SAM Questionnaire

Congenital Anomalies in the Newborn and Infant

Thomas P. Naidich, MD

1. With regard to the Amnionic Band Sequence, which one of the following most nearly describes the expected abnormalities?
   A. Holoprosencephaly with dorsal cyst
   B. Hydranencephaly
   C. Amputation of digits and Asymmetric facial clefts
   D. Polymicrogyria
   E. Conjoined twins

Correct Answer: C

Rationale
The Amnionic band sequence is associated with linear and circumferential mesodermal bands that constrict the early fetal tissue, resulting in auto-amputation of digits and limbs, and linear clefts of the face and head.

None of the other conditions is typically associated with the amnionic band sequence

References
1. Ware & Walsh [in] SA Moody 1999 Fig 1 p. 530

2. With regard to holoprosencephaly, which one of the following answers most clearly characterizes the alobar form of holoprosencephaly?
   A. Nearly complete formation of the interhemispheric fissure and lateral ventricles
   B. Nearly complete formation of the interhemispheric fissure and lateral ventricles with prominent dorsal cyst
   C. Partial formation of the interhemispheric fissure and lateral ventricles
   D. Partial formation of the interhemispheric fissure and lateral ventricles with prominent dorsal cyst
   E. No formation of the interhemispheric fissure or lateral ventricles, with or without dorsal cyst

Correct Answer: E

Rationale
In the alobar form, there is complete failure of separation of the prosencephalon into paired telencephalic hemispheres, with no interhemispheric fissure and no lateral ventricles. A dorsal cyst may be present or not.

The other answers are wrong because they specifically state that there is at least some formation of interhemispheric cyst and lateral ventricles indicating some differentiation of the telencephalic structures.
3. **In North America, the most common form of cephalocele is which one of the following?**
   A. Basal (i.e. transsphenoidal)
   B. Frontonasal
   C. Parietal
   D. Occipital
   E. Cervico-occipital

**Correct Answer: D**

**Rationale**
Of all cephaloceles seen in North America, the commonest by far is the occipital cephalocele. The others are far rarer.

**References**
1. Ware & Walsh [in] SA Moody 1999 Fig 1 p. 530

**Fetal MRI of CNS Brain Anomalies**
*Robert Zimmerman, MD*

4. **Bickers Adams Syndrome affects:**
   A. Infants with Dandy Walker Syndrome
   B. Only female infants
   C. Is chromosomal in origin, Xq 28y, Xq 27.3
   D. Is not associated with hydrocephalus
   E. Is not associated with mental retardation

**Correct Answer: C**

**Rationale**
Bickers Adams Syndrome affects male infants only, occurring on the x-chromosome and is seen in patients with aqueductal stenosis. As such, they have hydrocephalus secondary to the aqueductal stenosis. These infants are severely mentally retarded. The incidence is approximately 7% of male infants with aqueductal stenosis.

**Reference**

5. **Myelomeningocele repair in utero is:**
   A. Best accomplished after 30 weeks gestation
   B. Untethers the spinal cord in most cases
   C. Does not change the incidence of hydrocephalus in neonates
   D. Usually normalizes the posterior fossa structures, resolving caudalization
   E. Does not carry the risk of epidermoid formation at the site of repair

**Correct Answer: D**
Rationale
The time of operative repair is below 27 weeks of gestation, the surgery does not untether the spinal cord as it remains fixed to the operative site post surgically. However, as a result of the surgery, the posterior fossa structures usually return to the posterior fossa and do not remain caudalized. As a result of the surgery, the incidence of hydrocephalus is reduced by approximately 50%. However, the surgery is complicated in a small proportion by the formation of epidermoid tumors at the site of the myelomeningocele repair.

References

6. Insults to the fetal brain in utero on fetal MRI –
A. Are too difficult to see because of poor resolution on imaging
B. Are frequently not appreciated because fetal MRI are insensitive to blood products
C. Are not seen because diffusion sequences are ineffective because they are too long
D. Are not indicated because A,B, & C are contraindications
E. Correlate well with post natal imaging findings regarding infarction and hemorrhage

Correct Answer: E

Rationale
Correlate well with post natal imaging findings regarding infarction and hemorrhage.

Larger insults to the fetal brain in utero are well enough resolved that most can be recognized in utero with a combination of T2 and T1-weighted images. Echo-planar images are sensitive to blood products, demonstrating germinal matrix hemorrhage well. Diffusion sequences do work in fetal MRI. As a result, infarctions and hemorrhages producing injury to the fetal brain can be recognized with fetal MRI.

References

Hydrocephalus Update: Understanding and Assessing Hydrocephalus
Charles A. Raybaud, MD, FRCP(C)

7. In hydrocephalus, an abnormal transmantle pressure gradient explains the ventriculomegaly. What creates this gradient?
A. The back-pressure of CSF secreted by the choroid plexus in the obstructed ventricles
B. CSF absorption being maintained in the peripheral absorption sites
C. The retention of interstitial fluid into the parenchyma
D. The extracerebral spaces being more compliant than the obstructed ventricles
E. The lack of extracerebral CSF production

Correct Answer: D
References
1. Bonfanti Prog Neurobiol 2006
2. Fancy et al Ann Rev Neurosc 2011
3. Akbik et al Exp Neurol 2012

8. Periventricular interstitial edema is a prominent feature in some cases of hydrocephalus. Which of the following IS NOT true?
   A. It is associated with high ventricular/intracranial pressure
   B. It contributes to periventricular tissue damage
   C. It adds up to the high intracranial pressure
   D. It reflects an increased transependymal absorption
   E. It is caused by the compression of the subependymal veins

Correct Answer: D

References
1. Bonfanti Prog Neurobiol 2006
2. Fancy et al Ann Rev Neurosc 2011
3. Akbik et al Exp Neurol 2012

9. In hydrocephalus, which of the following IS NOT a factor of poor recovery of the cerebral mantle on imaging?
   A. Septic meningitis
   B. Parenchymal immaturity
   C. Intraventricular hemorrhage
   D. Long duration of hydrocephalus
   E. Co-existence of white matter injury

Correct Answer: B

References
1. Bonfanti Prog Neurobiol 2006
2. Fancy et al Ann Rev Neurosc 2011
3. Akbik et al Exp Neurol 2012

CNS Vascular Malformations: Diagnosis and Treatment
Darren B. Orbach, MD, PhD

10. Which of the following statements is correct?
   A. The term “hemangioma” is useful for characterizing a broad range of vascular malformations in children, both inside and outside the CNS.
   B. Infantile hemangioma is a vascular tumor of infancy that is always located on or immediately deep to the skin. It does not ever encroach on the CNS.
   C. Infantile hemangioma is a vascular tumor of infancy that is distinct from vascular malformations. Unlike hemangiomas, these latter are not tumors, and do not involute spontaneously.
   D. In PHACES, the infantile hemangioma invades the arterial supply to the brain, thereby posing a risk of vessel rupture.
   E. Diagnosing a new vascular mass seen on imaging in a 45 year old as a “hemangioma” makes perfect sense.

Correct Answer: C
Rationale
The distinction between vascular tumors and vascular malformations is central to understanding and treating vascular anomalies, despite the fact that older literature is replete with the use of “infantile hemangioma” to refer to all types of lesions. IH is a vascular tumor of infancy, with a proliferative phase typically during the first year of life, followed by an involutive phase over the next 4-5 years. Vascular malformations, on the other hand, grow with the child and do not involute.

Options A and E are not correct. See paragraph above.

Option B is not correct. IH can encroach into the skull and spine to insinuate itself, typically via neuroforamena. Even in such cases, mass effect and intracranial hemorrhage are extremely rare. The IH within the neuraxis typically exhibits the same natural history as the extra-CNS IH, with the same response profile to medication.

Option D is not correct. While PHACES is characterized by the presence of a regional infantile hemangioma, the arterial anomalies in PHACE do not result from direct vessel invasion by the IH. The arterial changes are often intracranial and relatively remote from the site of the IH.

References

11. Which of the following statements is correct?
   A. A diagnosis of vein of Galen malformation is one that carries a devastatingly high morbidity and mortality.
   B. Novel microsurgical approaches have become the standard of care for patients with vein of Galen malformations.
   C. The most feared morbidity of vein of Galen malformations is intracranial hemorrhage.
   D. If an infant with a vein of Galen is asymptomatic in infancy, the best course of action is to defer treatment for as many years as possible, as the risks of embolization are unacceptably high.
   E. Embolization of vein of Galen malformations in a timely fashion, as dictated by presenting symptoms (in the neonatal period in the setting of heart failure, at 3-6 months if asymptomatic), has revolutionized the prognosis of this condition, with most treated patients neurodevelopmentally normal or near normal.

Correct Answer: E

Rationale
While prior to the availability of embolization techniques, a diagnosis of VOGM was devastating, with severe morbidity and mortality rates approaching 90%. With the advent of management through embolization, over 75% of all VOGM patients treated at high volume centers are neurodevelopmentally intact, or suffer from mild and focal delays.

Options A and B are not correct. Open surgical management was the only option available prior to the development of endovascular techniques, but the location of the malformation renders open surgical approaches hazardous.
Option C is not correct. VOGM rarely present with hemorrhage. Morbidity is manifest as high-output heart failure, severe neurocognitive impairment and global loss of brain parenchyma.

Option D is not correct. Neonates with high-output heart failure and pulmonary hypertension need emergent treatment within days of birth. For those infants without cardiopulmonary symptoms, embolization is ideally performed between 2 and 6 months of life, in order to forestall the effects of chronically elevated venous sinus pressures, which can potentially result in global parenchymal brain loss.

References

12. The patient in the images to the right is 11 months old. Which of the following statements is correct?
A. The diagnosis is vein of Galen malformation.
B. The diagnosis is intracranial infantile hemangioma.
C. The diagnosis is dural sinus malformation.
D. The differential diagnosis is vein of Galen malformation versus dural sinus malformation, and these cannot be distinguished without a catheter angiogram.
E. The presence of enlarged superior ophthalmic veins in this patient implies a very poor prognosis.

Correct Answer: C

Rationale
The images depict an enlarged torcular and do not demonstrate enlargement of the deep venous system. Specifically, there is no dilatation of a persistent median vein of the prosencephalon, as would be seen in a case of VOAGM. The massively dilated torcular, along with tentorial vessels leading to it and the presence of arterial signal within the torcular on the TOF MRA, make dural sinus malformation the best diagnosis, among those presented here.

Options A and D are not correct. See the paragraph above.

Option B is not correct. There is no enhancing soft tissue mass seen.

Option E is not correct. Dilatation of the veins of the scalp, face, and neck results from elevated intrasinus pressure within the torcular and superior sagittal sinus. These dilated facial veins act as a pop-off valve, allowing the brain to drain via alternative pathways, and can forestall parenchymal brain injury related to the elevated venous pressure. With treatment of the DSM, the facial venous prominence typically abates.

References
13. Which of these pediatric groups is NOT at higher risk for ischemic stroke?
   A. Neonates
   B. Patient with sickle cell disease
   C. Patients with recent upper respiratory infections
   D. Prior radiation therapy
   E. Females

Correct Answer: E

Rationale
Females are not at increased overall risk for pediatric ischemic stroke. In fact some studies have shown a slightly higher risk of stroke in males.

Option A is incorrect. The risk of arterial ischemic stroke is high in neonates, approaching one in 4000.

Option B is incorrect. Patients with sickle cell disease are also at risk for both silent infarcts and overt symptomatic arterial ischemic infarcts.

Option C is incorrect. It has been shown that in children with ischemic stroke, there was a 12 fold increased risk if there was a recent (<3 days) visit for infection, most commonly upper respiratory infection.

Option D is incorrect. Children who have undergone radiation therapy for brain tumors are also at increased risk for ischemic stroke.

References

14. Which of these is the criteria for an abnormal transcranial Doppler velocity in patients with sickle cell disease according to the STOP (stroke prevention in sickle cell anemia) trial used for evaluation of sickle cell patients?
   A. Less than 170 cm/s.
   B. Greater than 170 cm/s.
   C. Greater than 200 cm/s.
   D. The STOP criteria is an MRI/MRA grading system and does not use transcranial Doppler velocities.

Correct Answer: C

Rationale
According to the risk stratification criteria established by the first stroke prevention in sickle cell anemia trial (STOP trial), transcranial Doppler (TCD) measurements of cerebral arterial vessels less than 170 cm/s are considered normal, those between 170 cm/s and 200 cm/s are considered borderline, and those above 200 cm/s are considered abnormal. These criteria are used for risk stratification of sickle cell disease patients. Options A and B are incorrect for the above reason.

Option D is incorrect. The STOP trial criteria are transcranial Doppler criteria rather than an MRI grading system.
15. Which of the following statements are correct?

A. Seizures are rarely one of the presenting symptoms of arterial ischemic stroke in children.
B. Most cases of arterial ischemic stroke in the neonatal are idiopathic.
C. Intracranial hemorrhage is common in young children with moyamoya disease.
D. Unilateral involvement is more common than bilateral involvement in idiopathic moyamoya disease.
E. Multiple exchange transfusions increase the risk of arterial ischemic stroke in children with sickle cell disease and elevated transcranial Doppler velocities.

Correct Answer: B

Rationale
In most cases of neonatal arterial ischemic stroke, the etiology may remain unknown.

Option A is incorrect. Seizures are a common symptom in pediatric arterial ischemic stroke. They are very common in neonatal and infantile stroke and decrease in older age groups. Seizures are quite rarely one of the presenting symptoms of arterial ischemic stroke in adults.

Option C is incorrect. Intracranial hemorrhage is uncommon in young patients with moyamoya disease, as opposed to adults with moyamoya disease. Ischemia is dominant in the pediatric age groups.

Option D is incorrect. Bilateral involvement is more common in idiopathic moyamoya disease.

Option E is incorrect. Exchange transfusions decrease the risk of arterial ischemic stroke in children with sickle cell disease and elevated transcranial Doppler velocities. They also decrease the chance of recurrence of stroke.

References
**Hypoxic Ischemic Injury in the Newborn**
Aylin Tekes, MD

16. Which of the following choices provide accurate information regarding HIE?
   A. Seizures have typical clinical presentation in the newborns
   B. Classic finding of HIE is seizures at day of life 5
   C. All patients with HIE are hypotonic at birth
   D. Therapeutic hypothermia is typically done in newborns less than 1800 gr, and younger than 35 gestational weeks
   E. None of the above

**Correct Answer: E**

**Rationale**
Clinical diagnosis of HIE can be challenging. Subclinical seizures are common in neonates yet typical tonic and/or clonic seizures are rare. Seizures typically happen in the first day of life in HIE. Although seen in the setting of HIE, hypotonia is not a must for diagnosis of encephalopathy. Therapeutic hypothermia is done in neonates ≥ 35 GW, and more than ≥ 1800 gr.

**Reference**

17. Which of the following has been postulated in the etiology/pathological mechanism of HIE?
   A. Infection
   B. Inflammation
   C. Failure of secondary energy metabolism and free radicals
   D. 1 and 3
   E. All of the above

**Correct Answer: E**

**Reference**

18. Choose the correct answer for imaging findings of HIE.
   A. Midbrain and brainstem injury is highly suggestive of severe insult such as acute complete placental abruption.
   B. Lack of T2 dark signal in PLIC in a 34 GW infant is indicative of moderate injury.
   C. Low resistive indices in the Circle of Willis, increased echogenicity of the brain parenchyma, slit-like ventricles are usually seen in head US in the acute phase of HIE.
   D. A and C
   E. All of the above.

**Correct Answer: D**

**Rationale**
Posterior limb of the internal capsule (PLIC) is not yet completely myelinated at 34 GW, therefore lack of dark T2 signal in the PLIC is not abnormal in this age group. MRI evidence of brainstem injury indicates severe insult. Head US is a valuable imaging tool in the acute phase of HIE and reveals signs of acute edema with increased echogenicity of the brain, reduced RI in the COW, and slit-like ventricles.
Reference

Supratentorial Tumors
Ashok Panigrahy, MD

19. Which pediatric tumor type is known to have translocation/activating mutations of the BRAF gene, constituting a promising clinical therapeutic pathway?
   A. Medulloblastoma
   B. Ependymoma
   C. Pilocytic Astrocytoma/optic pathway tumor
   D. Diffuse Intrinsic Pontine Glioma
   E. Hemangioblastoma

Correct Answer: C

References

20. The following are characteristics of supratentorial PNET except:
   A. Histologically similar to medulloblastoma
   B. Typically less aggressive than medulloblastoma
   C. Have unique molecular feature distinct from medulloblastoma
   D. Restrict Diffusion (low ADC)

Correct Answer: B

References

21. What is a distinguishing imaging feature of Craniopharyngiomas?
   A. Restrict diffusion MR signal
   B. Elevated MR perfusion
   C. Increased taurine on MR spectroscopy
   D. Rim calcifications on CT

Correct Answer: D

References
Infratentorial Tumors
Tina Young Poussaint, MD, FACP

22. The diffuse intrinsic brainstem glioma accounts for what percentage of brainstem gliomas?
   A. 10%
   B. 25%
   C. 35%
   D. 55%
   E. 80%

Correct Answer: E

Rationale
The majority of brainstem gliomas in childhood are the diffuse intrinsic type characterized by expansion of the pons and T2 prolongation.

Reference

23. Which tumor type is associated with basal cell nevus syndrome?
   A. Astrocytoma
   B. Schwannoma
   C. Subependymal giant cell tumor
   D. Hemangioblastoma
   E. Medulloblastoma

Correct Answer: E

Rationale
Basal cell nevus syndrome is a syndrome caused by mutations in the PTCH1 gene on chromosome 9. In this syndrome there are the development of basal cell carcinomas, keratocysts in the maxilla and mandible and medulloblastoma of the desmoplastic type due to aberrations in the sonic hedgehog pathway.

Option A incorrect: Astrocytomas have an increased association with neurofibromatosis type 1, the most common of the phakomatoses. Tumors seen in these patients include neurofibromas and astrocytomas.

Option B is incorrect: Schwannoma is associated with neurofibromatosis type 2. Tumors found in NF-2 include multiple inherited schwannomas, meningiomas, and ependymomas.

Option C is incorrect: Subependymal giant cell astrocytoma is associated with tuberous sclerosis. These patients have subependymal nodules, white matter abnormalities, and cortical tubers as well.

Option D is incorrect. Hemangioblastomas of the cerebellum, retina, and spine are associated with Von Hippel Lindau syndrome. Patients may also develop pancreatic cysts, islet cell tumors, pheochromocytomas, renal cysts, endolymphatic sac tumors, renal cell carcinoma, and epididymal cysts and cystadenomas.
References

24. Which is a feature of the brainstem lesions seen in NF-1?
   A. They are seen in 40% of children with NF-1
   B. They occur predominately in the pons
   C. They are high-grade and aggressive
   D. They are less frequently seen in the medulla
   E. They are low-grade, can regress and can be indolent

Correct Answer: E

Rationale
Brainstem lesions in NF-1 differ from brainstem lesions seen in the general population because they are commonly seen in the medulla followed by the midbrain, periaqueductal region and then the pons. In the general population, the majority of brainstem tumors are seen in the pons. These brainstem lesions are found in 20% of children with NF-1. They are usually low-grade, can regress and can be indolent.

Option A incorrect: Brainstem lesions are seen in 20% of children with NF-1.

Option B is incorrect: Brainstem lesions are commonly seen in the medulla in NF-1, not the pons.

Option C is incorrect: Brainstem lesions are low-grade, can regress and can be indolent.

Option D is incorrect. The brainstem lesions are commonly seen in the medulla.

Reference

Tumor Mimics
Thierry A. G. M. Huisman, MD

25. Which of the following statements is correct?
   A. Brain tumors are frequent in children
   B. Brain infections occur rare in children
   C. A rare manifestation of a common disease is less likely than a common manifestation of a rare disease
   D. A rare manifestation of a common disease is more likely than a common manifestation of a rare disease

Correct Answer: D
Rationale
Brain tumors are overall infrequent in children, alternative diagnosis should be considered first. In addition, a brain abscess may mimic a brain tumor and is seen much more frequent than a true brain neoplasm. Consequently it is very important to be aware of the old rule that a rare manifestation of a common disease is more likely than a common manifestation of a rare disease. Advanced imaging and correlation of the clinical and imaging findings is essential.

Reference
Huisman TA. Cancer Imaging 2009 Oct 2;9 S10-13

26. A classic brain abscess present with following signal characteristics:
A. DWI hyperintense, ADC hyperintense, T2-hyperintense, T1-hyperintense
B. DWI-hyperintense, ADC-hypointense, T2-hyperintense, T1-hyperintense
C. DWI-hyperintense, ADC hypointense, T2-hyperintense, T1-hypointense
D. DWI hypointense, ADC hyperintense, T2-hypointense, T1-hyperintense
E. DWI hypointense ADC hyperintense, T2-hyperintense, T1-hyperintense

Correct Answer: C

Rationale
Brain abscesses are DWI-hyperintense, ADC hypointense and T2-hyper/T1-hypointense. The pus within the center of the brain abscess typically exhibits restricted diffusion due to its consistency which results in reduced diffusion and consequently a low ADC value. On T2-weighted imaging the content of the abscess is typically hyperintense with a matching T1-hypointensity. Frequently the abscess wall with show a strong contrast enhancement which may appear somewhat irregular. Often the abscess is surrounded by extensive vasogenic edema.

Reference

27. Radiation necrosis after radiotherapy of a brain malignancy: Which statement is correct?
A. May mimic a recurrence or progression of the primary tumor
B. Is strictly limited to the radiation field
C. Contrast enhancement allows differentiation between necrosis and recurrent tumor
D. Always occurs in close temporal proximity to the treatment
E. Radiation necrosis typically has no mass effect

Correct Answer: A

Rationale
Radiation necrosis after radiation treatment for a brain malignancy may be a significant diagnostic challenge. They may indeed mimic tumor progression or recurrence. Unfortunately radiation related MRI signal changes or necrosis may also be observed outside of the primary field of radiation. The degree and pattern of contrast enhancement may mimic any kind of primary brain tumor and may change over time. In addition, radiation necrosis may be seen within a couple of days after radiation however may also become apparent many weeks or even months after treatment. Finally, radiation necrosis may have a significant mass effect on adjacent structures and consequently this imaging finding cannot be used to differentiate between necrosis and tumor recurrence.

Reference
Huisman TA. Cancer Imaging 2009 Oct 2;9 S10-13
**Leukodystrophies and Leukoencephalopathies**
Zoltan Patay, MD, PhD

28. Please choose the right answer. In mitochondrial cytopathies:
   A. Brain involvement is characterized by gray matter, in particular basal ganglia lesions exclusively
   B. Brain involvement may present with a “leukodystrophy-like” appearance
   C. Brain involvement is exceptional only
   D. Different mutations always present with different MR imaging phenotypes
   E. Initially brain lesions are characterized by increased diffusivity

Correct Answer: B

Rationale

Indeed, in some forms of mitochondrial cytopathies the MR imaging findings are suggestive of leukodystrophy. In the acute phase, in diffusion-weighted images the white matter lesions may be associated with restricted diffusivity (answer E is wrong) and the lesions rapidly burn-out leading to severe tissue rarefaction.

Brain involvement is common in mitochondrial cytopathies (answer C is wrong). Although gray matter nucleus involvement (typically remarkably symmetrical) in brain is frequent, white matter lesions may develop too (answer A is wrong), sometimes in addition to, more rarely without significant gray matter involvement.

Different mitochondrial DNA mutations may be associated with similar clinical-imaging phenotypes, or conversely, the same mutation may have different clinical and imaging manifestations (answer D is wrong).

Reference


29. Please choose the right answer:
   A. Increased head circumference is a characteristic feature of patients with Canavan disease
   B. In leukodystrophies, lesion patterns, including lesion gradients never change over time, therefore those have great value in the early imaging diagnosis
   C. Microcephalic leukodystrophies include L2-hydroxyglutaric aciduria, Alexander disease, and the vanishing white matter disease
   D. Head circumference changes are never seen in true leukodystrophies, only in acquired leukoencephalopathies
   E. In true leukodystrophies, lesion involvement of the cerebral white matter is always uniform and complete; therefore the concept of pattern recognition is not applicable to the diagnostic imaging evaluation of these conditions.

Correct Answer: A
Rationale

Head circumference changes in leukodystrophies are common, hence represent useful clinical and even imaging diagnostic clues (answer D is wrong). “Macrocephalic leukodystrophies” include megalencephalic leukodystrophy with subcortical cysts (MLC), the vanishing white matter disease, GM2 gangliosidosis and L-2-hydroxyglutaric aciduria (answer C is wrong) and is one of the hallmark clinical features of Canavan disease is macrocephaly (answer A is correct).

Microcephalic leukodystrophies include Aicardi-Goutiére syndrome, Cockayne disease and Pelizaeus-Merzbacher disease. Lesion patterns are often dynamic in leukodystrophies, therefore MRI may be negative initially and entirely non-specific in the burned-out phase (answer B is wrong). Since lesion involvement may not be uniform in some leukodystrophies and leukoencephalopathies, meticulous analysis of the involved and non-involved white matter structures and regions in MR images is important to accurately describe the actual lesion pattern and potentially correctly diagnose specific entities (answer E is wrong).

References


30. Please choose the right answer:

A. In metachromatic leukodystrophy the cerebrosides 3-sulphate content of myelin decreases from 30% to 3%  
B. In dysmyelinating diseases the myelin may become fragile and prone to breakdown  
C. Impaired myelin maintenance leads to delayed myelination but never to demyelination  
D. Galactosemia may present as leukodystrophy in MR images but proton MR spectroscopy has no value in the diagnostic workup  
E. Most entities related to a disorder of peroxisomal biogenesis are characterized by adult onset and relatively benign disease course

Correct Answer: B

Rationale

Myelin is a complex substance, composed of water, lipids and proteins in specific proportions. In dysmyelinating conditions the normal composition of myelin is altered, leading to potentially unstable myelin which may be prone to breakdown. In metachromatic leukodystrophy, due to a deficiency of the arylsulfatase A enzyme, cerebroside 3-sulphate accumulates and its concentration in the myelin increases from 3% to 30% (answer A is wrong).

Besides abnormal myelin build-up (dysmyelination), impaired myelin maintenance is another possible cause of demyelination (answer C is wrong), as in some of the inborn errors of methyl-transfer pathway. More profound metabolic derangements are usually associated with early onset, severe clinical disease phenotypes, therefore peroxisomal biogenesis disorders, which affect all or most peroxisomal enzymes, typically manifest in neonates and have poor prognosis (answer E is wrong), as opposed to single peroxisomal enzyme deficiencies which may have a later onset and occasionally a better prognosis too. Severe galactosemia may indeed present with a leukodystrophy-like appearance, which in extreme cases may mimic other leukodystrophies, but proton MR spectroscopy may aide with the correct diagnosis showing a peak doublet at the 3.67-3.74 ppm level (answer D is wrong).

Reference

Neurometabolic Disorders of the Newborn
Thierry A. G. M. Huisman, MD

31. Which of the following statements is correct in relation to neonatal neurometabolic disorders?
   A. Disorders of metabolism are collectively rare
   B. Early symptoms are often specific
   C. They often mimic more common neonatal diseases like HIE, sepsis and CHD
   D. Few neonatal neurometabolic disorders are treatable
   E. Neonatal hypoglycemic brain injury is the most common inborn error of metabolism

Correct Answer: C

Rationale
Disorders of metabolism are individually rare but collectively numerous. The early symptoms are frequently non-specific, and often mimic more common neonatal diseases like hypoxic-ischemic brain injury, neonatal sepsis of sequelae of congenital heart disease. Fortunately many neonatal neurometabolic disorders can be treated or the long lasting complications can be prevented or limited. Finally, neonatal hypoglycemic brain injury is not an inborn error of metabolism.

Reference

32. Which of the following statements is incorrect?
   A. Glucose is primary metabolic fuel of the brain
   B. Oxygen consumption is relatively low in the neonatal brain
   C. Critical lower limits of glucose are unknown and depends on demand (e.g. seizures, HIE)
   D. Glucose is being recruited from the hepatic glycogen storage (glycogenolysis and gluconeogenesis)
   E. Glucose production in neonate is 50% of adult level

Correct Answer: D

Rationale
Glucose production in neonate is 50% of adult level

Glucose is the primary metabolic fuel of the brain, the oxygen consumption of the neonatal brain is in contrast to the adult brain relatively low. The exact lower limits of glucose for adequate brain survival and function are unknown and depend on multiple factors including seizure activity and possible co-existent hypoxic ischemic brain injury. Glucose is stored as glycogen in the liver and consequently glucose is recruited from the hepatic glycogen storage in the neonatal time period. The glucose production in a neonate is about 2 to 3 times of the adult level.

Reference

33. Which imaging findings are typically seen in glutaric aciduria except for?
   A. Expanded CSF space anterior to the temporal lobes
   B. Widening of the Sylvian fissures
   C. Delayed white matter myelination
   D. Contrast enhancement of the mammillary bodies
   E. T2-hyperintensity of the central gray matter

Correct Answer: D
Rationale
Contrast enhancement of the mamillary bodies

The typical imaging features as described in glutaric aciduria type 1 are diverse and include expanded CSF space anterior to the temporal lobes, widening of Sylvian fissures, widened mesencephalic cistern, sulcal prominence and expanded pericerebral CSF space, ventriculomegaly, white-matter involvement, delayed myelination, high T2-signal of the corpus callosum, caudate nucleus, globus pallidus, putamen, thalamus, dentate nucleus, medial lemniscus, substantia nigra and the presence of a subdural collection. No increased enhancement of the mamillary bodies have been described.

Reference

Organic Acidurias and Aminoacidopathies
Susan Blaser, MD, FRCPC

34. Pick the incorrect statement.
   A. Organic acidopathies can be caused by defects in amino acid catabolism pathways, usually the result of deficient enzyme activity.
   B. Organic acids are comprised of an acid group, usually carboxylic acid (-COOH) and a compound specific side group (R).
   C. Amino acids also contain carboxylic acid and a compound specific side group, but in addition contain an amino group (-NH2)
   D. Lactic acid and uric acid are examples of amino acids
   E. Organic and amino acids are organic (carbon 'skeleton' containing) compounds

Correct Answer: D

Rationale
A. Correct, as amino acids are still organic acids once they lose their amino moiety during amino acid catabolism.
B. Correct
C. Correct
D. False, neither contain an amino side group.
E. Correct

References
35. Which statement is not true?
A. Infants who present with early-onset forms of amino and organic acid disorders do better than late-onset forms, due to better brain plasticity in the newborn.
B. PKU is the most common aminoacidemia found in North America, Western Europe, and the Middle East, but is infrequent in Japan and India.
C. Disorders involving amino and organic acid metabolism were formerly differentiated by their key diagnostic marker, for example, amino acids in blood or organic acids in urine.
D. As all carbon acids (including amino acids) contain a (-COOH) moiety, they can all be considered organic acids.
E. Increasingly, pre-symptomatic diagnoses of inborn errors of metabolism are being made by newborn screening (tandem mass spectrometry). Disorders may be missed, however, in ‘late-onset’ forms due to lack of sensitivity or incompleteness of the newborn screening panel.

Correct Answer: A

Rationale
A. False. Earlier onset implies a more severe enzyme deficiency. As the brain is undergoing rapid development at that time, damage is often severe.
B. Correct. PKU is more common in Caucasian populations and less common in African, Hispanic and Asian populations. Additionally, phenylalanine is involved in melanin pigment production, leading to lighter hair, eyes and skin in than unaffected siblings.
C. Correct
D. Correct
E. Correct. Each country, and even each state or province, tests for a different number and range of inborn errors of metabolism. Diagnosis at a later stage, with onset of symptoms, may require urine, blood or CSF testing, or specific enzyme or DNA analysis.

References

36. Match the disorder with the correct descriptive phrase.
A. Maple syrup urine disease
B. Urea cycle disorders
C. Non-ketotic hyperglycinemia
D. PKU
E. GAMT

1. Deficient Creatine peak on MR spectroscopy
2. Diffusion restriction of corticospinal tracts (early) and peak at 3.55 ppm
3. Myelin splitting of myelinated white matter leads to a specific pattern of cerebellar white matter edema and ‘four bright dots’ in the pons.
4. MRS of this disorder requires evaluation of the upfield spectrum, as the biochemical marker is found at 7.3 ppm.
5. ‘Depth-of-sulcus’ injury leading to ‘ulegyria’ in survivors.

Rationale
1. E- Deficient Creatine peak is found in GAMT (guanidinoacetate methyltransferase) deficiency, an inborn error of creatine synthesis.

2. C- Diffusion restriction of cortical spinal tracts and a glycine peak at 3.55 ppm are found in early Non-ketotic hyperglycinemia. Later, diffuse brain destruction, or end-stage brain, is non-specific.

3. A- Myelin splitting processes occur in areas where white matter is already myelinated. In the newborn, that would be the cerebellum and brainstem.

4. D- Phenylalanine (Phe) has an apparent T2 relaxation time of approximately 7.3 ppm, well out of the range of typically acquired spectra.

5. B- Early onset urea cycle disorders have a typical pattern of a ‘ribbon’ of diffusion restriction at the depth of the sulcus on DWI.

References