Case 298

2. Leigh syndrome

【Progress】

She is during observation under our hospital and university hospital with specific experts of metabolic diseases.

【Discussion】

Mitochondria contained in a segment of a single cell work to create energy of ATP from glucose, protein and lipid. Apart from nuclear DNA, mitochondria own circle DNA which produces mRNA, tRNA and protein for energy production (Because mitochondria have their own DNA, mitochondria are thought to have been incorporated in a cell in a process of cell evolution) (1, 2). tRNA interprets information from mRNA every three nucleotide codons: as an example, tRNA carries Leucin, one of amino acids to create protein, under codons of AAU responded from UUA of mRNA. tRNA modified by Taurin can also carry Leucin under codons of AAU responded from mRNA with nucleotides of UUG. In a short, normal pattern of taurine-modified tRNA can carry Leucin under codons of AAU from both codons of UUA and UUG of mRNA. Non-Taurin-modified tRNA can carry Leucin only under codons of AAU responded from UUA of mRNA but not under codons of AAU responded from UUG. This abnormality is called A3243G variation (3, 4). Then, a cell with mitochondria of A3243G abnormality has some disorder to create enzyme for producing ATP.

More or less, A3243G abnormality exists in a human. However, the rate of abnormality increases, abnormal expression emerges. When its abnormality incidences are during 60-75%, adult type MELAS (18 age or more) appears, when during 75-92%, infantile MELAS (less than 18 age) appears, and when > 92%, Leigh disease appears (3-7).

Leigh disease is a disease with poor prognosis. Most patients with Leigh disease pass away by 12 years (7). When the lesion appears in brain stem, fatal respiratory failure occurs. Its initiation usually occurs in less than 2 years after birth but can initiate at late age of around 3 or 4 years. At first, abnormal findings appear in basal ganglion most on MRI, followed by white matter and finally on brain stem of respiratory center.

MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, stroke-like episodes) is categorized into two groups: infantile type (onset peak 16, life span = onset + mean 6 years), adult type (onset peak 32, life span = onset + mean 12 years) (4-6). Characteristic symptoms of infantile type are vomiting, convulsion, hemiparesis and hemianopsia. Those of adult type are diabetes mellitus and auditory disturbance later followed by visual disturbance (4). Image findings of CT and MRI are that infarction patterns do not meet vascular territories in young adults. The ischemic lesions are sometimes corresponded to symptoms: optical pathway damages to visual disturbances, auditory pathway damages to auditory disturbances (5, 6). It is borne in mind that in case of non-vascular territory infarction in young adults on CT or MRI, MELAS and sinus or venous thrombosis should be listed in differential diagnosis.

When symmetric damages of putamen, caudate nucleus and thalamus were found on MRI or CT, several diseases are listed: Creutzfeldt-Jacob disease, hypoglycemic encephalopathy, autoimmune encephalitis and subacute necrotizing encephalopathy called Leigh encephalopathy. Of these, Leigh encephalopathy appears in children while Creutzfeldt-Jacob disease, hypoglycemic encephalopathy and autoimmune encephalitis appear in adult.

In our case, she experienced convulsion and vomiting twice by time of age, four. Brain CT showed the lesion with high attenuation of putamen, caudate nucleus and white matter of frontal lobe and MRI with T1WI, T2WI and Diffusion WI did show no abnormality, indicative of small hemorrhage. Then, she was in the process of under observation, suggestive of Leigh syndrome or child type MELAS.

【Summary】

We presented a 4-year-old girl with vomiting and convulsion. Laboratory test revealed high values of lactic acid. Brain CT showed high attenuation at white matter of frontal lobe, caudate nucleus and putamen. It indicated possible Leigh encephalopathy or child type MELAS. It is borne in mind that both Leigh disease and MELAS are mitochondria disorder disease which cannot create proper enzyme to produce ATP. Leigh disease onset below age of 3 and pass away until age of 12, while infantile MELAS onset at peak of age of 16 and pass away 6 years later and adult MELAS onset at peak of 32 and pass away 12 years later. Leigh encephalopathy initiates from the lesion with basal ganglion or white matter and ends with brain stem, indicative of fatal destiny. In MELAS, CT and MRI show infarction patterns do not meet vascular territories in young adults, corresponded to symptoms of hemiparesis and visual center pathway. When symmetric damages of putamen, caudate nucleus and thalamus were found on MRI or CT, several diseases are listed: Creutzfeldt-Jacob disease, hypoglycemic encephalopathy, autoimmune encephalitis and subacute necrotizing encephalopathy called Leigh encephalopathy. Of these, Leigh encephalopathy appears in children while Creutzfeldt-Jacob disease, hypoglycemic encephalopathy and autoimmune encephalitis appear in adult.

【References】

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