Neurogenetics in Pediatric Neurologic Disorders

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Why Neurogenetics Matters

- Genetic factors underlie many pediatric neurologic disorders
- Early diagnosis can improve outcomes
- Guides treatment and prognosis

Basic Concepts in Neurogenetics

- Genes, mutations, inheritance patterns
- Genetic heterogeneity: one phenotype, many genes
- Common testing methods: karyotype, CMA, WES, WGS

When to Suspect a Genetic Cause

- Global developmental delay or regression
- Dysmorphic features or congenital anomalies
- Family history of neurologic or genetic disease

Common Genetic Neurologic Disorders

- Epileptic syndromes (e.g., SCN1A, KCNQ2 mutations)
- Neurodevelopmental disorders (e.g., Rett, Fragile X)
- Neuromuscular diseases (e.g., DMD, SMA)
- Neurocutaneous syndromes (e.g., TSC, NF1)

Genetic Epilepsies: Examples

- Dravet Syndrome (SCN1A)
- Benign familial neonatal seizures (KCNQ2)
- Lissencephaly (PAFAH1B1, TUBA1A)

Neurodevelopmental Disorders

Autism spectrum disorder: monogenic in ~10-20%

Intellectual disability: chromosomal and single gene causes

Many have overlapping features and etiologies

Neurocutaneous Syndromes

- Tuberous sclerosis complex (TSC1, TSC2)
- Neurofibromatosis type 1 (NF1 gene)
- Clinical diagnosis supported by genetics

Approach to Genetic Testing

First-line: CMA for global delay, dysmorphism

WES/WGS: for undiagnosed complex cases

Consider targeted gene panels for epilepsy or neuromuscular concerns

Genetic Counseling in Practice

- Important before and after testing
- Interpretation of results: pathogenic vs VUS
- Communicating risk and recurrence

Case 1: Genetic Epilepsy

2-year-old with febrile and afebrile seizures

Normal MRI, developmental slowing

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WES → SCN1A pathogenic variant → Dravet Syndrome

Case 2: Regression + Hypotonia

6-month-old with milestone loss

Elevated lactate, basal ganglia lesions on MRI

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Mitochondrial panel: SURF1 mutation → Leigh syndrome

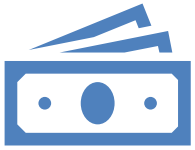
Current Advances in Neurogenetics

NEXT-GEN SEQUENCING (NGS), WGS BECOMING MORE ACCESSIBLE

GENE THERAPY (E.G., SMA)

MULTIDISCIPLINARY GENOMIC CLINICS

Ethical & Practical Considerations



Cost and insurance

Incidental findings

Limitations of testing and interpretation

Take-Home Messages

Genetics is key in pediatric neurology

Recognize when to refer or test

Early diagnosis can guide therapy and counseling

Questions & Discussion

- Thank you for your attention.