PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA (PEO): PRESENTATION OF A MITOCHONDRIAL MYOPATHY ACCOMPANIED BY ELECTRON MICROSCOPE

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Abstract

Kearns-Sayre syndrome is a mitochondrial disease, presenting findings before the age of 20 and characterized by chronic progressive external ophthalmoplegia and pigmentary retinal degeneration. It affects many organs, resulting in a very wide spectrum of complications.

In this work, a 24-year-old female, whose complaints first started at the age of 12, showing progressing external ophthalmoplegia and diagnosed with Kearns-Sayre disease following mitochondrial changes in muscle electron microscope investigation was presented. Ways of diagnosing in mitochondrial diseases, especially those in children were tried to be evaluated.


Keywords: Kearns-Sayre syndrome, mitochondrial diseases, progressive external ophthalmoplegia, electron microscope.

Introduction

Mitochondrial disease include a group of systemic diseases that include structural or functional anomalies and show clinical and biochemical heterogeneity. Kearns-Sayre syndrome (KSS) is a mitochondrial disease resulting from mitochondrial DNA deletion1,2. This aspect was first mentioned in 1962 by Luft et al. In this disease, mitochondries produce energy without control due to failure in oxidation phosphorylation. However, this energy is not stored as ATP. Resulting energy is recorded as heat3.

In 1958, Kearns and Sayre described a syndrome with external ophthalmoplegia, pigmentary degeneration of the retina and complete heart block. Progressive external ophthalmoplegia (PEO) clinically follows a benign route. Ophthalmoplegia without diplopia is characterized by ptosis and weakness of extremities in different degrees. They showed abnormal mitochondries by using Gomori’s trichrome stain in muscle biopsies and after this, most of ocular myopathy cases were accepted as mitochondrial myopathies4.

Mitochondrial dysfunction and lack of energy supply to tissues because of inability to make oxidative phosphorylation play roles in the pathogenesis of the disease. Basically, despite presence of this lack of energy in all tissues, tissues with higher energy requirement like central nervous system, retina, heart muscle and skeletal muscles are affected more. As a result of this different level of effect, clinical findings are very diverse5.

We found it appropriate to present the case with external ophthalmoplegia starting before the age of 20 and showing progression, whose myopathy was identified by mitochondrial changes shown in the muscle electron microscope investigation, in order to discuss the separation from other possible diagnosis criteria.
Case Report

Complaints of HA, 24-year-old female patient, started at the age of 12, describing problems in far sight and reading the blackboard. She did not describe double vision in the inquiry. Lowering of the right eyelid was told to her by a doctor making medical examination in the school. This lowering did not change between morning and evening. Later, left eyelid also started to lower. In 2-3 years, dysfunction started in eyelid movements and total ophthalmoplegia developed. Diplopia was not identified. In 1996, she was diagnosed with Myastenia Gravis and started to receive mestinon treatment. She did not show any benefits from this treatment. In 1997, decremental response was achieved in repetitive stimulation. She underwent a thymectomy operation, but did not show any benefits. She did not have family history.

Neurological examination displayed limitation of horizontal and vertical eye movements in both eyes (Figures 1, 2, 3, 4). She had bilateral ptosis and complaint of pain during vertical and horizontal movements of the eyes. Light reflexes were normal. Pupils were isochoric. Eye bottom examination was normal. All extremities showed 4/5 muscle power. Brain stem and deep tendon reflexes were normal. There were no pathologic reflexes.

Cerebellar system examination was normal. Cranial MR and thyroid function tests were normal. ANA, Asthma and cardiolipin antibodies were within normal limits. Eye bottom and light reflex was normal. CK, ECG, USG were normal. ECO showed left ventricle diastolic dysfunction. Anti HBs was positive. ASO and CRP were normal.

Sedimentation (S): 22 – 31 mmHg/s. ENMG motor and sensory transmission speed measurements were normal. In the needle EMG, short time low amp. Polyphasic MUP’s in proximal muscles were visualized. Repetitive stimulation was normal. Muscle biopsy material from deltoid muscle was investigated with electron microscope.

Enlargement of mitochondries and common cristolisis findings were shown. Z bands were noticed to be irregular, or even to disappear completely in some places. Loss of myofilaments were noticeable in places were Z bands disappeared (Figures 5, 6, 7, 8).

Figure 1.2.3.4. Neurological examination displayed limitation of horizontal and vertical eye movements in both eyes.
Figure 5. Common crystalisis in mitochondrions. It is seen that crystals of some are deleted completely and these have transformed into giant mitochondrions, having vacuolar vision. Obvious deletion in Z bands and loss myofilaments are also visible (Uranyl acetate -Lead citrate, X 12000).

Figure 6. Mitochondrions are seen to have grown and common crystalisis visible. It is noticeable that Z bands are irregular in places, completely deleted in some others. Myofilaments obviously deleted where Z bands are completely deleted (Uranyl acetate -Lead citrate, X 12000).

Discussion

Kearns-Sayre syndrome, which is seen in early adolescence, was first identified in 1958 \(^4\). This disease, resulting from sporadic mitochondrial DNA deletion, is not hereditary\(^1\). Analyses of muscle tissues have shown mitochondrial DNA deletion in approximately 80% of cases\(^2\).

Kearns-Sayre syndrome is characterized by chronic progressive external ophthalmoplegia, pigmentary retina and heart transmission failures. Progressive external ophthalmoplegia is a syndrome defined by clinical attributes. This syndrome is generally defined by progressive ptosis, external ophthalmoplegia, bilateral strain, strain of muscles innervated by more than one nerve, protection of the pupil, slow progression, lack of remission, presence of cardiac strain and lack of findings of a specific disease.
Mitochondrial diseases that include a heterogen group disease often cause diagnosis confusion for the clinician. Diagnosis of mitochondrial diseases can be made by detection of anomalies in muscle biopsy and number and structure of mitochondries. In order to make the diagnosis definite, staining techniques like Gomori’s trichrome, cytochrome oxidase, succinic dehydrogenase and NADH should be applied to skeletal muscle biopsy sections. The importance of muscle histology is that it easily differentiates the disease from other diagnoses. Lipid droplets can be seen among myofibrils. These droplets are specific to Kearne-Sayre and Peo and are not seen in Melas and Merrf.

Mitochondrions are the energy stations of the cell and mitochondries constantly divide and multiply in order to supply energy to the cell in the presence of defective mitochodries, especially due to mutation. However, this multiplication does not have any benefit, apart from formation of new defective mitochondrias.

As a result, as clinical findings related to inability to supply sufficient energy to the cell develop, defective mitochondrias accumulate in groups. This accumulation is more intense in subsarcolemmal area and is easily visible in TEM investigation.

Due to aging and oxidant stresses, non-functional defective mitochondrias might accumulate. Therefore, for diagnosis of mitochondrial diseases, apart from TEM, lack of COX activity in ragged blue fibers in combined enzyme staining and SDH staining enables the definite diagnosis of mitochondrial myopathies.

Conclusions

Mitochondrial diseases that include a heterogen group disease often cause diagnosis confusion for the clinician. Mitochondrial changes shown in the muscle electron microscope investigation.

Declaration of Interest

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References