ICD-10-CM Codes for Leukodystrophies

Global Leukodystrophy Initiative (GLIA)

Josh Bonkowsky, MD, PhD

Monika Baker

Primary Children's Hospital
Department of Pediatrics, University of Utah

Intermountain Primary Children's Hospital

RARE DISEASES CLINICAL RESEARCH NETWORK

GLOBAL LEUKODYSTROPHY INITIATIVE

HEALTH UNIVERSITY OF UTAH

What is a Leukodystrophy?

- Genetic disease of the white matter in the brain and/or spinal cord
  - involving myelin (glia), astrocytes, and/or microglia

- First recognized in the late 1800s

- Over the past 15 years, with MRI and genetic testing, the extent of leukodystrophy disease has become more apparent

- Greek root *leuko* (*λευκο*) (white)

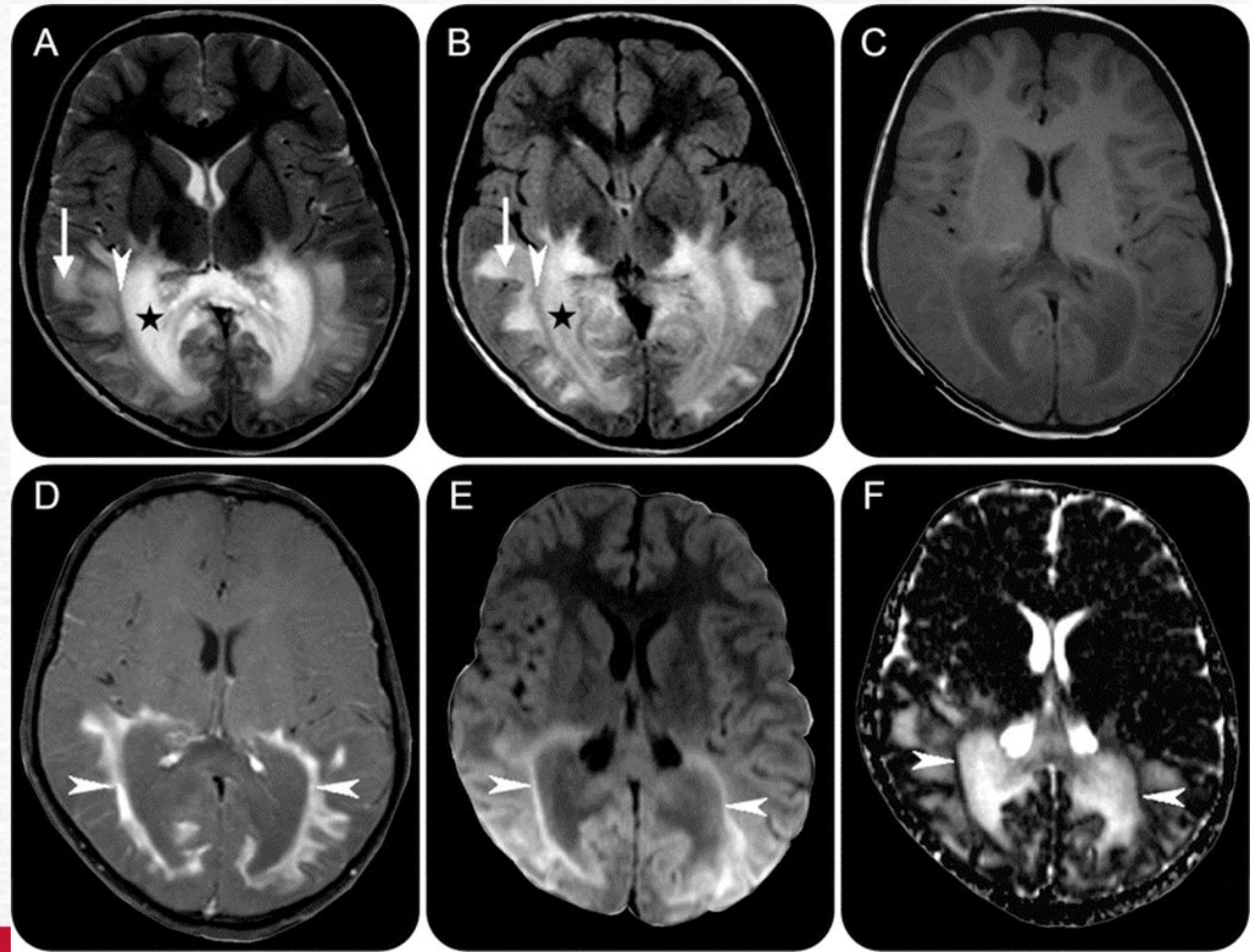
- Myelin sheath: insulation for axons

Intermountain Primary Children's Hospital

HEALTH UNIVERSITY OF UTAH

Leukodystrophies

- Leukodystrophies are a diverse group of diseases
- >400 known different genes
  - Distinct clinical trajectories
  - Distinct treatments
  - Rare and orphan conditions
- Death in 30% by age 8



Intermountain
Primary Children's Hospital

Leukodystrophy Epidemiology

- 1 in 4,000 live births (overall)
  - Nearly as common as cystic fibrosis (1 in 3,000 Caucasian live births)
  - Each individual leukodystrophies is less common
    - For example, Adrenoleukodystrophy affects 1 in 15,000 live births
  - But overall "incidence" has increased, as conditions previously mis-diagnosed are correctly identified
- Affects all ages, races, and ethnicities
  - Minority patients are underdiagnosed
    - almost 50% missing diagnoses in Hispanic and African-American individuals

Clinical features of leukodystrophies

- Onset can range from prenatal to adulthood
- Symptoms
  - Infant/toddler onset
    - developmental delay
    - regression of skills
    - seizures
  - Juvenile/adult onset
    - loss of coordination
    - loss of vision or intellectual skills
    - Psychiatric disturbances
- *Rapid diagnosis is critical* because effective treatment is only possible in a narrow time window

What is the problem?

- Up until 10-15 years ago, only a few leukodystrophies were known, and these have their own codes in ICD-10-CM (ALD, MLD, Krabbe)
- **Now, more than 400 different distinct genetic leukodystrophies are known**
- There are now specific treatments for 4 different leukodystrophies (MLD, ALD, Krabbe, Canavan)
- There are clinical trials in process for another 30+ different leukodystrophies (VWM, AGS, …)
- Research, clinical trials, and clinical care are constrained because of the lack of specific codes

Problems with not having specific ICD-10-CM codes

- Difficult to determine prevalence of specific disorders
- Don’t have a structured way of representing specific leukodystrophies for research purposes
- Unable to track disease progression, compare care at different centers, etc.
- Unable to do clinical trial readiness
- Clinically, patients are incorrectly assigned codes

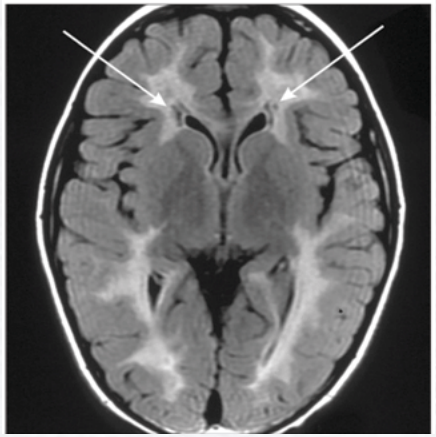
Current ICD-10-CM Codes for Leukodystrophies

- Only 6 Leukodystrophies have their own specific ICD-10-CM code
  - The creation of the specific existing codes has empowered clinical trials, newborn screening, etc.
- <u>Most others (400+) are grouped into a single code</u>

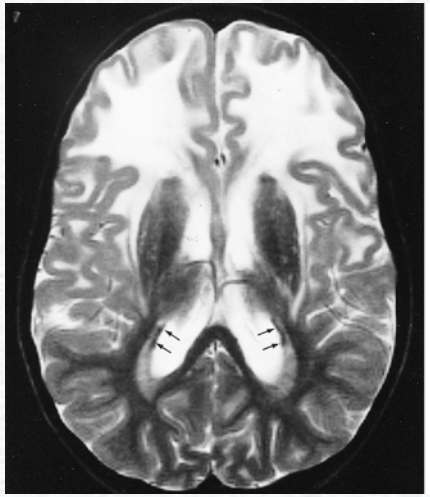
Proposal

- Create ICD-10-CM codes for those 33 leukodystrophies (and 46 total codes), including:
  - more common leukodystrophies
  - leukodystrophies in clinical trials or clinical trial readiness

Examples?



- Leukodystrophy with Vanishing White Matter
  - caused by mutation in *EIF2B 1-5*
  - progressive, fatal disease course, marked by episodic deterioration and seizures
  - often mis-classified as Metachromatic Leukodystrophy or Multiple Sclerosis
  - Clinical trial underway currently, 2 more drugs for clinical trials in Q4 2022



- Alexander disease
  - slowly progressive disease, striking all ages from infants to adults
  - “Dementia”-like disease progression
  - caused by mutations in *GFAP* gene
  - Clinical trial with an anti-sense oligonucleotide therapy underway

- Aicardi—Goutieres Syndrome
  - often misdiagnosed as a congenital infection
  - brain and other systems affected (skin, joints, heart)
  - caused by mutations in genes *TREX1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1,* or *ADAR*
  - treatment with baricitinib proven effective (Vanderver et al, 2020, NEJM)

in
n’s Hospital
HEALTH
UNIVERSITY OF UTAH

Source of Proposal

- GLIA-CTN and collaborators
  - Global Leukodystrophy Initiative Clinical Trials Network
    - includes (all of the) specialists from across the U.S.
      - MGH, Stanford, CHOP, Johns Hopkins, Emory, Utah…
  - Partners: family and patient organizations
    - United Leukodystrophy Foundation
    - Hunter's Hope

GLOBAL LEUKODYSTROPHY INITIATIVE

HUNTER'S HOPE

united LEUKODYSTROPHY FOUNDATION

Clinical examples

1. An 8 year old African-American boy is admitted to the hospital with new onset weakness and white matter abnormalities
   1. there is no code for Aicardi-Goutieres Syndrome, so he is diagnosed with “Multiple Sclerosis”, and started incorrectly on a medicine
2. A 1 year-old Hispanic toddler has a leukodystrophy
   1. there is no code for Pelizaeus-Merzbacher disease, so he is given the generic “Sphingolipidosis” code
   2. A year later, a clinical trial opens for PMD, but a review of the hospital charts does not identify him, and his family is not informed of the trial
3. A 10 year old Caucasian girl is found to have elevated very long chain fatty acids and a leukodystrophy
   1. There is no code for Peroxisomal D-bifunctional enzyme deficiency
   2. She is incorrectly diagnosed with Adrenoleukodystrophy, even though this disease does not affect girls under the age of 30

Conclusions

- Specific ICD-10-CM codes for leukodystrophies are needed
- Now is the time
  - Direct impact on clinical care; patients awaiting treatments (AGS); clinical trials (VWM); and clinical trial readiness (PMD)…
  - These diseases have hundreds of millions of dollars of impact on patients, families, and the healthcare system
    - source, Ghabash et al., 2021, 2022; Richards et al., 2015; Bonkowsky et al., 2010

Capitol Reef National Park, Utah

HEALTH
UNIVERSITY OF UTAH