

Chronic Progressive External Ophthalmoplegia

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Citation

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Abstract

Introduction: Kearns Sayre syndrome is a rare form of mitochondrial myopathy. We report a case of an 18 year old male who had chronic progressive external ophthalmoplegia diagnosed as Kearns – Sayre syndrome.

Case Report: An 18 year old male presented with gradually progressive drooping of both upper lids since three years, associated with limited movements of eyeball in all directions. Window defects were seen on fundus fluorescein angiography. Electromyography showed defibrillation and decreased amplitude in favor of myopathy. Audiometry showed evidence of bilateral sensorineural deafness at higher frequencies. Biopsy of orbicularis oculi showed muscle fibers of varying size, some of which were normal in size with evident cross striations while others were atrophied and degenerated and showed intense eosinophilia in Massons trihome stain suggesting the diagnosis of chronic progressive external ophthalmoplegia with Kearns- Sayre syndrome.

Conclusion: Kearns-Sayre Syndrome is a form of mitochondrial myopathy. Regular followup is required to detect if there is development of cardiac conduction defects. Ocular examination and cardiac screening of family members is recommended.

INTRODUCTION

Mitochondrial myopathies presenting as chronic progressive external ophthalmoplegia (CPEO) are Kearns-Sayre syndrome (KSS), isolated ocular form, oculofacial syndrome. Kearns-Sayre syndrome is a rare disorder. We report a case of an 18 year old male who had CPEO diagnosed as Kearns – Sayre syndrome.

CASE REPORT

An 18 year old male presented to us with chief complaints of gradually progressive drooping of both upper lids since three years associated with limited eye movements in both eyes (Figure 1).

Figure 1

Figure 1: Clinical Photograph of the patient showing bilateral severe Ptosis



There was no history of diplopia or pain. There was no history of remissions or fluctuations, fatigability, trauma. There was no history of change in speech, hearing loss. His patients were non-consanguineous. His built was normal to his age. On examination secondary sexual characters were well developed.

Examination of central nervous system and cardiovascular examination did not reveal any abnormality. On ocular examination visual acuity was 6/12 in the right eye 6/9 in the left eye. Lid crease was absent in both the eyes. Amount of ptosis was 4mm on both sides. Ocular movements were absent in all the gazes. Bell's and Marcus-Gunn phenomenon were absent. Pupillary reactions, both direct and consensual were present and brisk. Rest of the anterior and posterior segment examination was normal. Fundus examination did not reveal any retinal pigmentary abnormality. But on fundus fluorescein angiography window defects were seen. Perimetry was normal. All the systemic investigations including serum creatine, phosphokinase, liver function tests, lactate/pyruvic acid levels, serum calcium, sodium, potassium, random blood sugar, were unremarkable. Electrocardiography and echocardiography were normal. Electromyography showed defibrillation and decreased amplitude in favor of myopathy. Audiometry showed evidence of bilateral sensorineural deafness at higher frequencies. There was no enlargement of muscle or evidence of any mass lesion on CT orbit. MRI Head was normal. Biopsy of orbicularis oculi showed muscle fibers of varying size, some of which were normal in size with evident cross striations while others were atrophied and degenerated and showed intense eosinophilia in Masson's trichrome stain (Figure 2A and 2B).

Figure 2

Figure 2A: Section showing muscle fibers of varying size, with evident cross striations while others were atrophied and degenerated (H& E, 100X).

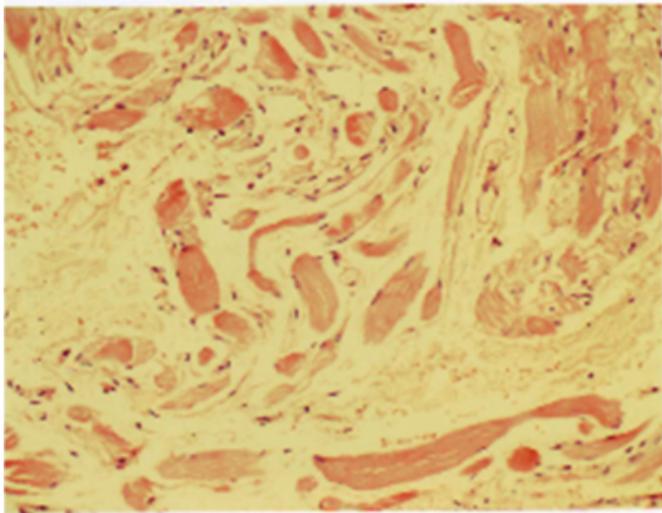
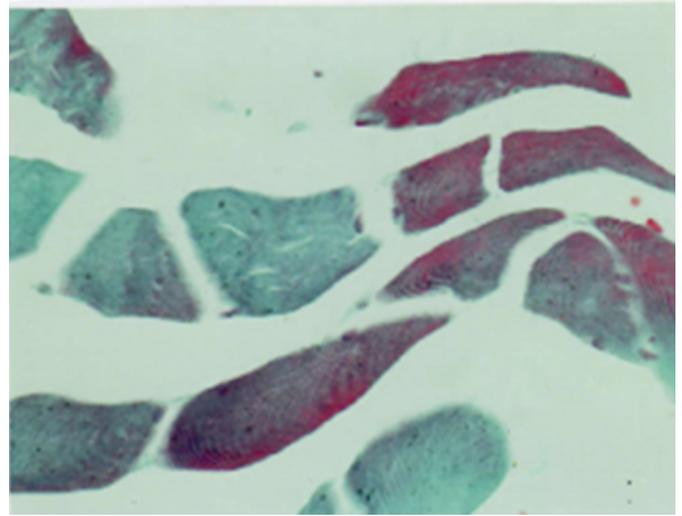


Figure 3

Figure 2B: Microscopic section of degenerated extraocular muscle showing intense eosinophilia in Masson's trichrome stain (200X)



With all these findings a diagnosis of chronic progressive external ophthalmoplegia was made. We started the patient on multivitamins. At six months follow-up there was no improvement in ocular movements.

DISCUSSION

Kearns-Sayre Syndrome is a form of mitochondrial myopathy. It is defined by triad of clinical findings: onset before age 20, CPEO, pigmentary retinopathy plus any one of following: complete heart block, CSF protein >1.0g/l, cerebellar ataxia¹. Some patients may not fulfill all the criteria for KSS. Our patient had age of onset < 20 years, external ophthalmoplegia and ptosis, retinal pigmentary changes on FFA. Kearns-Sayre syndrome is a rare disorder. It is a sporadic disease in which there is M/C deletion removes bp 4977 of mtDNA². Mutations are also reported³. At the onset of the disease no clinical, morphologic or molecular features can predict whether CPEO will remain isolated or become part of multisystem disease. Ophthalmoplegia is usually symmetric. Pigmentary retinopathy confines to the post pole with a mottled appearance of retinal pigment⁴. Other cardinal systemic manifestations are cardiac conduction defects, elevated CSF protein, abnormal muscle mitochondria, and spongiform encephalopathy⁵.

Associated manifestations are short stature, deafness⁶, cerebellar ataxia, mild corticospinal signs, descending myopathy of face and limbs, subnormal intelligence, slowed EEG, aseptic meningitis (by history), demyelinating

radiculopathy, hyperglycemic acidotic coma^{7,8}. Endocrinological sings include Diabetes Mellitus (13%), hypogonadism, Growth Hormone deficiency, adrenal dysfunction, hypoparathyroidism, and skeletal and dental anomalies⁹. Risk of recurrence among the offspring of affected women was 4.11%. Affected mothers on an average have a risk of about 1 in 24 births¹⁰. In s study in 21 patients MRI abnormalities were found in 20 patients. Most frequent abnormalities were widespread white matter hyperintensity in 19 patients, supratentorial cortical atrophy in 13 patients¹¹. Absence of basal ganglia hyperintensity was correlated with Kearns-Sayre Syndrome¹¹. Most common MRI finding reported in Kearns-Sayre Syndrome is supratentorial and infratentorial atrophy¹¹. Early EMG and muscle biopsy examination facilitate early diagnosis. Death is mostly attributed to heard block. Sudden death is also reported with this disease. Treatment tried is Ubidecarenone or coenzyme Q 10 has been noted to be deficiency¹². This coenzyme is essential for normal mitochondrial respiration. Treatment with coenzyme Q 10 of patients with mitochondrial cytopathies has resulted in improved pyruvate metabolism, cardiac function, exercise intolerance, CSF levels and ataxia but no effect on ophthalmoplegia, ptosis or retinopathy¹³. Regular follow up is required to pick up if there is development of cardiac conduction defects. Ocular examination and cardiologic screening of family members is recommended.

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References

1. Kearns TP, and Sayre GP. Retinitis pigmentosa, external ophthalmoplegia, and complete heart block. Arch Ophthalmol 1958;60; 80-289.
2. Holt IL, Harding AE, and Morgan-Hughes JA: Deletions of mitochondrial DN in patients with mitochondrial myopathies. Nature 1988;331;717-719.
3. Andrew M. Schaefer, Emma L. Blakely, Philip G. Griffiths, Douglass M. Turnbull, Robert W. Taylor. Ophthalmoplegia due to mitochondrial DNA disease: The need for genetic diagnosis..Muscle and nerve 104-107 28 Mar 2005.
4. Erdbrink WL. Ocular myopathy associated with retinitis pigmentosa. Arch Ophthalmol 1957;57:335-338.
5. Anan R, Nakagawa M, Miyata M et al. Cardiac involvement in mitochondrial diseases. A study on 17 patients with documented mitochondrial DNA defects. Circulation 1995 Feb 15; 91(4): 955-961.
6. Zwirner P, Willichowski E. Progressive sensorineural loss in children with mitochondrial encephalomyopathies myopathies. Laryngoscope 2001; 111: 515-521.
7. Bosbach S, Kornblum C, Schroder R, Wagner M. Executive and visuospatial deficits in patients with chronic progressive external ophthalmoplegia with kearns Sayre syndrome. Brain 2003;126:1231-40
8. Saudifer PH. Chronic progressive ophthalmoplegia of myopathic origin J Neurol neurosurg and psychiatry. 1946; 9:81-83.
9. Harvey JN, Barnett D. Endocrine dysfunction in Kearns-Sayre syndrome. Clin Endocrinol 1992; 37:97-103
10. Chinnery PF, DiMauro S, Shanske S. Risk of developing a mitochondrial DNA deletion disorder. Lancet 2004; 364:592-596
11. Hector Manuel BC, Valee JN, Daouda L et al. Brain Magnetic Resonance imaging findings in patients with mitochondrial cytopathies. Arch Neurol 2005;62: 737-742
12. Bresolin N, Bet L, Binda A et al. Clinical and biochemical correlations in mitochondrial myopathies treated with coenzyme Q10. Neurology 1988; 38: 892-9
13. Sommer F, Fotzsch R, Pillunat LE et al. Diagnostic and therapeutic problems in chronic progressive external ophthalmologia. Klin Monatsbl Augen 2003; 220:315-319.

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