ICD-10-CM Codes for Leukodystrophies

Global Leukodystrophy Initiative (GLIA)

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RARE DISEASES CLINICAL RESEARCH NETWORK

GLOBAL LEUKODYSTROPHY INITIATIVE

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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

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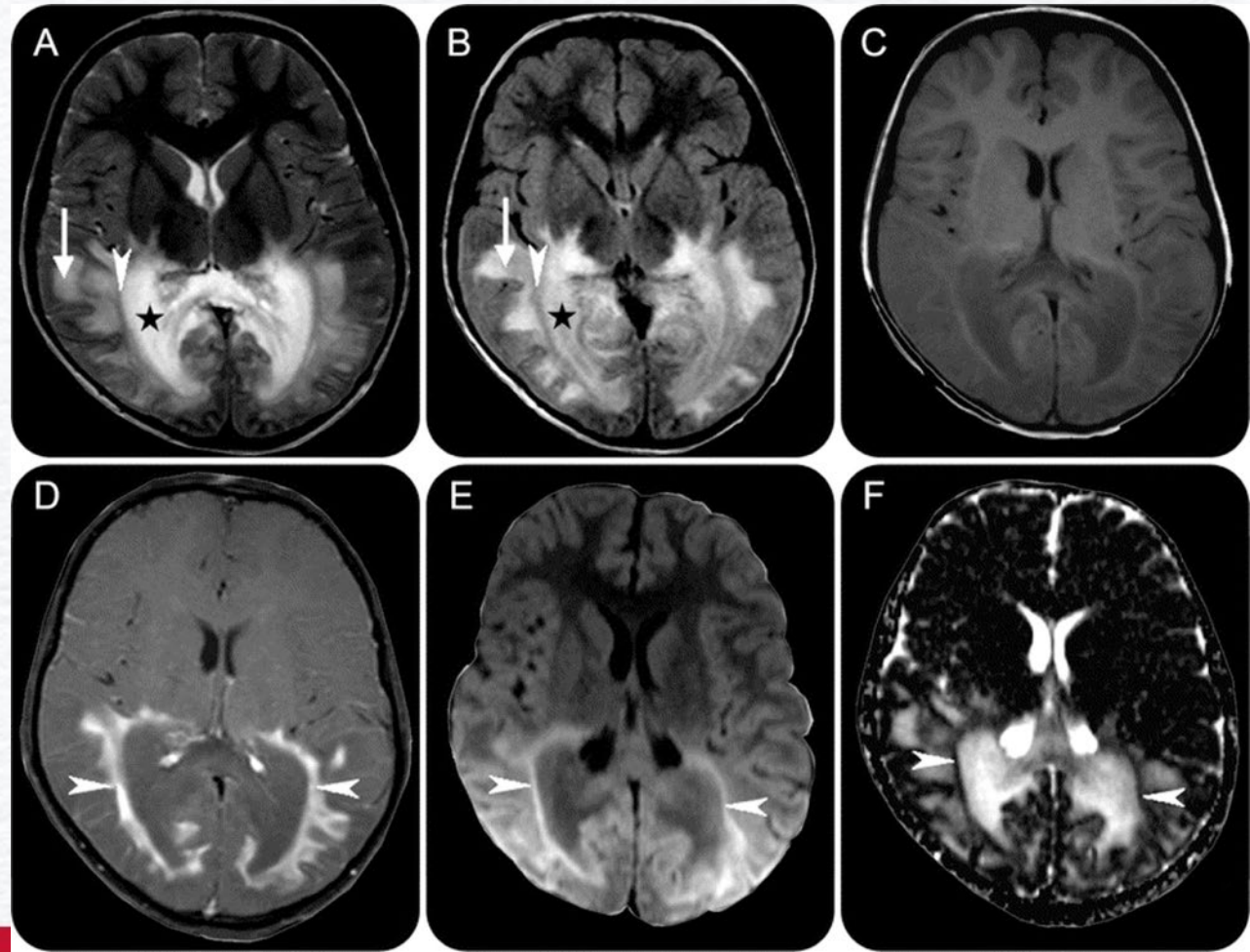
Leukodystrophies

- Leukodystrophies are a diverse group of diseases
- >400 known different genes
  - Unique clinical feature
  - Distinct treatments
  - New cures
- Death in 30% by age 8



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Leukodystrophy Epidemiology

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

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
  - Progression to coma and death
- *Rapid diagnosis is critical* because effective treatment is only possible in a narrow time window

Current Status

- 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, Zellweger)
- Now, more than 400 unique leukodystrophies are known
- There are now specific treatments for 5 different leukodystrophies (MLD, ALD, Krabbe, Canavan, AGS)
- There are clinical trials in process for another 30+ different leukodystrophies (VWM, Alexander disease, …)

Current Coding Classification Challenges

- Inability to track disease progression, compare care at different centers, etc.
- Participation in clinical trials is limited
- Difficult to determine prevalence of specific disorders
- Lack of structured way to represent specific leukodystrophies for research purposes

Current ICD-10-CM Codes for Leukodystrophies

- Only 4 Leukodystrophies have their own specific ICD-10-CM code
  - The existing codes has empowered treatments, clinical trials, newborn screening, etc.
- Most others (400+) are grouped into a single code

Objective of Proposal

- Create ICD-10-CM codes for leukodystrophies:
  - Most common (e.g. VWM)
  - With treatment (e.g. AGS)
  - In clinical trials (e.g. Alexander disease)

- **Revised proposal based on March 2022 feedback**
  - Reduced total number of ICD codes proposed
  - Solicited additional expert guidance (AAP)
  - Further (correctly) organized codes appropriately

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

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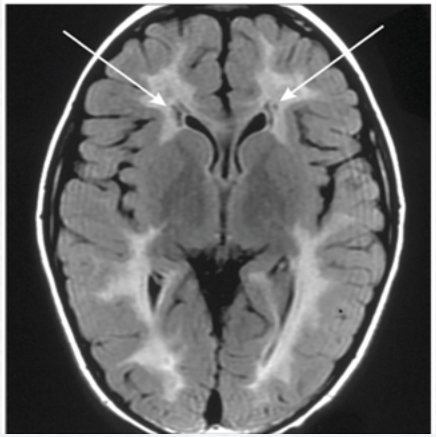
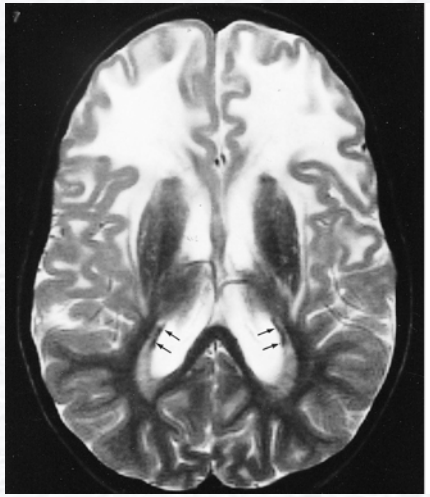
HUNTER'S HOPE

united LEUKODYSTROPHY FOUNDATION

Examples of Specific Leukodystrophies



- 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 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)

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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 the generic “Leukodystrophy” code, and is not started correctly on baricitinib
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 a demyelinating leukodystrophy
   1. There is no code for Vanishing White Matter disease
   2. She is incorrectly diagnosed with multiple sclerosis and placed on an immunosuppressant medicine

Conclusions

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

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