Kearns-Sayre Syndrome: A rare neuromuscular cause of ocular motility disorder- A Case Report

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Introduction
Muscular disorders of mitochondrial etiology are not so uncommon, but less well recognized. Among the mitochondrial cytopathies of ocular significance, the most commonly encountered entities are the isolated Chronic Progressive External Ophthalmoplegia (CPEO) and the Kearns-Sayre syndrome (KSS), which are termed ‘ophthalmoplegia plus’ because of the progressive nature of ophthalmoplegia. Kearns-Sayre syndrome, though primarily a myopathy, is actually a CNS syndrome with frequent neuromuscular findings of peripheral neuropathy, ataxia, spasticity, deafness, retinopathy, optic atrophy and dementia. The condition is characterized by its onset prior to age 15, presence of chronic progressive external ophthalmoplegia, pigmentary retinopathy and one among the following: - Heart Block, Cerebellar defects or a CSF protein of over 100 mg/dL. Here we present a case of an incomplete form of KSS, which may evolve into a complete form.

Case Report
A 12 year old boy presented with progressive drooping of his upper eyelids. On detailed probing into the history, there was no diurnal variation for the ptosis and he had associated night blindness also. He was the second child of a non-consanguinous marriage, whose birth, growth and development had been normal. His parents and siblings were healthy.

On our preliminary examination, there was ptosis, with a levator function of 1 mm both eyes, external ophthalmoplegia affecting all movements of the eyes and a chin lift. There were no signs of vitamin A deficiency. The anterior segment examination was within normal limits including the pupils and the visual acuity was 6/6 both eyes. General examination revealed short stature and an accessory thumb in his left hand. He had normal intelligence and on detailed CNS examination, the muscle power, tone and reflexes were normal along with a normal skull and spine. The cardiovascular and gastrointestinal systems also appeared to be normal.

It was during the fundus evaluation that we suspected KSS since he had an unusual pigment motting of the retina, especially of the posterior pole, with absence of bone spicules. Disc and vessels appeared normal. Patient was sent to cardiology to rule out any cardiac conduction problems and to neuromedicine to pick up any additional neurological finding, if present.

The results were: The Complete Blood Count, S. Lactate & S. Pyruvate - Normal, The Blood sugar & Thyroid Function Tests - Normal, The ECG & Echocardiogram - Normal. The Pure Tone Audiogram showed no sensoryneural hearing loss and The MRI Brain & Orbit showed normal study. A Muscle Biopsy was not done.

But even with the investigation part as normal, with the clinical findings alone, we were strongly in favour of KSS since the child was as young as 12 years and the fact that the complete array of clinical signs are present only by about 20 years of age. And though the diagnosis was enthusiastically made, we could not do much in terms of treatment, except for the bilateral frontalis sling surgery which we did for his ptosis.

Discussion
Kearns-Sayre syndrome was recognized as a clinical entity in 1958 when Kearns & Sayre described the classic triad of Progressive External Ophthalmoplegia; atypical RP & complete heart block in one patient. It’s primarily a mitochondrial cytopathy of sporadic incidence, attributed to large scale deletions in mitochondrial DNA, leading to a disruption in the morphology and function of mitochondria. This results in defects in pyruvate utilization, oxidative phosphorylation and respiratory chain function. The mitochondrial myopathies are the most important cause for ‘progressive’ ophthalmoplegia; the others being Muscular dystrophies and vitamin E deficiency. A higher concentration of mitochondria in the extraocular muscles than in other skeletal muscles accounts for the predominance of ocular motility problems in this disease. There is an entity of Isolated CPEO apart from the KSS; with absence of systemic features. Identical skeletal muscle mitochondrial DNA deletions have been found in KSS and Isolated CPEO suggesting that they are the same disease; only difference being that in Isolated CPEO, deletion is found only in the muscle tissue.

Multiple organ systems are affected in KSS, predominantly the CNS, skeletal muscle & heart. It’s characterized by the obligatory triad of: onset before age 20; pigmentary retinopathy & PEO. In addition at least one of the following features are seen: cardiac conduction block, CSF protein>100 mg/dl, cerebellar ataxia.

The cardiac conduction defects and arrhythmia can occur at any time during the disease course. Endocrine disturbances which are associated include diabetes mellitus, hypothyroidism, hypoparathyroidism, growth retardation and short stature; and hypogonadism, all due to the
respective hormonal’s deficiencies.

Investigations may show elevated S. pyruvate and lactate levels as a result of increased anaerobic metabolism. Muscle Biopsy stained with Gomori trichome stain shows a dark red color of muscle fibres, (hence called ‘ragged red fibres’) due to the high ratios of mutated mitochondria containing inclusions.

The management aspect of this classic neuromuscular disorder is disappointing. Ubiquinone or CoE Q10 which is essential for the normal mitochondrial respiration may be tried. Though it may improve the cardiac function and exercise tolerance; it has no effect on ophthalmoplegia, ptosis or pigmentary retinopathy. Thiamine, Folic acid & L-carnitine have been tried to improve the metabolic failure. But a pacemaker insertion is important if a conduction deficit is present which will prevent the occurrence of sudden death. From the ophthalmologic side, the only management procedures are; a muscle surgery for strabismus and a sling surgery for ptosis.

**Conclusion**

Kearns-Sayre syndrome is only one among the rare systemic disorders whose predominant manifestations pertain to the eye. Many systemic syndromes may go unnoticed if a complete ocular evaluation and systemic work up are not done, particularly in the paediatric population. A detailed history is also as important as a systemic work up. When people present with PEO, it’s very important to do a dilated fundus examination and an associated heart block is to be ruled out along with elaborate laboratory investigations to support the diagnosis.

**References**
