Profile of infants with neonatal-onset epilepsy (genetic and metabolic causes): single center study

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OBJECTIVE

To determine the metabolic and genetic causes among infants presenting with neonatal-onset epilepsy in single center study over a period of 22 years (2000-2023).

METHODS

We retrospectively reviewed the medical records of 55 patients admitted to KFMMC, Dhahran, Saudi Arabia with different types of neonatal epilepsy . Metabolic screening for inborn error of metabolism and neurotransmitter disorders was performed. (Tandem MS spectrometry, Serum Amino acid profiles, Ammonia, Lactate, Acylcarnitine profile, CSF neurotransmitters (glycine, glucose, ect).

Beside serial EEGs, in all patients MRI brain was performed (some of them MRI spectroscopy added).

The genetic testing is done at (Bioscientia, Germany). The types of genetic testing requested are; either karyotype, FISH, CGH array, NGS gene panel, or whole exome sequencing (WES). WES interpenetrated as pathogenic, likely pathogenic or VUS

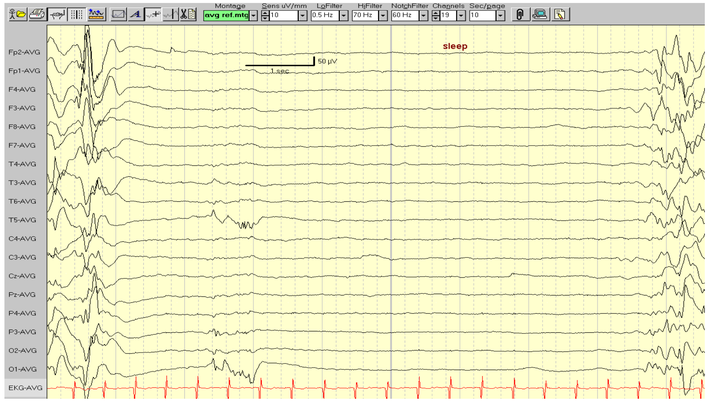

Figure 1: EEG in infant with STXBPI encephalopathy showing burst-suppression pattern (Ohtahara syndrome)

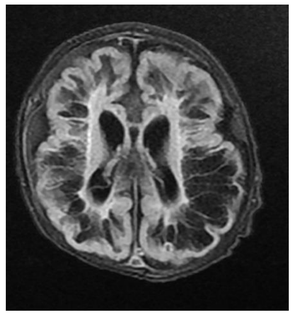

Figure 2: T1 weighted MRI with cystic encephalomalacia in an infant with Molybdenum cofactor deficiency(MOCS1 gene)

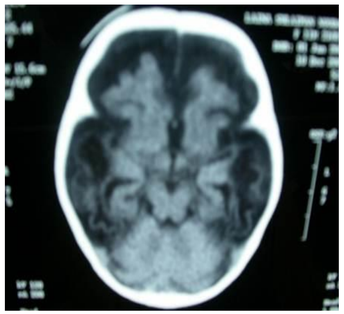

Figure 3: CT brain showing severe brain atrophy in neonate with primary lactic acidosis (Cytochrome C oxidase deficiency)

RERULTS

55 neonates found to have genetic and metabolic causes of their epilepsy.

Genetic: KCNQ2 (n=7), SLC13A59 (n=3), STXBP1, SCN2A, DMXL1, TSC2, TSC1, TCF4, FOXP1, GABBR2, KANSL1, EHMT1. ***chromosomal*** (Ip36 deletion, Wolf-Hirschhorn syndrome, partial trisomy18, mosaic Patau).***Metabolic:*** SOUX, MOCS1(2), PEX1 Zellweger (3), PNPO(2), ALDH7A1(2) ASNS gene

Non-kenotic hyperglycinemia (3), Urea cycle defects(2), Organic acidemias (N=7), MSUD (2), ***mitochondrial*** (TIMM50,HTRA2, COQ8A (2), Cytochrome C oxidase deficiency)

CONCLUSIONS

Due to high prevalence of consanguineous marriage in Arabia epilepsy due to genetic and metabolic diseases are common and now possible to be diagnosed early due to availability of genetic testing. So early management with antiepileptics, special diets, cofactor supplementation can cure or alter the prognosis of these disorders. Likewise early genetic counseling and PGD can be offered to families with incurable diseases.