

Metabolic and Genetic Mimics of Child Abuse

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Disclosures

- Dr. Christian provides medical-legal expert work in child abuse cases
- Dr. Christian is NOT a geneticist nor metabolic specialist. She is a general and child abuse pediatrician!

Objectives

- Increase awareness of the differential diagnosis of child abuse
- Provide recommendations for initial screening tests for metabolic/ genetic diseases in cases of suspected abuse, guided by presenting "injury"

We see what we look for,
we look for what we know.

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REVIEW ARTICLE

Genetic Influences on Outcome Following Traumatic Brain Injury

Barry D. Jordan

Several genes have been implicated as influencing the outcome following traumatic brain injury (TBI). Currently the most extensively studied gene is apolipoprotein E (APOE). However, several other genes have been investigated and/or speculated. These include APOE promoter, catechol-o-methyltransferase (COMT), dopamine D2 receptor (DRD2), interleukin, p53, and CACNA1A genes. The following paper will review the current state of knowledge regarding genetic influences on outcome following TBI and discuss possible mechanisms and methodological considerations.

Clinical Clues to Differentiating Metabolic and Genetic Diseases from Abuse

- Infants who present in the first 2 weeks of life
- History of chronic, multisystem disease
- Unusual physical exam findings
- “Injuries” that are atypical for abuse
- Abnormal laboratory results out of proportion
 - Liver enzymes that don’t return to normal
 - Coagulation abnormalities
- Clinical course that deviates from expected
- In some cases, parental ‘dysfunction’ led to delay in diagnosis

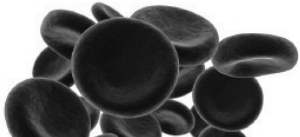
**Metabolic and Genetic
Mimickers of Child Abuse**

- Diseases that mimic Abusive Head Trauma (AHT)
- Diseases that mimic cutaneous injuries
- Diseases that mimic inflicted fractures
- Diseases that mimic sexual abuse
- Diseases that mimic child neglect
- Diseases that mimic “medical child abuse” (MSBP)

Diseases that mimic AHT

- Disease that predispose to intracranial hemorrhage
 - Coagulopathy
 - Integrity of vasculature
 - Influences of cerebral atrophy
 - Glutaric aciduria, Osteogenesis imperfecta, Ehlers Danlos syndrome, Menkes kinky hair syndrome, liver disease, primary coagulopathies
- Diseases that predispose to ALTE/ SIDS

Coagulopathy



Coagulopathy and ICH

- Hemophilia (Factor VIII & IX deficiency)
 - Severe and Moderate deficiency
 - Including SDH
- Liver Disease with associated Vit K deficiency
 - Including SDH
- Other Factor deficiencies
 - Factor XIII deficiency

CT findings in *Spontaneous* ICH Due to Coagulopathy in Children

Disorder (n)	Location of Bleed	Other findings
Hemophilia A (2)	SDH, SAH, ICH	Midline shift, edema
Hemophilia B (3)	SDH, SAH, ICH	Midline shift
VWD (1) [1y/o]	SDH, SAH	
Thrombocytopenia (2)	Thalamic, ICH	Focal edema
Platelet Dysfunction (2) [5mo, 10 y/o]	SDH, Cerebellar	Old hemorrhage
Vitamin K def. (3)	SDH, SAH, ICH	Midline shift, edema

Shih, et al. Neuroradiology 1993;35:629-21

7-week-old born by forceps
Vomiting, irritability, seizures
Bleeding from nose

CT- Acute occipital SDH
RH in right eye
Normal SS

NI PT, PTT
Prolonged Bleeding Time
(> 15 minutes)

Further evaluation revealed...

Hermansky-Pudlak Syndrome

- Autosomal recessive disorder
- Characterized by:
 - Oculocutaneous albinism
 - Bleeding diathesis due to platelet abnormality and impaired aggregation
- Usually a mild bleeding disorder

Cobalamine C Defect (Vit B12 enzyme)

- Case report of a 5-week-old infant with encephalopathy and 'HUS' picture
 - Sibling had died a 4 mo with ?propionic acidemia
 - SDH, IVH, RH with vitreous heme
- methylmalonic aciduria and homocystinuria
- Inc plasma homocysteine, MMA
 - Fibroblast complementation study: Cobalamine defect
- Elevated homocystine may predispose to spontaneous intracranial hemorrhage
 - Vascular endothelial damage
 - Baby also had coagulopathy, thrombocytopenia



Frances PJ, et al. Eur J Pediatr 2004;163:420-1

Pediatric
Neurosurgery

Original Paper

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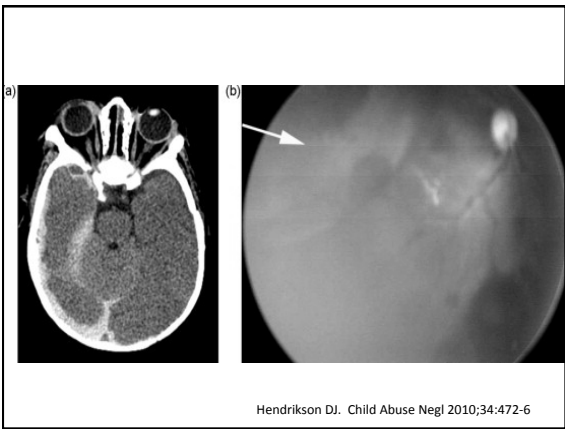
Intracranial Hemorrhage and Vitamin K Deficiency Associated with Biliary Atresia: Summary of 15 Cases and Review of the Literature

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Hendrickson DJ, et al. An inborn error of bile salt transport with features mimicking AHT. Child Abuse Negl 2010;34:472-6.

- 8-mo-old girl limp, unresponsive, ear bleed
- Sclera mildly icteric, mild hepatomegaly
- Acute SDH and retinal hemorrhages
- PMHx-
 - Vit D def & hypocalcemia at 5 mo
 - FTT
- PTT > 150 INR > test limit; improved with Vit K
- LFTs mildly elevated, inc. Bili, nl GGT
- Extensive eval revealed Progressive familial intrahepatic cholestasis Type 2
- Infant had liver transplant



Bile Salt Transport Defect


- Multiple inherited defects are known in bile acid synthesis, conjugation, and transport
- In this patient a mutation (ABCB11) eradicated bile salt export protein expression
 - Impaired transport of bile salts into bile
 - Prevented absorption of fat-soluble vitamins
- Coagulopathy was identified as the cause for subdural and retinal hemorrhage
 - Retinal detachment related to hypoalbuminemia

Glutaric aciduria Type I

- Deficiency of glutaryl-CoA dehydrogenase
 - Metabolism of lysine, tryptophan
- Autosomal recessive disorder
- Encephalopathy in late infancy, childhood
 - Acute dystonic-dyskenetic syndrome
- Diagnosis
 - Glutarate, 3-OH glutarate & glutaconate in urine
 - Deficiency of glutaric dehydrogenase in leukocytes or fibroblasts
 - Assess carnitine levels
- Newborn screens done with Tandem MS

GAI- Imaging



- FRONTOTEMPORAL ATROPHY
 - Widened insular cisterns
- Changes in basal ganglia
- White matter hypodensities
- Subdural effusions
 - SDH occur in conjunction with significant frontotemporal atrophy
 - Generally appear as chronic SDH
- RH are described

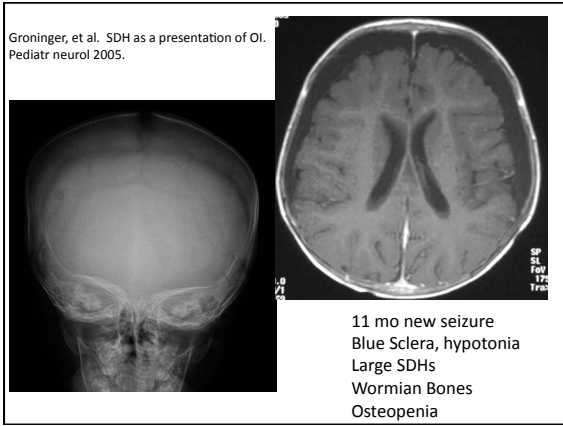


Morris, et al. Glutaric aciduria and suspected child abuse. Archives of Disease in Childhood 1999;80:404-405

Disorders of Collagen


- Osteogenesis Imperfecta
 - Acute and chronic SDH have described
 - Reports of SDH with trauma...
 - In severe OI, without trauma
- Ehlers Danlos Syndrome
 - Report of recurrent SDH a presentation
 - Infant with acute and chronic SDH, RH and prolonged bleeding time

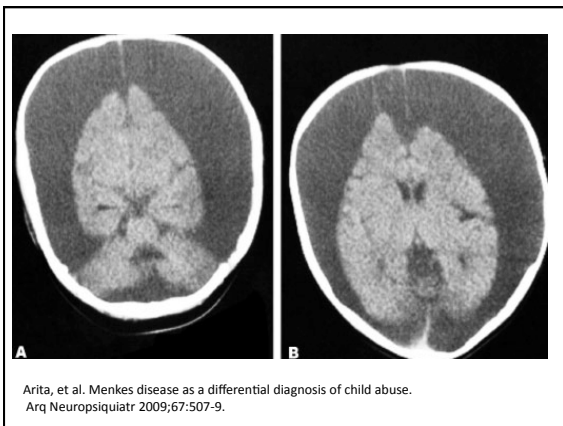





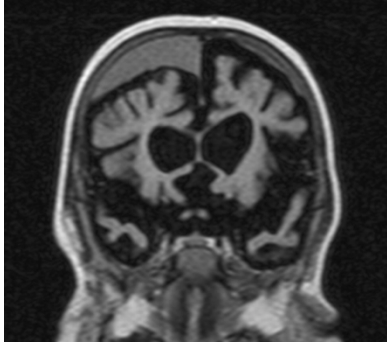
Menkes Kinky Hair Syndrome

- X-linked recessive disorder of copper metabolism
- Clinical triad:
 - Developmental delay
 - Progressive neurologic degeneration
 - Hair abnormalities
- Decreased serum ceruloplasm
- Decreased serum copper
- Subdural Collections due to:
 - Brain atrophy
 - Failure in elastin and collagen cross-linking



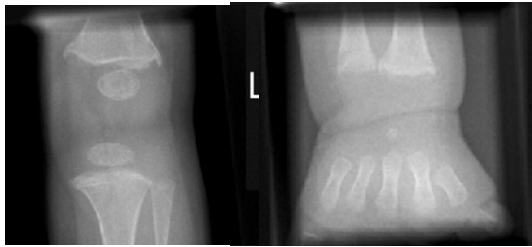


Bacopoulou, F et al. Menkes Dz mimicking non-accidental injury. Arch Dis Child 2006;91:919



ADC

Figure 2 metaphyseal irregularity and spurring.

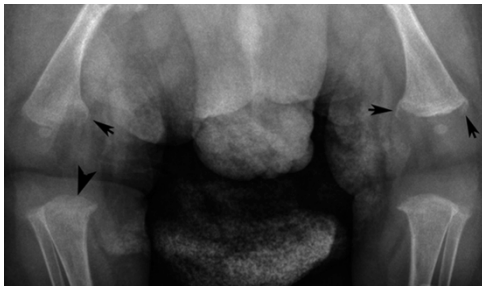


Bacopoulou, F et al. Arch Dis Child 2006;91:919

ADC

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Case 2: Bilateral knees show severe osteoporosis, poor mineralization, and femoral metaphyseal spurs reminiscent of Menke kinky hair syndrome (arrows).



Marquardt M L et al. Pediatrics 2012;130:e695-e698

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PEDIATRICS

Clinical Evaluation for Diseases that mimic AHT

- History
 - “We don’t know what happened”
- Physical Examination
 - Head circumference abnormalities
 - Ectodermal examination
 - Hair, teeth, skin
 - Eye examination, including sclera
 - Feel the abdomen
- Neurologic examination

Initial Screening Labs: AHT

- Screening for coagulopathy
 - CBC with platelet count
 - PT/activated PTT/ INR
 - Factor VIII, Factor IX levels
 - DIC panel (D-dimer and fibrinogen)
- Complete chemistry panel, including LFTs, electrolytes
- Plasma amino acids, urine organic acids
- Acylcarnitine profile
- Review newborn screen
- Follow up on abnormal laboratory values
- Consult your local hematologist, geneticist

Diseases that predispose to CUTANEOUS BLEEDING...scars, etc

- Disease that predispose to bleeding
 - Abnormalities of Coagulation
 - Both primary coagulopathies
 - Diseases with secondary coagulopathy
 - Integrity of vasculature
- Diseases with skin findings that mimic bruising, burns or scarring
 - Vasculopathies
 - Inherited dermatologic diseases

Ehlers-Danlos Syndrome

- 6-year-old child with 4 ED visits in 2 months for lacerations requiring sutures
 - Report made to child welfare
 - Family “ignored” investigation; brought to court
 - Medical and psychological evaluation ordered
- Mult scars, bruises, skin shiny, paper thin
- Scars healed by secondary intention
- Slightly dysmorphic
- Hyperextensible joints and hyperelastic skin

Owen SM, Durst RD. Ehlers-Danlos syndrome simulating child abuse. Arch Dermatol 1984;120:97-101.



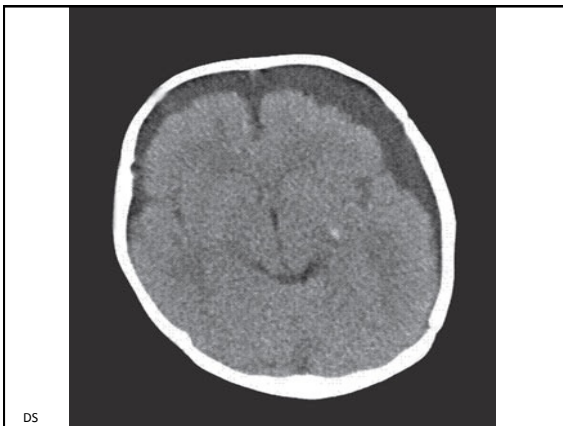
Ehlers-Danlos Syndrome

- Inherited connective tissue disorder
- Characterized by joint hypermobility and skin hyperelasticity
- Clinical signs:
 - Extensive cutaneous injury with gaping wounds after mild trauma
 - “Cigarette paper” scars
 - Easy bruising
 - Habitual dislocation of the joints

Degos Syndrome

- 6-month-old boy with skin ulcers and focal seizures
 - Mult 7-10 mm monomorphic ulcers
 - red margin, white atrophic centers
 - Trunk, limbs, scrotum
- CT & MRI – Bilateral SDH, no intracerebral lesions
- ?child abuse vs. vasculitis
- Child developed further seizures,
 - MRI showed mult cerebral infarctions
- Skin biopsy revealed Degos Syndrome
- Baby ultimately died

Moss C, et al. Degos disease: a new simulator of non-accidental injury. *Developmental Med Child Neurol* 2009;51:647-50.





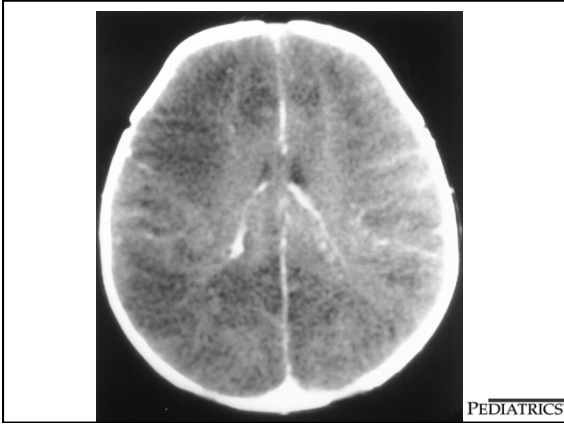
Incontinentia Pigmenti- 2 case reports

- 6-day-old girl with seizures
 - Bilateral RH
 - Hyperpigmented macules on thorax and limbs
 - Ecchymoses over buttocks
 - CT with diffuse infarcts and edema
- Diagnosed with “SBS” and transferred for further care...
 - Dermatologist to the rescue!!

Ciarallo L, Paller AS. Two cases of incontinentia Pigmenti simulating child abuse. Pediatrics 1997;100:e6







Incontinentia Pigmenti

- X-linked dominant disorder
- Characterized by dermatologic, dental and, less frequently, ocular and neurologic abnormalities
- Cutaneous findings are diagnostic:
 - All four stages show patterning along Blaschko's lines

Initial Screening Labs: Cutaneous

- Screening for coagulopathy
 - CBC with platelet count
 - PT/ aPTT/INR
 - Factor VIII level
 - Factor IX level
 - VWF antigen
 - Ristocetin cofactor
- Consult Genetics, Dermatology, Hematology as needed

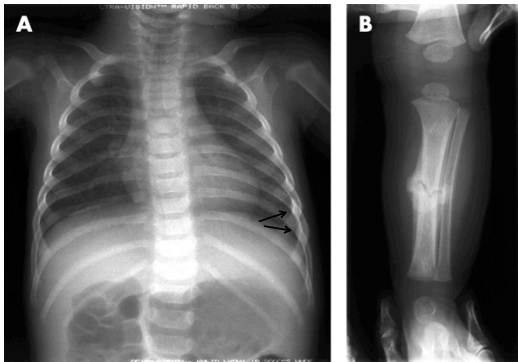
Diseases that Predispose to Fractures

- Genetic disorders with Osteopenia/ Osteoporosis
 - Osteogenesis Imperfecta
 - Job syndrome
 - Menkes Kinky hair syndrome
 - Biliary atresia with vitamin D deficiency
 - Fanconi syndrome
- Disorders that predispose to Trauma
 - Hereditary Sensory Neuropathy

Job Syndrome: Recurrent fractures in an infant

- 2.8 kg FT newborn with mild PS
- Developed severe eczema by 2 months
- Hospitalized at 4 mo with FTT, eczema
 - Dysmorphic- nl karyotype and FISH for 22q11
- Hosp at 6 mo with eczema, wrist laceration
 - SS fracture of tib/fib with callous, rib fractures
- Placed in Foster care
 - Developed *S. aureus* abscess
- Serum IgE- > 1,600

Walsh J, Reardon W. Job syndrome masquerading as non-accidental trauma. Arch Dis Child 2008;93:65-7



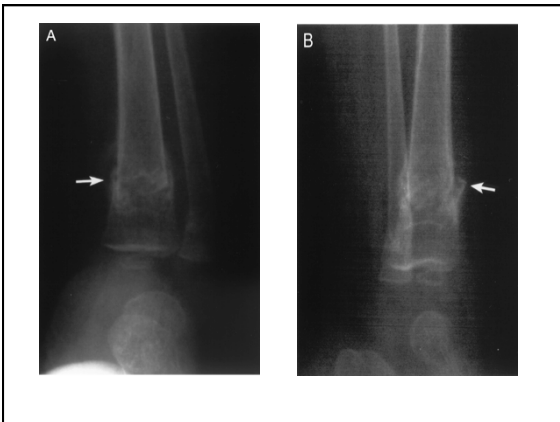
Walsh J, Reardon W. Job syndrome masquerading as non-accidental trauma. Arch Dis Child 2008;93:65-7

Job Syndrome

- A rare primary immunologic disorder
 - STAT3 gene
- Characterized by hyperimmunoglobulin E
- Associated with:
 - Eczema
 - Craniosynostosis
 - Skull plasticity
 - Molluscum contagiosum
 - Recurrent staphylococcal skin abscesses
 - Recurrent fractures

Biliary Atresia

- Osseous abnormalities found in many children with biliary atresia
 - Cortical thinning
 - Trabecular bone loss
 - Changes of rickets
- Fractures in 11% of patients with biliary atresia
- In one study, 4/10 children with biliary atresia had evidence of rickets



Initial Screening Labs: fractures

- Careful evaluation of radiographs
- Screen for mineralization deficiency
 - Ca, PO4, Alk Phos
 - 25-OH vitamin D, PTH
 - Urine calcium, phosphate
- Consider genetic testing for OI, EDS, Menkes
 - Can also consider fibroblast collagen analysis

Genetic diseases that mimic Sexual Abuse

- Crohn's Disease
- Myotonic Dystrophy

Eur J Pediatr (2000) 159: 539–541

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ORIGINAL PAPER

Lucrecia Suárez · Amaya Bélanger-Quintana · Hector Escobar
Gemma de Blas · Jesus Benítez · Eduardo Lobo · Fuencisla de Miguel
Juan Manuel Aparicio

**Suspected sexual abuse:
an unusual presentation form
of congenital myotonic dystrophy**

Received: 13 April 1999 / Accepted: 31 January 2000

Abstract In children, anal abnormalities due to various causes may be confused with sexual abuse. We present the case of a child in whom the suspicion of abuse due to anal dilatation led to the previously unknown diagnosis of myotonic dystrophy. Myopathic involvement of the perianal musculature is a known feature of congenital myotonic dystrophy that usually appears in late childhood or adolescence.

Conclusion We stress the importance of considering an underlying myopathic condition in the differential diagnosis of anal laxity. Further studies, such as anal ultrasonography, may help when the diagnosis of abuse is not clear.

Key words Sexual abuse · Anal dilatation · Myotonic dystrophy · Child

Conclusions

- There is a differential diagnosis for everything
- Recognizing rare diseases requires
 - Consideration that alternatives exist
 - careful observation and physical examination
 - close scrutiny of screening labs
 - monitoring of the patient’s clinical course
 - embracing the concept of consultation!
