**High-dose Nicotinamide rescues from ‘Early-onset, progressive encephalopathy with brain edema and/or leukoencephalopathy-1 (PEBEL-1)’: All hope is not lost!**

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***Objective***: Early-onset progressive encephalopathy with brain edema and/or leukoencephalopathy-1(PEBEL-1) is lethal condition, caused by mutation in NAD(P)HX Epimerase (NAXE) gene. There are 20 reported cases and only one-fourth survivors.

We report two cases who improved and developing well following high dose nicotinamide therapy.

***Methods***: Case series

***Results***: Case 1: 16 months-old girl with mild developmental delay presented with acute neuroregression, seizures and rapidly progressive encephalopathy, following febrile illness, necessitating mechanical ventilation. She had GCS 3/15, bilateral external ophthalmoplegia, absent breathing, autonomic instability and bilateral pyramidal dysfunction. Her MRI brain and metabolic work-up were normal. There were two sibling deaths in infancy, with developmental delay, acute encephalopathy, hypoventilation and neuroregression. The index child’s whole exome sequencing (WES) revealed homozygous pathogenic *NAXE* mutation. Following Nicotinamide supplementation (200 mg/day), she showed remarkable improvement. At 4 years, she is running, indicating daily needs, follows gestures, but has profound sensori-neural hearing loss (SNHL), short stature and epilepsy.

Case 2: A 14 months-old girl presented with acute-onset SNHL following febrile illness and walking difficulty. Her MRI and metabolic work-up were unremarkable. Her elder sister had neuroregression and acute-onset esotropia and died at 27 months age, with rapidly progressive encephalopathy and respiratory failure. WES of index child revealed homozygous pathogenic mutation in NAXE gene. After starting Nicotinamide (200 mg/day), her motor functions improved dramatically, but has severe SNHL.

***Conclusion***: PEBEL-1 due to NAXE mutations is rare and often fatal condition. Early diagnosis and timely initiation of high dose nicotinamide can facilitate good recovery, and prevents neurological crises.