A Dynamic Genetic Testing Approach for Neurological Disorders in Pediatric Neurogenetic Case-Management Councils

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INTRODUCTON

- Genetic diagnosis is essential for;
  - Management of neurogenetic diseases
  - Determining treatment options as well as precision therapy
- However there certain important clinical challenges ;
  - Which genetic test should be chosen to reach the earliest and most accurate diagnosis?
  - Correct interpretation of appropriate tests--enhances early definitive diagnosis
  - Multidisciplinary collaborative approach ensures more accurate interpretation of findings and results

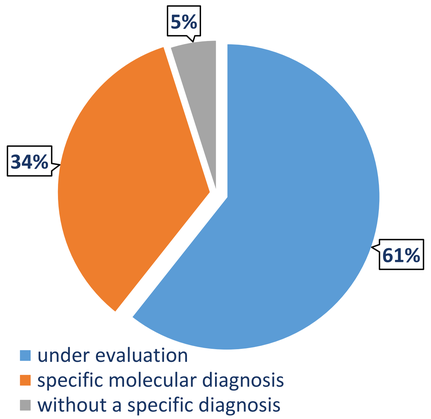

Figure 1: The diagnostic yield of genetic tests with a dynamic approachment in neuro-genetics councils

OBJECTIVE

- To evaluate the diagnostic yield of genetic tests with a dynamic approachment in a neuro-genetics council

MATERIAL & METHOD

- A case series including 61 patients with clinical diagnosis of a neurological disorder
- The Pediatric Neurogenetic Case-Management Councils at Ege University Children's Hospital
- Which genetic test should be used to reveal a genetic molecular diagnosis; karyotyping, microarray, gene panels, clinical exome, and whole exome sequencing

RESULTS

- Twenty- one patients **(34.4%)** had a genetic molecular diagnosis using dynamic testing approach **(Table 1)**
  - 17 -- with NGS
  - 3 -- with CMA (microarray)
  - 1 -- with MLPA
- Thirty-seven patients **(60.6%)** -- still under evaluation for additional genetic testing or reanalysis of sequencing data
- 3 patients **(5%)** – no specific molecular diagnosis with studied genetic tests

Table 1: Genetic landscape of the cohort

Patient no	Clinical Diagnosis	Gene	Mutation
P-15	Epilepsy	**SCN1A**	c. 206C>T
P-24	Epilepsy	**SCN1A**	c.5740C>T
P-40	Epilepsy	**SCN1A**	c.827A>C
P-61	Epilepsy	**SCN1A**	c.4903T>G
P-57	Epilepsy	PRUNE1	c.[874_875insA ; 874_875insA]
P-43	Epilepsy	NARS2	c.[418C>T ; c.1253G>A]
P-6	Epilepsy	PIGN	c.[1034C>T; c.2575delA]
P-4	Epilepsy	IQSEC2	c.1591C>T
P-19	Epilepsy	DPAGT	c.[341C>G ; 341C>G]
P-31	Muscular dystrophy	COL6A2	c.[1856_1858delTCA ; 1856_1858delTCA]
P-25	Muscular dystrophy	DMD	c.186+1G>T
P-27	Congenital myasthenia	CHRNA1	c.[1072C>T ; 1072C>T]
P-5	Spinocerebellar ataxia	SACS	c.[2686-2690del ; 2686-2690del]
P-57	Developmental delay, Polyneuropath	PIEZ02	c.[744delT ; 744delT]
P-3	Developmental delay, Polyneuropath	PRPS1	c.25G>T
P-39	Ophtalmoplegi	MGME1	c.[563delC ; 563delC]
P-1	Hypotonia, kyphosis, ventriculomega		46,XY,t(13;12)(p21q13);arr.chr12q15q21.33 (70,478,077-92,171,460)*1
P-10	Epilepsy, mental retardation, autism		18q21.2q23 (51,544,371-78,014,123)*1
P-23	Epilepsy, global developmental delay, hypotonia		15q11.2q13.2 (22,770,421-30,366,247)*1
P-59	Muscular dystrophy	DMD	Exon 45-48 del

CONCLUSIONS

- The dynamic genetic testing approach for neurological disorders provided;
  - earlier determination of the treatable causes
  - more specific molecular diagnosis, leading to precision medicine

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