

Viewing Time

The program will take up to one hour to complete.

Target Audience

This program is designed for primary care physicians.

Other health care professionals working with patients and their families may also find this program of interest.

Faculty Disclosure

It is the policy of Children's Hospitals and Clinics of Minnesota to ensure balance, independence, objectivity, and scientific rigor in all its educational programs. Our faculty have been asked to disclose to our program audience any real or apparent conflicts of interest related to the content of their presentation. They have also been requested to let you know when any product mentioned in their presentation is not labeled for the use under discussion or is still under investigation.

Faculty Disclosure

Erin Osterholm, MD, has disclosed no actual or potential conflict of interest in relation to this educational activity.

During this educational activity **Dr. Osterholm** will not be discussing the use of any commercial or investigational product not approved for any purpose by the FDA.

Case Presentation: "5-Month-Old Female with Seizures"

Erin Osterholm, MD
Pediatric Chief Resident
Children's Hospitals and Clinics of Minnesota

Case Presentation: "5-Month-Old Female with Seizures"

A lecture presenting a case that was seen in a local primary care clinic, discussing the workup and diagnosis of the case and reviewing the literature pertinent to the discussion.

Program Objectives

Upon completion of this program, participants should be able to:

- Inform participants of unusual presentations of common pediatric problems.
- Identify specific difficulties in the diagnosis of specific problems.
- Discuss potential difficulties in the management of pediatric problems.

Disclaimer

Children's Hospitals and Clinics of Minnesota accepts no responsibility for the materials presented through these Grand Rounds seminars. Each professional host assumes all responsibility for maintaining confidentiality or obtaining authorization, in accordance with all applicable laws.

Accreditation

Children's Hospitals and Clinics of Minnesota is accredited by the Minnesota Medical Association to provide continuing medical education for physicians. Children's Hospitals and Clinics of Minnesota designates this educational activity for a maximum of 1 AMA PRA Category 1 Credits™ toward the AMA Physician's Recognition Award. Each physician should only claim those credits that he/she actually spent in the activity.

Receiving CME Credit

To receive CME credit you must view the entire program and complete the evaluation form at the end.

"5 month old female with seizures"

Erin Osterholm, MD
Grand Rounds-St. Paul Children's Hospital
June 5, 2008

Our case begins in Pediatric Clinic

- CC: Possible seizures.
- HPI: 5 month old female arrives to peds clinic a few hours prior to her scheduled well child check after her grandmother noted an episode of staring and unresponsiveness, eyes rolling back, and some shaking movements of extremities.
- She has been in her father's care for the past few days and he notes she was having a few of these episodes each day, but he did not think they were seizures.
- When grandmother witnessed an episode today, she immediately brought the child into the clinic.

Erin Osterholm, MD
Case Presentation:
"5-Month-Old Female with Seizures"

Peds Clinic Visit

- ▶ Upon arrival, she has no seizure activity, is sleeping comfortably in her carseat.
- ▶ Prior to 3 days ago, she had no signs of illness.
- ▶ No fevers.
- ▶ Eating normally.
- ▶ No emesis, some loose stools.
- ▶ No rash.
- ▶ No respiratory difficulty.
- ▶ No meds, no allergies.
- ▶ No recent exposures.

Past Medical History

- ▶ Birth history-Born at 38 weeks via NSVD, complicated by maternal substance abuse. Maternal toxicology screen positive for THC at birth.
- ▶ Hospitalized at 6 weeks of age for pyelonephritis (had normal VCUG and renal ultrasound).
- ▶ History of fall down steps onto concrete in her car seat while being carried by mom age 3 months. Not evaluated medically at that time.

Social History

- ▶ Patient is currently in the custody of her father and paternal grandmother.
- ▶ A few weeks ago, mother was arrested and remains in jail after a physical altercation with father while he was holding the baby. The baby was scratched and hit in the head with fist several times. She underwent a Head CT and ED evaluation at the time with no pathology noted.

Social History

- ▶ Mother had 3 previous children who have all died before 2 months of age.
- ▶ Half-brother died age 6 weeks secondary to overlying suffocation/SIDS.
- ▶ Half-sibling-stillborn at term after maternal drug overdose.
- ▶ Half-brother died age 2 weeks in unsafe sleep environment/SIDS.
- ▶ CPS involved.

Additional Family History

- ▶ Half sibling with seizures-age 7 (in foster care)
- ▶ Maternal uncle-seizure disorder
- ▶ 2 maternal aunts-SLE
- ▶ Maternal grandfather-polycystic kidney disease.

Peds Clinic Course

- ▶ During clinic visit, she is noted to have another seizure.
- ▶ Event started with staring, then upward eye movements, left arm stiffening, then tonic clonic movements of left arm and then extension/stiffening bilaterally of both lower extremities.
- ▶ Event lasted about 4 minutes and patient was immediately moved to the PICU from the clinic.
- ▶ She had no respiratory distress during the episode.

Erin Osterholm, MD
 Case Presentation:
 "5-Month-Old Female with Seizures"

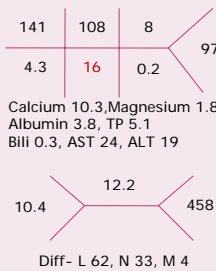
PICU Admission

- ▶ HPI: Seizure in clinic lasted 4 mins and resolved spontaneously. Pt arrives to ICU somewhat sleepy, but arousable. Family notes diarrhea x 3 days, no additional ROS.
- ▶ PMHX/Social Hx-reviewed in detail
- ▶ Notes some developmental concerns-poor head control, does not roll, unable to tripod, does make appropriate vocalizations.

Admission Physical Exam

- ▶ Wt 6kg (15%), Length 60cm (7%), OFC 40cm (7%)
- ▶ T 36, RR 40, P 140, BP 84/58, Sat 98%
- ▶ General-easily arousable, but sleepy, tracking with eyes, intermittently crying, but consolable.
- ▶ HEENT-AF soft and flat, plagiocephaly on R posterior occiput, PERLL, EOM intact, fundi poorly visualized, OP clear, normal TMs.
- ▶ Neck-supple, nontender, poor head control when in sitting position.
- ▶ CV/RESP/ABD/EXT-normal
- ▶ Skin-few petechiae on arm in area of tourniquet for blood draw
- ▶ NEURO-alerts with exam, poor head control, strength and tone mildly decreased, symmetric and brisk DTR.

Admission Laboratory Data



Urinalysis- SG 1.015, pH 6, mod blood, no protein, no ketones, neg nitrite, positive LE, 6-20 WBC, 0-5 RBC
 UC-pending
 Blood culture-pending

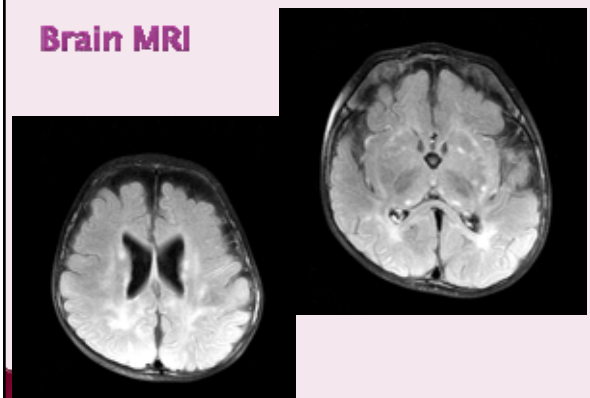
PICU Assessment and Plans

- ▶ A: 5 month old female with new onset seizures, with history of past head trauma and concern for non-accidental trauma as possible etiology. Also, with likely UTI possibly lowering seizure threshold.
- ▶ Plans:
 1. NEURO- neurology consult, recommends EEG today, load with Keppra after EEG and then start maintenance dose of 20mg/kg div tid, obtain head MRI.
 2. FEN-maintenance IVF, regular diet.
 3. ID/Renal-Monitor cultures, start ceftriaxone for UTI, consider repeat renal ultrasound.

Electroencephalogram

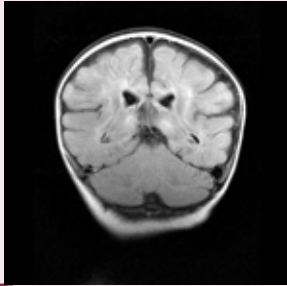
- ▶ Reading- Markedly abnormal EEG, abundant sharp activity in the right posterior quadrant that could be seen in relationship to seizures or structural abnormality in this area, or in some cases blindness.
- ▶ Absence of normal background patterns and brief intervals of generalized suppression- implying diffuse cerebral dysfunction, relatively severe, but nonspecific as to etiology.

Brain MRI



Erin Osterholm, MD
Case Presentation:
"5-Month-Old Female with Seizures"

Brain MRI



Reading:
-Sulcal hyperintensity and enhancement in bilateral cerebral sulci, suggestive of meningeal process, either engorgement of leptomeningeal vessels with status epilepticus or meningeal inflammation.
-T2 hyperintense foci in bilateral thalami, basal ganglia, and periventricular white matter- could be small infarcts.
-Cerebral volume loss- prominent in frontal lobe. Constellation of findings worrisome for nonaccidental trauma.

PICU Day 1

- ▶ Radiologist calls team with concerns of meningeal inflammation and possible sequelae of trauma on MRI.
- ▶ Lumbar puncture completed.
- ▶ CSF gram stain-no WBC, no organisms, protein 18, glucose 58, 8 RBC, 6 Nucleated cells, Diff L 58%, Mono 17%, Macro 25%, cultures and herpes PCR pending.
- ▶ SCAN team consulted.
- ▶ Ophthalmology consulted.
- ▶ Vancomycin and acyclovir added to ceftriaxone.

PICU Day 2

- ▶ S: Quite fussy overnight, but no additional seizure activity, remains afebrile, tolerating po.
- ▶ O: Urine culture with >100,000 gram negative rods, CSF-NGTD, Blood NGTD, HSV PCR-negative, lytes normal with exception of CO2 of 20 (nml 22-30).
- ▶ Optho exam-no ocular evidence of trauma
- ▶ SCAN team recommends skeletal survey which is negative for any fractures.
- ▶ Remains on vanco/ceftriaxone (acyclovir discontinued).

NEUROLOGY CONSULT

- ▶ Neurology reviews history and previous records from outside hospital evaluation of possible trauma about 4 weeks ago.
- ▶ CT scan from this visit was read as "pattern of mild parenchymal volume loss primarily frontal lobe."
- ▶ Neuro exam is normal with the exception of poor truncal tone and slightly brisk DTR in lower extremities.
- ▶ Reviews abnormal EEG and MRI.

NEURO Impression/Recs

- ▶ 5 month old female with concerning history for traumatic brain injury with EEG spikes in the right posterior quadrant-likely localization related seizures with generalization.
- ▶ Rec-Continue Keppra for now although it is unclear if she will need prolonged anticonvulsant medications.
- ▶ Careful developmental follow-up and referral to OT/PT recommended.

Day 3-Transfer to peds floor

- ▶ OT does developmental assessment and reports she is more like a 2 month old developmentally-poor head and trunk control, unable to lift head when prone, unable to take weight when placed in stand, not observed to roll, not visually tracking an object, does coo and vocalize.
- ▶ Pt has 2 brief seizures about 30 seconds each with arms and legs straightening, both L>R. Neurologist contacted and additional load of Keppra and increased dose given.

Hospital Day 4-7

- ▶ Renal ultrasound reveals normal kidneys.
- ▶ She receives 7 days of IV Ceftriaxone for Klebsiella UTI (pansensitive) with plans for 3 days of orals.
- ▶ Has multiple, short (<20 second) seizures on days 4-5.
- ▶ Repeat EEG on Day 6-unchanged from previous.
- ▶ Has several dose adjustments of antiepileptic med with improved seizure control.
- ▶ CPS/SW coordinate discharge to paternal grandmother's custody with supervised maternal visitation after release from jail.
- ▶ OT and brain injury team will follow-up with ongoing neuro-developmental evaluations, neuro to see in 1 week and repeat MRI at that time.

ED Visit -36 hours after hospital discharge

- ▶ CC: Seizure
- ▶ Pt here with 3 breakthrough convulsive episodes. Pt reported to be very fussy, then have a shrill, loud cry, followed by neck stiffening, L leg shaking, then involving whole body. First episode earlier today, lasted about 5 mins, second episode-tonight, about 7 mins, given diastat, and third upon arrival to ED-given IV lorazepam.
- ▶ Kepra level day prior to d/c was <5.

Hospital Admission #2

- ▶ Per neuro recs, receives additional Kepra load and increased maintenance dose IV.
- ▶ Does not require additional lorazepam.
- ▶ Admission BMP again with low HCO₃ of 17 with gap of 15-attributed to increased oxygen consumption with repeated seizures. Bicarb increased to 24 after 36 hours of IV rehydration.
- ▶ UTI oral treatment completed.
- ▶ Unable to coordinate sedation for MRI-to be done as outpt.
- ▶ Discharged on HD #3 on increased Kepra dose.

13 days later-ED visit

- ▶ CC: 3 seizures in past day.
- ▶ HPI: Father reports pt has been crying nearly inconsolably, with increased seizure frequency to 3x/day, all tonic clonic with episodes lasting 2-5 mins.
- ▶ PE: VSS, notable for a fussy infant, decreased motor tone/head control, remainder of exam normal.
- ▶ Labs-normal electrolytes with the exception of slightly elevated chloride to 111 and decreased CO₂ to 14 with anion gap of 16, normal CBC, normal UA-no ketones.

Hospital Admission #3

- ▶ 5 month old female with seizure disorder presenting with increasing irritability and seizure frequency, also with metabolic acidosis that seems to be recurrent.
- ▶ Admitting team reviews previous BMPs-all 8 previous samples have had a low bicarb in the 14-20 range with the exception of a single 24 after aggressive fluid rehydration. Anion gap has been 12-17 even without recent seizure.
- ▶ Given infant's poor development, seizures, and acidosis, team plans to evaluate for inborn error of metabolism and renal tubular acidosis.

Hospital Admission #3 Plans

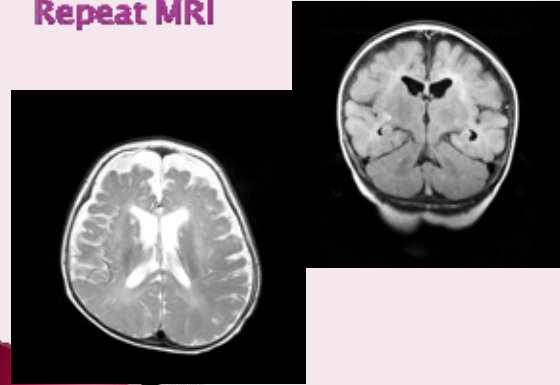
- ▶ Discussed with metabolism consult over the phone, will send urine organic acids, plasma amino acids, qualitative plasma acylcarnitines, and urine acylglycines.
- ▶ Recommended patient receive D10 IVF as needed for hydration.
- ▶ Lactate 3.8 (normal 0.7-2.1) and ammonia 77 (normal 25-94)
- ▶ Pt to be seen in metabolic clinic once labs return or sooner if decompensates.

Erin Osterholm, MD
Case Presentation:
"5-Month-Old Female with Seizures"

Hospital Admission #3

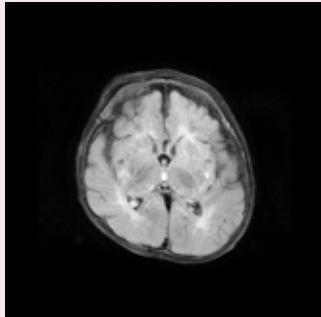
- ▶ EEG repeated-still markedly abnormal with spikes, polyspikes, and slow waves-now in bilateral posterior quadrants (prev localized to right).
- ▶ Severe degree of diffuse cerebral dysfunction with absence of normal background patterns.
- ▶ One seizure noted during admission lasting about 4 mins-Keppra increased to 40mg/kg/day.
- ▶ MRI repeated.

Repeat MRI



MRI

Reading- Evolution of some of the T2 hyperintensities in the thalami and basal ganglia, likely infarcts. New areas of lacunar infarct in caudate nuclei. Cerebral volume loss as before.



Hospital Discharge-Day 3

- ▶ Few seizure episodes during the admission.
- ▶ Pt weaned off IVF and taking po well.
- ▶ Bicarb increased to 22.
- ▶ Continues on Keppra now QID.
- ▶ Plans for follow-up with neurology in about 1 week and Genetics/metabolism in 2 weeks.
- ▶ Outpt OT/PT scheduled.

Metabolic Clinic

- ▶ CC: Seizures, hypotonia, and global developmental delays.
- ▶ HPI: 6 month old female with seizures for the past 2 months, abnormal MRI, and abnormal EEG. Currently, she is having up to 3 episodes/day of tilting her head back and jerking her limbs for < 1 min. These episodes are occurring most when she is falling asleep or just waking. She has seemed more lethargic to grandma for the past few days.

Metabolic Clinic Visit

- ▶ ROS:
 - ▶ Loose mucous containing stools daily.
 - ▶ Hands and feet seem swollen.
 - ▶ Intermittent rash on arms/legs.
 - ▶ Persistent cool extremities.
 - ▶ Hypotonia, developmental delays
 - ▶ No fevers.
- ▶ PMHx
 - ▶ Reviews UTI hospitalization, possible head trauma x 2, normal NMS, Birth Weight 5lb 6oz
 - ▶ Reviews complex social history.

Erin Osterholm, MD
 Case Presentation:
 "5-Month-Old Female with Seizures"

Physical Examination

- ▶ Wt 6.2kg, Ht 64cm, OFC 40.5cm
- ▶ Gen-alert, active
- ▶ HEENT-plagiocephaly, otherwise normal
- ▶ Neck-poor head control
- ▶ CV-normal
- ▶ RESP-normal
- ▶ ABD-normal, no HSM
- ▶ GU-normal
- ▶ NEURO-normal CN, normal muscle bulk, severe hypotonia, DTR-hyperreflexia with sustained ankle clonus, significant head lag.
- ▶ Skin-petechial rash over forearms

Review of previous labs

- ▶ Last MRI-cerebral volume loss (prominent in frontal lobes), infarcts in lenticulostriate distribution.
- ▶ EEG-complete loss of normal background and diffuse irritative CNS dysfunction.

140	111	7	87
5	14	0.2	

Lactate 3.2
 Ammonia 48
 INR 1.04
 PTT 32
 Hgb 11.1
 Platelet 423
 Levitracetam 32.9

Send out labs begin to return

- ▶ **Plasma amino acids:** The plasma amino acid pattern is not consistent with a known disorder of amino acid metabolism.
- ▶ **Plasma quantitative acylcarnitines:** Elevated C4 acylcarnitine species (butyryl- and isobutyrylcarnitine) at 1.64.
- ▶ This isolated finding is suggestive of either a diagnosis of SCAD (short chain acyl-CoA dehydrogenase) deficiency or IBD (isobutyryl-CoA dehydrogenase deficiency). Consider urine organic acids, C4-acylcarnitine, and acylglycines to differentiate.

Newborn Screen ACT Sheet—American College of Medical Genetics

- [Elevated C4 Acylcarnitine]**
- ▶ **Short-Chain Acyl-CoA Dehydrogenase (SCAD) Deficiency**
 - ▶ **Differential Diagnosis:** SCAD; Isobutyryl-CoA dehydrogenase (IBDH) deficiency (also referred to as IBG); and Ethylmalonic acid encephalopathy (EMA).
 - ▶ **Condition Description:**
 - ▶ **SCAD deficiency is a fatty acid oxidation (FAO) disorder.** FAO occurs during prolonged fasting and/or periods of increased energy demands (fever, stress) when energy production relies increasingly on fat metabolism.
 - ▶ **IBG is from IBDH deficiency.** IBDH is an enzyme involved in degradation of valine.
 - ▶ **EMA** is a related disorder that seems to be due to a defective mitochondrial matrix protein, the precise function of which is yet unknown.
 - ▶ In all three conditions, potentially toxic derivatives accumulate.

ACT Sheet Elevated C4 Acylcarnitine

- ▶ You should take the following IMMEDIATE actions:
 - Contact the family and determine clinical status (poor feeding, vomiting, lethargy).
 - Consultation with pediatric metabolic specialist.
 - See and evaluate infant (hypoglycemia, lethargy, metabolic acidosis).
 - Emergency treatment if symptomatic.
 - Initiate timely confirmatory testing as recommended by specialist.
 - Educate family about signs/symptoms and need for urgent treatment with illness.
 - Report finding to newborn screening program.

ACT Sheet—Elevated C4 Acylcarnitine

- ▶ **Diagnostic Evaluation:**
- ▶ **In SCAD deficiency,** urine organic acids show increased ethylmalonic acid.
- ▶ **In IBG,** plasma and urine acylcarnitines will show increased C4-acylcarnitine and urine OA will show isobutyrylglycine.
- ▶ **In EMA encephalopathy,** plasma acylcarnitines will typically show C4 and C5-acylcarnitine, and urine organic acids will show increased ethylmalonic acid and isovalerylglycine. The diagnosis is confirmed by ETHE1 gene sequencing.

ACT Sheet-Elevated C4 Acylcarnitine

- ▶ **Clinical Expectations:**
- ▶ **SCAD deficiency** can have variable presentation, although affected neonates can be very ill with vomiting, lethargy, seizures, and hypoketotic hypoglycemia. **Tx with avoiding fasting and vitamin/co-factor supplementation.**
- ▶ **EMA encephalopathy** presents in infancy with developmental delay, diarrhea and petechiae.

- ▶ Back to our case...

Additional send-outs return

- ▶ **Acylglycines urine-** multiple abnormally high glycines including ethylmalonic acid.
- ▶ Interpretation-profile is suggestive of diagnosis of ethylmalonic encephalopathy. Consider testing the ETHE1 gene for mutations in order to confirm the diagnosis.
- ▶ **Urine organic acids-** highly elevated ethylmalonic acid along with the presence of isobutyrylglycine and 2-methylbutyrylglycine is consistent with the diagnosis of ethylmalonic aciduria. Clinical correlation required.

Metabolic assessment

- ▶ 6 month old female with probable ethylmalonic encephalopathy with severe neurological impairment and infantile spasms/seizures. History of possible trauma in past likely unrelated to current neurologic status.
- ▶ Plans-
- ▶ Emergency letter given to family for times of illness documenting IVF needs, indicated laboratory studies, and emergency contacts.
- ▶ Send carnitine levels, C4-acylcarnitine, obtain skin biopsy for fibroblast culture.
- ▶ Start carnitine 1.6ml tid.
- ▶ Follow-up in one month.

3 weeks later

- ▶ Hospitalized with increasing seizure frequency (baseline 3x/day), now increased to 7-8 seizures/day lasting several minutes.
- ▶ Significant diarrhea x 7 days.
- ▶ Admission bicarbonate 16 with lactate of 6.
- ▶ Rehydrated with D10 ½ NS and given IV carnitine with resolution of acidosis and diarrhea.
- ▶ Discharged on HD #3.

2 days later

- ▶ Seen in metabolic clinic.
- ▶ HPI- Pt having increased watery diarrhea, increased lethargy, had 2 witnessed seizures in clinic.
- ▶ Transferred to inpatient status, very sleepy on arrival, poor head control, disconjugate gaze, poor eye contact, hyperreflexia, with obvious developmental delays.
- ▶ CO2 low at 12 with anion gap of 19, lactate 7.2, infectious work-up sent and pending.
- ▶ Difficult IV access-received D10 once established.

Erin Osterholm, MD
Case Presentation:
"5-Month-Old Female with Seizures"

Hospital admission #6

- ▶ Given that this patient will likely continue to have diarrhea and repeated admissions for acidosis secondary to her underlying metabolic condition, it would be in her best interest to have more permanent venous access.
- ▶ Port-a cath is placed Day 3.
- ▶ Pt has several seizures the day after port placement, continues on IVF and then discharged to home on Day 5.

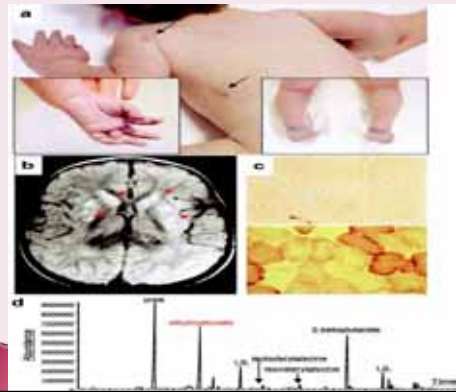
Current status

- ▶ She has currently been admitted for the 8th time in 4 months for severe acidosis and increasing seizure frequency.
- ▶ She continues to demonstrate progressive truncal hypotonia, distal hypertonicity, mucoid diarrhea, intractable seizures, and now emerging concerns for dysphagia.
- ▶ Her OFC has fallen to <3rd percentile, weight <3rd percentile.
- ▶ She is followed by metabolism, neurology, OT/PT, and pediatrics.
- ▶ Grandmother is aware of her poor prognosis and continues to be her primary caregiver.

Ethylmalonic Encephalopathy

- ▶ First described in 1991 by Burlina et al., most common in individuals of Mediterranean and Arab descent.
- ▶ Characterized by ethylmalonic and methylsuccinic aciduria and lactic acidemia.
- ▶ Associated with developmental delay, acrocyanosis, petechiae, and chronic diarrhea.
- ▶ In 2004, Tiranti et al reported only 30 cases of EMA encephalopathy worldwide, but the actual incidence may be underestimated because the biochemical phenotype may be incorrectly attributed to other metabolic disorders (particularly defects in mitochondrial electron-transfer).

Clinical features

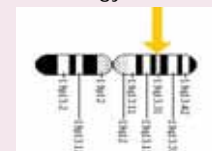


Clinical features

- ▶ Signs and symptoms are usually present in the first few months of life.
- ▶ Neurologic symptoms are progressive with most affected individuals surviving only into early childhood.
- ▶ A few individuals with a milder, more chronic form have been reported.
- ▶ No treatment is currently available although carnitine is given to enhance the formation and excretion of acylcarnitine conjugates thought to be toxic to the brain, liver, and kidneys.

Ethylmalonic encephalopathy

- ▶ The underlying metabolic defect is unknown, but seems to be due to a defective mitochondrial matrix protein.
- ▶ Molecular genetics-The ETHE1 gene has been identified as the site of mutations causing EE.
- ▶ It has been demonstrated that the ETHE1 protein is targeted to mitochondria and internalized into the matrix indicating an important role in mitochondrial homeostasis and energy metabolism.
- ▶ ETHE 1 gene has been mapped to chromosome 19 q 13.32



Take home points

- ▶ It is important to recognize, work-up, and treat increased anion gap metabolic acidosis in early infancy EVEN IF the newborn metabolic screen is NORMAL.
- ▶ Initial evaluation of suspected metabolic condition includes pH, CO₂, ammonia, lactate, pyruvate, glucose, lytes, BUN/Cr, CBC, and ketones.
- ▶ Consultation with a pediatric metabolic specialist can help direct the need for tests such as plasma amino acids, urine organic acids, acylglycines, and acylcarnitines.

- ▶ Children with FAO disorders are susceptible to metabolic decompensation during episodes of fasting or increased energy demand/catabolism (ie illness, trauma, surgery).
- ▶ During decompensation, children generally need IVF with a GIR based on the estimated hepatic glucose production rate.
- ▶ Na HCO₃ may be needed for acidosis.
- ▶ Prompt recognition of decompensation may prevent life-threatening acidosis.

References

- ▶ Koeberl, D et al. Rare Disorders of Metabolism with Elevated Butyryl- and Isobutyrylcarnitine Detected by Tandem Mass Spectrometry Newborn Screening. *J International Pediatric Research*. 53:219-223: 2003
- ▶ McKusick, Victor. Ethylmalonic encephalopathy. *Online Mendelian Inheritance of Man*. Feb 2004.
- ▶ Merinero, B. et al. Persistent increase of plasma butyryl/isobutyrylcarnitine concentrations as marker of SCAD defect and ethylmalonic encephalopathy. *J Inherited Metabolic Disease*. 22: 2006.
- ▶ Tiranti, V. et al. Ethylmalonic Encephalopathy is Caused by Mutations in ETHE 1, a Gene Encoding a Mitochondrial Matrix Protein. *Am J Hum Genet*. 74:239-252: 2004.
- ▶ www.aemg.net/resources/policies/ACT. Newborn screening ACT sheet-Elevated C4 acylcarnitine. American College of Medical Genetics 2006.

Comments
and
Questions

*Thanks for viewing
this presentation!*



*To receive CME credit, please click
the CME Eval button below
and complete the form.*