A Rare Mitochondrial disease; Naxe Gene Mutation

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Introduction

Infantile-onset mitochondrial diseases affecting the respiratory chain reactions can cause severe symptoms including neurological manifestations. NAD(P)X epimerase is an enzyme required in the maintenance of cellular metabolism and homeostasis: it catalyzes a crucial step in the prevention of toxic metabolites accumulating during cellular metabolism.

NAD(P)X epimerase is encoded by *NAXE* whose mutations are inherited in autosomal recessive manner and are mainly characterized by severe progressive leukoencephalopathy and/or pellegra like skin findings.

Case report

18 months girl with consanguineous parents and developmental delay admitted to the hospital with inability to walk, strabismus, aphasia and change of consciousness which was started 2 days ago. She had an upper respiratory tract infection 1 week ago. At 6 months of age she had seizure like symptoms, all investigations (metabolic/electrophysiologic/neuroimaging) were normal, but valproic acid(VPA) was started 3 months ago. On the physical examination; she was unconscious, but reacts to pain and hypotonic. She had facial weakness, and neck stiffness. She was intubated. All laboratory findings were normal except CSF lactate which was 31,3 mg/dL and CSF pressure was 40 cmH2O. There were cerebellitis, striatal edema and longituidinal myelitis in the neuroimaging. Intravenous ımmunglobulin, pulse steroid and antibiotics were started. We considered mitochondrial disease as differential diagnosis, so VPA was stopped, mitochondrial supplementations(vitamins) were started. Because of the radiological progression plasma exchange was started. Unfortunately, she was unresponsive to the treatment. On the 19th day she had erythematous bullous skin lesions(Figure1), local/systemic steroid treatment was not succesful. A new homozygous mutation in the NAXE gene was identified by whole exome sequencing. Now, she is tetraparetic, has tracheostomy tube and in persistent vegetative stage.

Discussion

A new mutation of Naxe gene was detected in this case which was added to the existing knowledge on NAXE and its role in mitochondrial function.

Kremer et al. revealed *NAXE* gene mutations with whole exome sequencing in four children with (sub-) acute-onset ataxia, cerebellar edema, spinal myelopathy and skin lesions. All affected patients had elevated Lactate levels in cerebrospinal fluid. Disease onset was during the second year of life and clinical signs as well as episodes of deterioration were triggered by febrile infections. Disease course was rapidly progressive, leading to coma, global brain atrophy, and finally to death in all affected individuals. They are similar to our case in terms of clinical, radiological and CSF findings, except the age of the onset.

Supplementation with nicotinic acid has been suggested in the literature, considering impaired NAD metabolism, but our patient didn't benefit from supplementation therapy including all mitochondrial vitamins.

Conclusion

NAXE gene mutation-related encephalopathy is a rare condition, it should be considered as a differential diagnosis of early onset progressive encephalopathy and longuitidinal myelitis after a febrile infection.

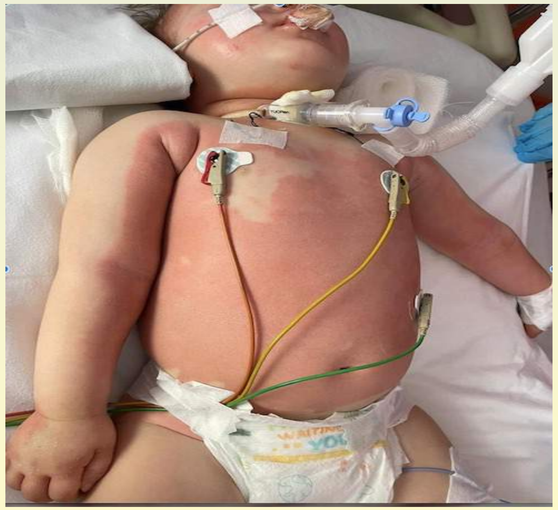

Figure 1: Skin lesions of the patient with Naxe Gene mutation

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