World Journal of Current Medical and Pharmaceutical Research
Content available at www.wjcmpr.com ISSN: 2582-0222

A REVIEW ON: KEARNS-SAYRE SYNDROME (KSS)

Thentu Vimalavathi, Kowlu Ramu, Nalla Eswara Rao. Chandaka Madhu
Gokul College of Pharmacy, Piridi, Bobbil, Vizianagaram, Andhra Pradesh -535558

Article History
Received on: 14-05-2025
Revised on: 09-06-2025
Accepted on: 16-07-2025

Abstract

Kearns-Sayre Syndrome (KSS) is a rare mitochondrial disorder characterized by progressive external ophthalmoplegia (PEO), pigmentary retinopathy, and cardiac conduction defects, typically presenting before the age of 20. It results from large-scale deletions or mutations in mitochondrial DNA (mtDNA), leading to impaired oxidative phosphorylation and decreased ATP production, especially in high-energy-demand tissues such as the eyes, heart, brain, and muscles. KSS follows a non-Mendelian, usually sporadic pattern of inheritance due to the unique properties of mtDNA. Patients often experience ptosis, muscle weakness, hearing loss, cerebellar ataxia, short stature, endocrine dysfunctions, and cognitive decline. Diagnosis is based on clinical presentation, supported by genetic testing, muscle biopsy, and imaging studies. Although there is no cure, treatment is supportive, including pacemaker implantation for cardiac issues, ptosis surgery, hormone replacement, and supplements like coenzyme Q10 and carnitine. KSS can overlap with other mitochondrial syndromes, including Pearson syndrome and progressive external ophthalmoplegia as isolated presentations. Early diagnosis and multidisciplinary management are critical for improving quality of life and minimizing complications.

Keywords: Kearns-Sayre Syndrome (KSS), Mitochondrial disorder, Mitochondrial DNA (mtDNA) deletions, Progressive external ophthalmoplegia (PEO), Pigmentary retinopathy.

***Corresponding Author**
Thentu Vimalavathi

DOI: https://doi.org/10.37022/wjcmpr.v7i2.362

INTRODUCTION

Kearns-Sayre Syndrome (KSS) is a **mitochondrial myopathy**, a neuromuscular disorder caused by defects in the mitochondria. It typically begins before the age of 20 and is characterized by [1].

Progressive external ophthalmoplegia (PEO) – weakness or paralysis of the eye muscles

Progressive External Ophthalmoplegia (PEO) is a rare neuromuscular disorder characterized by a gradual weakening or paralysis of the extraocular muscles, which control voluntary eye movements [2]. The most common clinical features of PEO include progressive ptosis (drooping of one or both eyelids), restricted eye movements (especially upward or lateral gaze), and in some cases, double vision (diplopia) [3]. As the condition advances, patients may develop a fixed or expressionless gaze due to the near-total immobility of the eyes. PEO often presents before the age of 20 when it is part of a multisystem mitochondrial disorder like Kearns-Sayre Syndrome (KSS), although it can also appear as an isolated condition or be associated with other mitochondrial myopathies [4].

The underlying cause of PEO typically involves mutations or large-scale deletions in mitochondrial DNA (mtDNA), which impair the function of mitochondria-the cellular structures responsible for energy (ATP) production [5]. Some cases also result from mutations in nuclear genes that affect mitochondrial function, such as POLG or TWNK. Because the extraocular muscles have high energy demands, mitochondrial dysfunction severely affects their performance, leading to the characteristic symptoms of the disorder. A muscle biopsy in affected individuals often reveals "ragged red fibers," indicating the accumulation of defective mitochondria [6].

Diagnosis is primarily clinical but supported by genetic testing, muscle biopsy, electromyography (EMG), and neuroimaging to rule out other neuromuscular diseases [7]. Treatment options for PEO are limited and mainly supportive. Surgical correction may be considered for ptosis if vision becomes obstructed, and prism glasses can help manage diplopia. Nutritional supplements like coenzyme Q10 or L-carnitine are sometimes prescribed, though their efficacy varies. Regular monitoring is important, especially in syndromic cases, due to possible involvement of cardiac or endocrine systems [8].

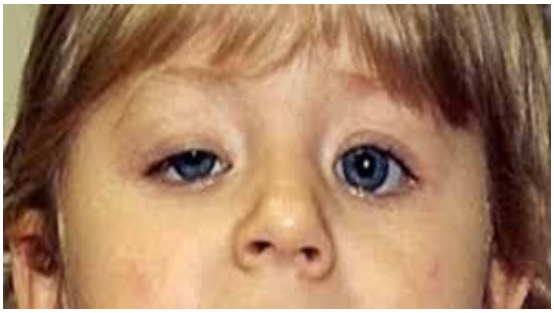

Fig 01: Kearns-Sayre syndrome-Medline genetics

Pigmentary Retinopathy a type of vision loss involving retinal degeneration

Pigmentary Retinopathy is a broad term referring to a group of retinal disorders characterized by abnormal pigmentation in the retina, most commonly seen as clumps or streaks of pigment resembling bone spicules when viewed during an eye exam [9]. This condition is often associated with progressive degeneration of the photoreceptor cells-particularly the rods, which are responsible for vision in low-light conditions. As a result, one of the earliest symptoms of pigmentary retinopathy is **night blindness** (nyctalopia), followed by a gradual loss of **peripheral vision**, which may progress to tunnel vision and, in some cases, complete blindness [10]. Although pigmentary retinopathy can occur as an isolated inherited retinal dystrophy (like in **retinitis pigmentosa**), it is also commonly found as part of broader syndromic conditions, including **Kearns-Sayre Syndrome (KSS)**, **Usher syndrome**, and other mitochondrial or systemic disorders [11].

In the context of **Kearns-Sayre Syndrome**, pigmentary retinopathy is typically part of a triad of core features, alongside progressive external ophthalmoplegia (PEO) and cardiac conduction defects. 12The retinal changes in KSS are due to **mitochondrial dysfunction** in retinal cells, which compromises their energy supply and leads to cell death and pigment dispersion. The progression is usually slow, and central vision is often preserved until the later stages. Diagnosis is made through **ophthalmoscopic examination**, **optical coherence tomography (OCT)**, and **electroretinography (ERG)**, which can show reduced rod and cone responses. There is currently **no cure** for pigmentary retinopathy, but low-vision aids, protective sunglasses, and vitamin A supplementation (in certain inherited forms) may help manage symptoms and slow progression [13]. Genetic counseling and regular ophthalmologic follow-up are recommended, especially when the condition is part of a broader genetic or mitochondrial syndrome [14].

Fig 02: Pigmentary retinopathy

KSS is considered a **multisystem disorder**, meaning it can affect the heart, muscles, endocrine system, ears, and central nervous system.

CAUSES

KSS is caused by **deletions or mutations in mitochondrial DNA (mtDNA)**. These deletions are usually:

- **Sporadic** (not inherited from parents)
- Involve large-scale deletions (typically 1.3–10 kilobases)

Since mitochondria have their own DNA (separate from nuclear DNA), the disorder follows a **non-Mendelian pattern of inheritance**, often arising spontaneously.

Kearns-Sayre Syndrome (KSS) is primarily caused by large-scale deletions or, less commonly, point mutations in mitochondrial DNA (mtDNA). These genetic alterations disrupt the genes responsible for oxidative phosphorylation, the critical process by which mitochondria produce adenosine triphosphate (ATP), the energy currency of the cell [15]. As a result, cells, particularly those in high-energy-demand tissues such as the muscles, brain, heart, and eyes, experience an energy deficit. The most frequently observed mtDNA deletions in KSS range from 1.3 to 10 kilobases and lead to a malfunction of the electron transport chain, which directly impairs ATP synthesis.16 Due to the phenomenon of heteroplasmy, where both normal and mutated mtDNA coexist in varying proportions within cells, the severity and distribution of symptoms can vary widely depending on the tissue-specific load of mutated mtDNA. Clinically, this mitochondrial dysfunction manifests as progressive external ophthalmoplegia, pigmentary retinopathy, cardiac conduction abnormalities, cerebellar ataxia, and cognitive impairment. These symptoms are directly linked to the reduced energy availability in affected tissues. Ultimately, KSS illustrates how mtDNA deletions can severely impact cellular energy metabolism and lead to a complex, multisystem disorder.

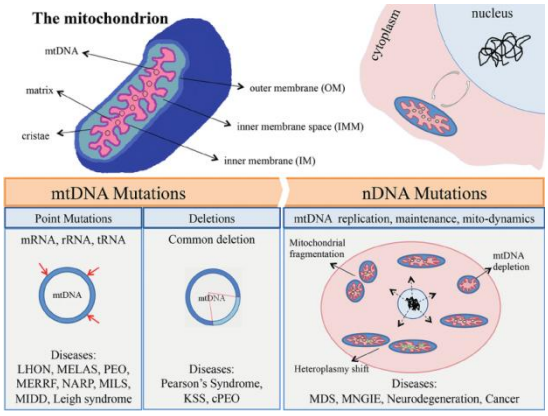

Fig 03: Mutations in DNA

TYPES

Kearns-Sayre Syndrome is sometimes considered part of a **spectrum of mitochondrial disorders**, and not typically divided into formal subtypes. However, it overlaps with other mitochondrial conditions such as:

- **Progressive External Ophthalmoplegia (PEO)** alone
- **Pearson Syndrome** (in infancy; may evolve into KSS in survivors)

- **MELAS and MERRF** (other mitochondrial encephalomyopathies with different mutations)

SIGNS AND SYMPTOMS

KSS typically manifests before age 20 and includes:

Ocular symptoms

- **Progressive external ophthalmoplegia** (inability to move eyes)
- **Ptosis** (drooping eyelids)
- **Pigmentary retinopathy** (vision problems, especially night blindness)

Systemic symptoms

- **Cardiac conduction defects** (can lead to heart block or sudden death)
- **Ataxia** (coordination problems)
- **Muscle weakness**
- **Short stature**
- **Hearing loss**
- **Endocrine issues** (diabetes, hypoparathyroidism, hypothyroidism)
- **Cognitive impairment** or **encephalopathy** in severe cases

MECHANISM OF ACTION

KSS arises due to **defective mitochondrial oxidative phosphorylation**, which impairs the body's ability to produce energy efficiently.

Key Mechanisms

- Mitochondria are responsible for producing **ATP** (energy) via the **electron transport chain**.
- Large-scale deletions in mtDNA disrupt genes essential for this process.
- Cells with **high energy demands** (e.g., muscle, nerve, retinal cells, heart) are most affected.
- **Heteroplasmy** (mixture of normal and mutant mtDNA in cells) contributes to variable severity and symptoms.

TREATMENT

There is **no cure** for KSS. Treatment is **symptomatic and supportive**, aiming to manage complications:

Cardiac

- **Pacemaker implantation** for conduction defects
- Regular **ECG monitoring**

Ocular

- **Ptosis surgery** if vision is impaired
- **Visual aids** for retinal degeneration

Systemic/Metabolic:

- **Cochlear implants** for hearing loss
- **Endocrine therapy** (e.g., insulin, hormone replacement)
- **Coenzyme Q10**, **carnitine**, and **B vitamins** supplements (though evidence is limited)

General:

- **Physical therapy** for muscle weakness
- **Genetic counselling**

Table 01: Summery of the following

Feature	Details
Onset	Usually before age 20
Cause	Mitochondrial DNA deletions (sporadic)
Main Symptoms	PEO, pigmentary retinopathy, heart block
Other Involvement	Hearing loss, diabetes, ataxia, short stature
Inheritance	Usually sporadic (not inherited)
Treatment	Supportive care, pacemaker, supplements

CONCLUSION

Kearns-Sayre Syndrome (KSS) is a rare and severe mitochondrial disorder caused by genetic mutations in mitochondrial DNA. It primarily affects the eyes, causing progressive external ophthalmoplegia (weakness or paralysis of eye muscles) and pigmentary retinopathy (a degenerative eye condition that can lead to vision loss). Additionally, KSS involves other systems, commonly impacting the heart with cardiac conduction defects, and potentially leading to short stature, hearing loss, ataxia (problems with coordination and balance), and endocrine disorders such as diabetes. While there is no cure, a multidisciplinary approach focusing on early diagnosis and symptomatic management can significantly improve quality of life and outcomes. Timely interventions like pacemakers for heart block are crucial for managing life-threatening complications. Research into therapies to improve mitochondrial function and potentially halt or slow disease progression holds promise for the future.

Funding

Nil

Conflict of Interest

Authors are declared that no conflict of interest.

Acknowledgement

Not Declared

Informed Consent and Ethical Statement

Not Applicable

Author Contributions

Not Declared

REFERENCES

1. Gropman, A. L. (2004). The neurological presentations of childhood and adult mitochondrial disease: established syndromes and phenotypic variations. *Mitochondrion*, *4*(5–6), 503–520. https://doi.org/10.1016/j.mito.2004.07.009
2. Ettinger, A. B., & Weisbrot, D. M. (2014). *Neurologic Differential Diagnosis: A Case-Based Approach*. Cambridge University Press.
3. Toukhy, E. a. E. (2020). *Oculoplastic surgery: A Practical Guide to Common Disorders*. Springer.

4. Hankey, G., & Wardlaw, J. (2008). *Clinical neurology*. CRC Press.
5. Taanman, J., & Kroon, A. M. (2019). Mitochondrial DNA: structure, genetics, replication and defects. In *Elsevier eBooks* (pp. 127–152). https://doi.org/10.1016/b978-0-12-811752-1.00005-5
6. Warner, T. T., & Hammans, S. R. (2008). *Practical Guide to Neurogenetics E-Book*. Elsevier Health Sciences.
7. Acar, T., Demirel, E. A., Afşar, N., Akçalı, A., Demir, G. A., Alagöz, A. N., Mengi, T. A., Arsava, E. M., Ayta, S., Bebek, N., Bilgiç, B., Boz, C., Çakar, A., Çelebisoy, N., Çevik, M. U., Delen, F., Tekçe, H. D., Ekmekçi, H., Elmalı, A. D., . . . Yön, M. İ. (2020). The COVID-19 from Neurological Overview. *Turkish Journal of Neurology*, *26*(2), 58–108. https://doi.org/10.4274/tnd.2020.73669
8. Hauser, S., & Josephson, S. (2013). *Harrison's Neurology in Clinical Medicine, 3E*. McGraw Hill Professional.
9. Maharana, P. K., Sharma, N., & Kumar, A. (2024). *Ophthalmology Clinics-I for Postgraduates*. Jaypee Brothers Medical Publishers Pvt Limited.
10. Duker, J. S., Waheed, N. K., & Goldman, D. (2021). *Handbook of Retinal OCT: Optical Coherence Tomography E-Book*. Elsevier Health Sciences.
11. Roberts, F., & Thum, C. K. (2016). *Lee's ophthalmic histopathology*. Springer.
12. Pascual, J. M. (2017). *Progressive brain disorders in childhood*. Cambridge University Press.
13. Brodsky, M. C. (2010). *Pediatric Neuro-Ophthalmology*. Springer Science & Business Media
14. Bunik, M., Levin, M. J., Abzug, M. J., & Schreiner, T. L. (2024). *CURRENT Diagnosis & Treatment Pediatrics, 27th Edition*. McGraw Hill Professional.
15. Minczuk, M., &Rorbach, J. (2020). *Mitochondrial gene expression: Methods and Protocols*. Humana.
16. Warnecke, T., Dziewas, R., &Langmore, S. (2021). *Neurogenic dysphagia*. Springer Nature.