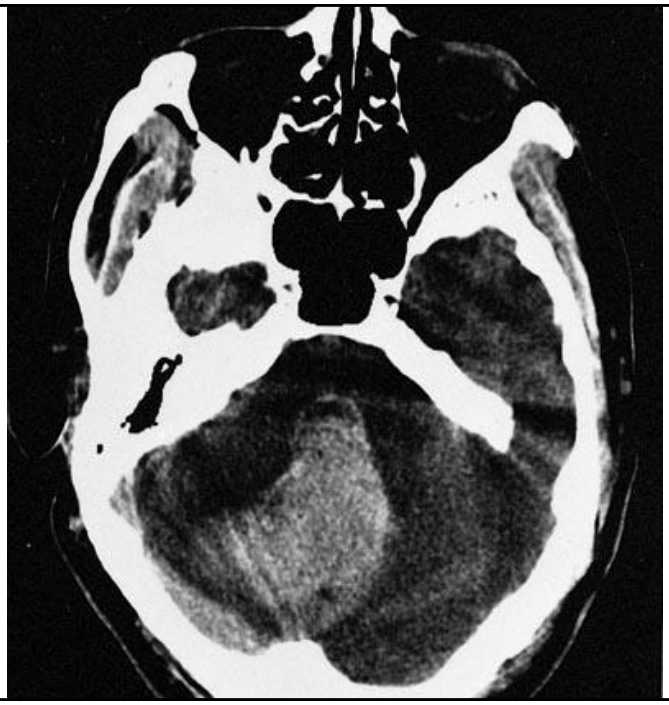
- Acute cerebellar ataxia/post-infectious encephalomyelitis
- Drug intoxication
- Posterior fossa tumor
- Cerebellar hemorrhage or subdural hemorrhage
- Head trauma
- Guillain-Barré syndrome (Miller-Fisher variant)
- Labyrinthitis
- Neuroblastoma
- Metabolic disease: Hartnup disease, maple syrup urine disease, pyruvate decarboxylase deficiency, familial periodic ataxia
- Functional neurologic disorder (“FND,” conversion disorder”)

20

ACUTE ATAXIA
Management

- Search for and treat underlying cause
- Head CT or brain MRI
- Toxicology screen
- Chest x-ray/abdominal ultrasound
- +/- Lumbar puncture

21



22

CASE 3

You are stat paged about an 18-year-old female teen on the ward with asthma, sickle cell disease, and history of substance use disorder. She is obtunded. How do you begin to think through her differential diagnosis for this change?

ALTERED MENTAL STATUS ("△MS") ENCEPHALOPATHY AND COMA

Signs

Structural

- Consciousness static
- Asymmetric exam
- Unifocal seizures
- Impaired pupillary reactivity, possibly papilledema

"Metabolic" (i.e., infectious, toxic, metabolic, endocrinologic, etc.)

- Fluctuating consciousness
- Symmetric exam
- Multifocal seizures
- Tremor, asterixis, myoclonus
- Hypo- or hyper-thermia

ENCEPHALOPATHY AND COMA
Management

- **A**irway with cervical spine immobilization
- **B**reathing
- **C**irculation
- **D**-stick
- **O**xygen
- **N**aloxone 0.1 mg/kg IV, IM, SQ, or ETT
- **T**hiamine 100 mg before starting glucose in teens
- Assess vital signs and Glasgow Coma Scale
- Physical and neurological exam

ENCEPHALOPATHY AND COMA
Evaluation

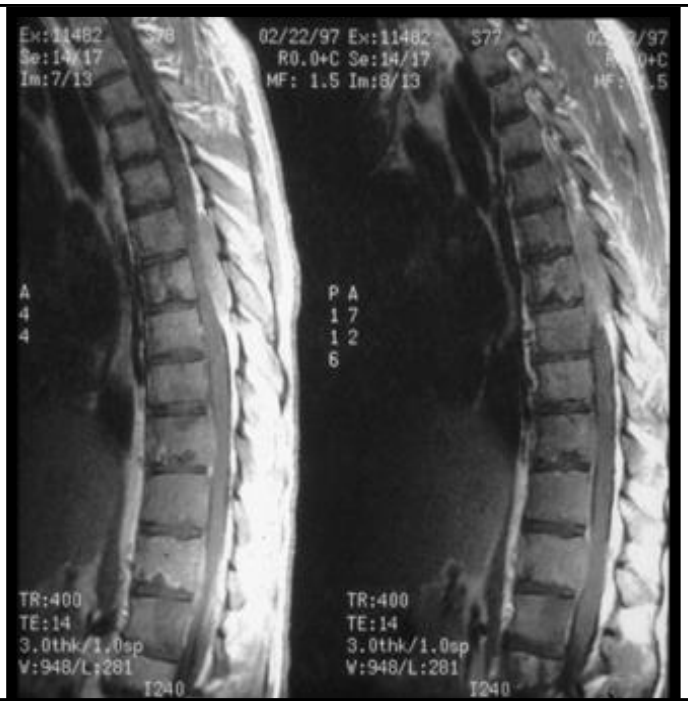
- Complete history and physical exam
- Electrolytes, chemistry, CBC
- Toxicology screen
- Blood and urine cultures, if febrile
- Consider NH_3, venous pH, lactate/pyruvate, urine ketones, perhaps in adolescent or young adult B12, TFTs, ESR
- Head CT or MRI
- Lumbar puncture, particularly if febrile } highest yield
- EEG

J Pediatr 2018;200:218

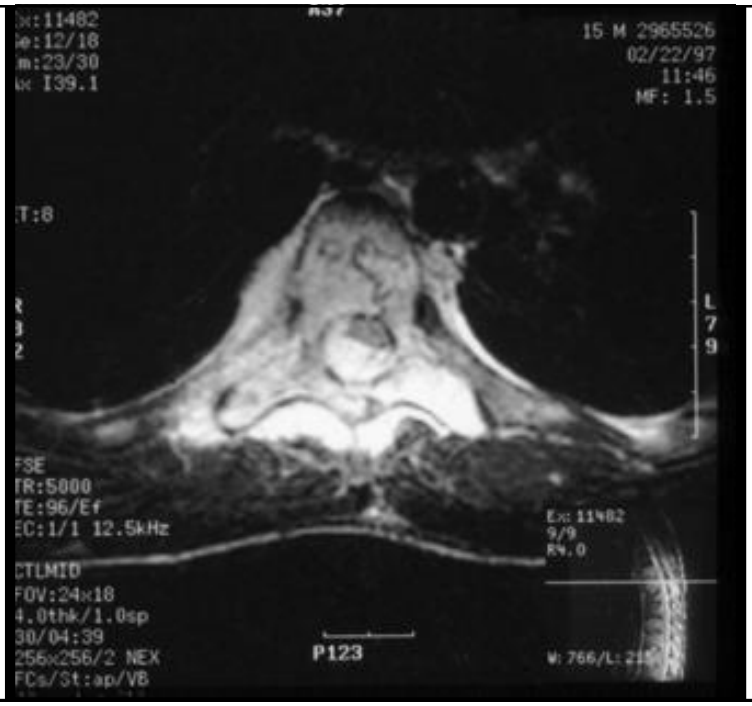
CASE 4

A 10-year-old is admitted for evaluation of a 2-week history of lower back pain, progressive gait difficulty, and urinary retention. Head circumference is 55.0 cm (90%).

27



28



29

CASE 5

A 15-year-old girl is rushed to the emergency department after slipping off a diving board and striking her head on cement. On physical examination, her mental status evaluation results are completely normal. She can abduct her upper extremities at the shoulder, but cannot flex or extend her arms and minimally moves her fingers. She cannot move her limp lower extremities. You order emergent magnetic resonance imaging of the brain and spine.

30

CASE 5

Of the following, the MOST important therapy to implement before the patient is sent for imaging is

A. fosphenytoin 18 phenytoin equivalents/kg intravenously
B. immobilization of the neck and body
C. low-molecular weight heparin 1 mg/kg subcutaneously
D. mannitol 1 g/kg intravenously
E. methylprednisolone 30 mg/kg intravenously

Answer: B, immobilization of the neck and body

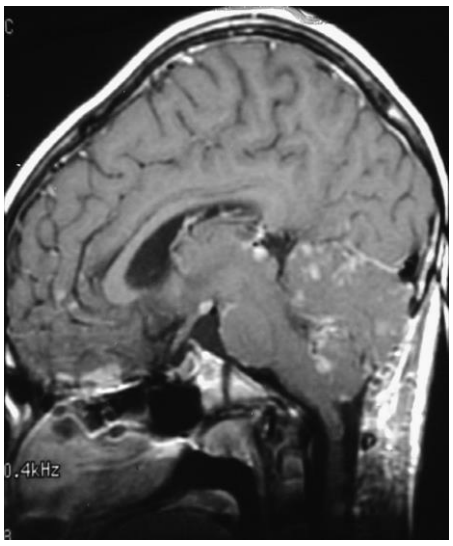
- Common sites for fracture dislocation spinal cord injuries are C1 through C2, C5 through C6, and T12 through L1 spinal segments
- If there is high index of suspicion for spinal trauma, as for the girl described in the vignette, prompt immobilization of the neck and body is paramount
- Methylprednisolone is no longer universally viewed to effect improved outcome
- Dexamethasone is used more often for vasogenic edema with spinal cord tumors, and has not been fully investigated for trauma
- Anticonvulsants are sometimes used after head trauma, though controversial
- Mannitol would be used for increased intracranial pressure

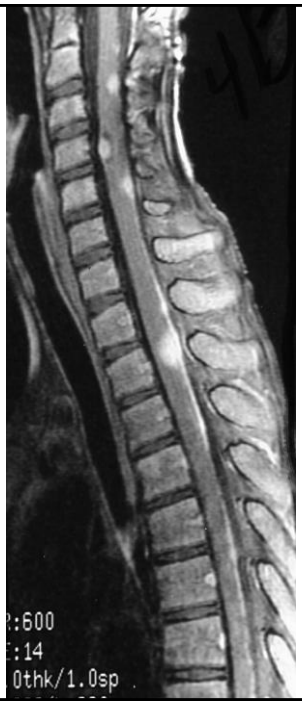
SPINAL CORD COMPRESSION
Differential Diagnosis

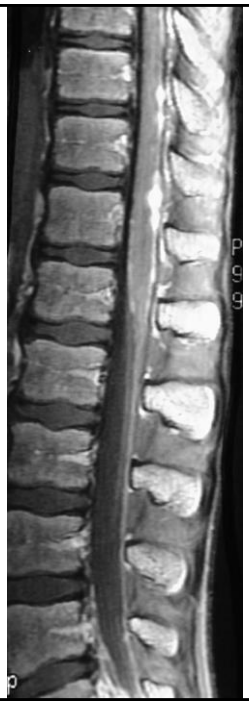
- Tumor through intervertebral foramina (neuroblastoma, lymphoma, Ewing sarcoma, neurofibroma)
- Dural metastatic tumor (neuroblastoma)
- Subarachnoid tumor (leukemia and drop metastases from medulloblastoma, PNET, ependymoma, germ cell tumors, and high-grade gliomas)
- Posttraumatic bone displacement
- Posttraumatic hematoma
- Compression fracture
- Epidural abscess
- Transverse myelitis

Left scoliosis has a higher incidence of an underlying neurological problem

33







34

SPINAL CORD COMPRESSION
Management

- Immobilization, if any hint of trauma
- Secure airway, ventilation/oxygenation, circulation
- For trauma, no steroids most often, or methylprednisolone started in first 3 to 8 hours
- For tumor, dexamethasone 1 mg/kg IV
- Emergency complete spine MRI
- For tumor, surgical decompression or radiotherapy

CASE 6

A 15-year-old girl presents to the emergency department with a month-long history of droopy eyes and face, worse at day's end. Chewing is difficult. Now she complains of difficulty holding her head and raising her arms. Head circumference is 53.0 cm (25%).

CASE 7

A 4-month-old is brought to the emergency department by his parents for evaluation of bilateral droopy eyes. His mother believes this has developed just over the last week. The child recently started taking cereal in addition to breastfeeding and has been constipated. Physical examination reveals droopy eyelids and 1+ deep tendon reflexes diffusely.

CASE 7

Of the following, the MOST likely diagnosis is

A. botulism
B. blepharophimosis syndrome
C. congenital ptosis
D. muscular dystrophy
E. myasthenia gravis

Answer: A, botulism

- Ptosis + decreased deep tendon reflexes indicates myopathy or neuromuscular junction problem
- Muscular dystrophies do not have ptosis (except myotonic dystrophy)
- Myasthenia has variable ptosis
- Blepharophimosis syndrome - autosomal dominant condition producing bilateral and severe ptosis as well as other abnormalities, e.g., constricted lids, increased distance between the medial canthi, absent epicanthal folds, flat nasal bridge, low-set ears
- Congenital ptosis would be present from birth

CASE 8

A 10-year-old boy has experienced increasing generalized weakness over the past 2 months. Now he has difficulty rising from a chair or climbing stairs. On physical examination, he has notable symmetric weakness at the shoulders and hips. Deep tendon reflexes are 2+ (normal) bilaterally, and results of the sensory examination are normal. There is no rash. Serum aspartate aminotransferase concentration is 343 U/L and the lactate dehydrogenase level is 848 U/L.

CASE 8

Of the following, the test MOST likely to help establish this child's diagnosis is

A. edrophonium test
B. lumbar puncture
C. magnetic resonance imaging (MRI) of the spine
D. serum creatine kinase measurement
E. urine porphobilinogen measurement

ACUTE FLACCID WEAKNESS

Yes, you can localize the lesion!

- Cerebral: alteration of behavior, development; visual field loss; seizure; speech loss
- Brainstem: cranial neuropathies
- Spine: bilateral or unilateral extremities, sensory level, bowel/bladder changes, back pain
- Nerve: distal weakness, symmetric, depressed DTRs
- Neuromuscular junction: rostral>caudal; fatigable
- Muscular: proximal weakness, symmetric

ACUTE FLACCID WEAKNESS
Differential Diagnosis

- Tumor
- Transverse myelitis
- Acute flaccid myelitis, associated with enterovirus D68
- Spinal arteriovenous malformation
- Epidural abscess
- Poliomyelitis (also coxsackie and echovirus)
- Guillain-Barré syndrome, West Nile virus
- Toxins - organophosphates, carbamates, lead, arsenic, thallium, dapsone
- Tick paralysis
- Diphtheria
- Acute intermittent porphyria
- Myasthenia gravis
- Botulism
- Acute myopathy (acute infectious myositis, McArdle's disease, MERRF)
- Periodic paralysis

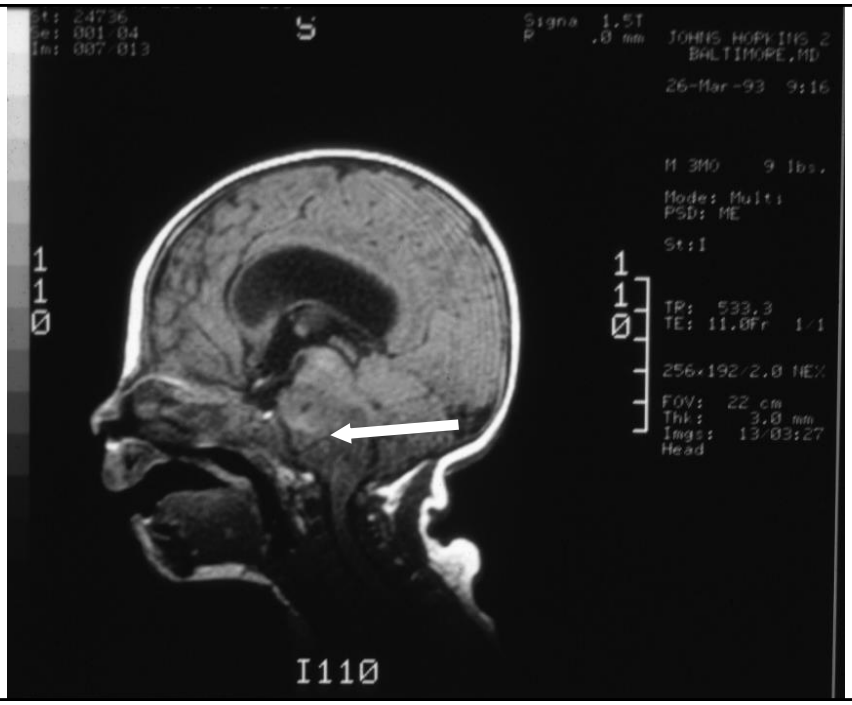
ACUTE FLACCID WEAKNESS
Management

- Search for underlying diagnosis
- Monitor forced vital capacity
  - FVC LESS THAN 10-15 cc/kg HERALDS THE NEED TO INTUBATE
- Measure urine post-void residual
- Spinal MRI
- Lumbar puncture
- Check potassium, creatine kinase, urine porphobilinogen
- NCV/EMG

CASE 9

You’re asked to check in on a 3-month-old male admitted by a community physician for a left facial palsy and torticollis. Your exam also shows apparent left facial numbness and equivocal hearing. Head circumference is 42.0 cm (95%).

45



46

CASE 10

A 7-year-old girl has had weakness of the right side of her face for 4 days following a systemic viral infection 2 weeks ago. She denies any hearing difficulty or hyperacusis and claims that tearing and taste are normal. Physical examination reveals weakness of the upper and lower face and an inability to close the right eye. Deep tendon reflexes are normal.

CASE 10

Of the following, the MOST appropriate next step is

A. application of an ocular lubricant at night
B. initiation of amoxicillin
C. magnetic resonance imaging of the brain
D. nerve conduction velocities/electromyography
E. prescription of oral acyclovir

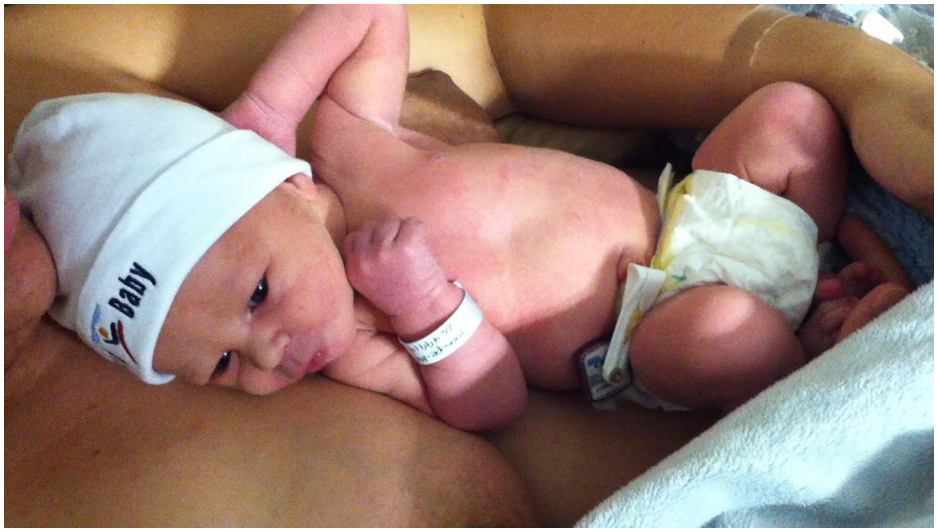
Answer: A

FACIAL PALSY
Differential Diagnosis

- Bell's palsy
- Guillain-Barré syndrome (Miller-Fisher variant)
- Mastoiditis
- Otitis media (Gradenigo syndrome)
- Herpes zoster (Ramsay-Hunt syndrome)
- Parotitis
- Other infections: Lyme disease, mononucleosis, diphtheria, West Nile
- Sarcoidosis
- Muscular disorders: myotonic dystrophy, facioscapulohumeral dystrophy
- Brainstem tumor
- Schwannoma
- Forceps delivery
- Asymmetric crying facies (sometimes associated with velocardiofacial syndrome, 22q11.2 microdeletion syndrome)

FACIAL PALSY
Management

- Localize facial nerve lesion
- Search for underlying diagnosis
- Treatment of Bell's palsy with steroids and/or acyclovir controversial
- AAN practice parameter: early treatment with oral steroids is probably effective to improve facial functional outcomes; acyclovir in combination with oral acyclovir is possibly effective (*Neurology* 2001;56:830 and 2012, 79:2209)
- Prevent corneal exposure



51

CASE 11

Of the following, the MOST likely diagnosis is

A. cerebral palsy
B. hyperekplexia
C. neonatal abstinence syndrome
D. simple motor seizure
E. shuddering attacks

52

53

CASE 12

Of the following, the MOST likely diagnosis is

A. alternating hemiplegia of childhood
B. benign neonatal sleep myoclonus
C. generalized tonic-clonic seizures
D. multifocal clonic seizures
E. myokymia

54

Benign Neonatal Sleep Myoclonus

- Onset at <1 month, resolution by 6 months
- Repetitive myoclonic jerks in sleep
- More prominent in distal limbs
- More prominent in lower extremities
- Focal or multifocal
- Unilateral or bilateral
- Occurs in clusters
- Movements stop when baby is woken from sleep

55

56

CASE 13

A 2-year-old girl presents to the emergency department 10 minutes after the sudden onset of ataxia and refusal to walk. She has vomited twice. According to her parents, she experienced similar episodes three times in the past 6 months. On a previous evaluation, results of oto-acoustic emission testing and computed tomography of the head were normal.

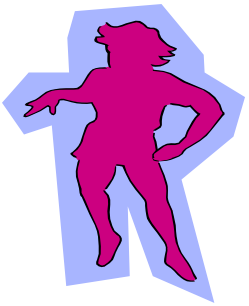
CASE 13

Of the following, the MOST likely diagnosis is

A. benign paroxysmal vertigo
B. complex partial epilepsy
C. medulloblastoma
D. Ménière disease
E. perilymphatic fistula

Answer: A, benign paroxysmal vertigo

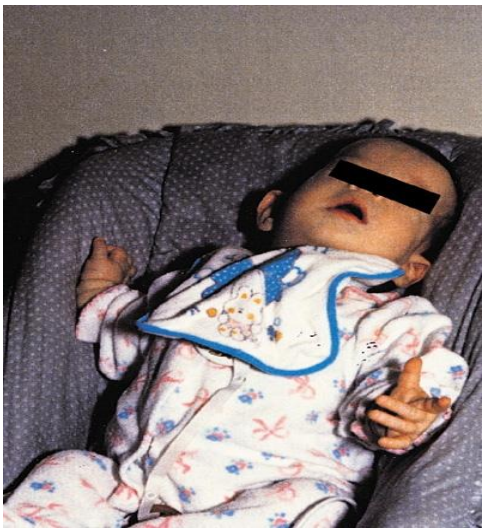
- Abrupt, brief episodes of vertigo with ataxia in children ages 2-6
- Child appears frightened, with pallor, and may indicate feeling dizzy
- Rapid eye movements or nystagmus may be observed if the eyes are open.
- Vomiting may be prominent
- No loss of consciousness
- Migraine variant
- Treatment is supportive



CASE 14

Your diagnosis?

Sandifer syndrome - episodic extension and lateral flexion of the head that occurs 4 months - 14 years, usually in association with feeding



PAROXYSMAL EVENTS

Not Everything that Shakes is a Seizure!

- **Neonatal apnea**
- **Breath-holding spells**
- **Syncope**
- **Dizziness**
- **Vertigo**
- **Migraine**
- **Acute confusional state**
- **Nightmares (REM)**
- **Night terrors (nREM)**
- **Somnambulism (nREM)**
- **Narcolepsy**
- **Cataplexy**
- **Tic**
- **Dystonia**
- **Myoclonus**
- **Shuddering attacks**
- **Hyperekplexia**
- **Episodic ataxia**
- **Paroyxysmal dyskinesias**
- **Spasmus nutans**
- **Daydreaming/attentional disorder**
- **Hyperventilation**
- **Prolonged QT syndrome**
- **Wolff-Parkinson-White syndrome**
- **Brugada syndrome**
- **Sandifer syndrome**
- **Transient ischemic attack**
- **Depression/fugue state**
- **Panic attack**
- **Paroxysmal behavior outburst**
- **Masturbation**
- **Psychogenic non-epileptic seizure (PNES)**

61

PAROXYSMAL EVENTS

Pearls

- For episodes that occur frequently, smart phone video is an excellent, cost-effective, first step.
- Eyes are open, not closed, during a seizure. Consider instead a psychogenic (i.e., non-electrical or behavioral) seizure.
- Patients with new-onset, daily seizures rarely have completely normal interictal EEGs.
- Seizures rarely produce "negative phenomena," such as pallor, cold, apnea, and bradycardia. Consider instead syncope, breath holding spells, or prematurity.
- Directed acts of violence are not a feature of epilepsy. Consider instead rage attacks or other behavioral disorders.
- Conversion disorder and malingering, which can manifest as psychogenic seizures, are uncommon in the first decade.

62

Table 3 Differential Diagnosis Between Psychogenic and Epileptic Seizures

Feature	Psychogenic seizure	Epileptic seizure
Onset	Usually gradual	Sudden
Duration	Often prolonged (several min)	Brief (1–2 min)
Injury and tongue biting	Rare	Common
Ictal eye closure	Common (resistance to passive eyelid opening)	Rare (eyes generally open)
Urinary incontinence	Rare	Common
Motor activity	Variable, forward pelvic thrusting, rolling side to side, "waxing and waning"	Stereotyped, coordinate tonic-clonic activity
Postictal confusion	Rare (a postictal crying is common)	Common
Triggers	Emotional disturbances	No
Reproduction of attack by suggestion	Sometimes	No
Ictal EEG findings	Normal	Frequently abnormal

Neurology: Clinical Practice 2022; 12:320

63

PAROXYSMAL EVENTS
Evaluation

- Complete history and physical exam
- Hyperventilation
- Electrolytes (with Ca^{+2}, Mg^{+}), BUN, liver function tests, CBC
- Toxicology screen
- Pregnancy test
- Head CT acutely; MRI is the preferred modality for nonurgent neuroimaging (*Neurology* 2000;55:616)
- EKG
- pH probe study?
- EEG, with hyperventilation and photic stimulation, after first seizure (*Neurology* 2000;55:616)
- Video-EEG monitoring

64

STATUS EPILEPTICUS

- Continuous seizure activity or serial seizures without return of consciousness, ≥ 5 minutes.
- May be convulsive or non-convulsive, generalized or partial.
- Causes: rule of fourths--febrile, prior symptomatic/noncompliance, new symptomatic, and idiopathic.
- Routine imaging not warranted in children ***Neurology* 2006;67:1542.**

65

DOES STATUS EPILEPTICUS CHANGE THINGS?

- Management needs to follow a well-conceptualized protocol for support and drug therapy
- Drug therapy for generalized convulsive status epilepticus usually starts with lorazepam 0.1 mg/kg>diazepam 0.1-0.3 mg/kg IV/PR, followed by fosphenytoin IV/IM>phenobarbital IV, both 18-20 mg/kg
- Prognosis: <5% mortality, predominantly in symptomatic cases; morbidity rather low in the absence of a progressive neurologic insult or metabolic disorder
- Do *not* treat a child chronically with an antiepileptic drug after febrile status epilepticus
- What about levetiracetam? IV? Now or on the way home? And nasal midazolam? Rectal diazepam?

66

67

As a result of attending this session, I encourage you to incorporate these changes in your practice

- **MOST IMPORTANT: To be able to manage increased intracranial pressure, acute weakness, status epilepticus, and spine trauma.**
- Distinguish acute weakness from acute ataxia
- Formulate management plans for status epilepticus, acute cord syndromes, and encephalopathy

68