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SCIENTIFIC ARTICLE - CASE REPORT

ANESTHESIA FOR KEARNS SAYRE SYNDROME: CASE REPORT

MATEUS FERREIRA DE SIQUEIRA E SILVA[1]; DIRCEU CASTRO PACHECO[1]; GUSTAVO SIQUEIRA ELMIRO[1]; GIULLIANO GARDENGHI[1,2]

1. Centro de Ensino e Treinamento da Clínica de Anestesia (CET - CLIANEST) - Goiânia - GO - Brazil
2. Hospital ENCORE, Aparecida de Goiânia - GO - Brazil

ABSTRACT

Introducion: Kearns-Sayre syndrome (KSS) is a very rare multisystem mitochondrial disease that occurs before the age of 20 and is characterized by a typical clinical triad: progressive external ophthalmoplegia with ptosis, pigmentary retinopathy and cardiac conduction abnormalities, including heart block. Other clinical manifestations may also include muscle weakness, symptoms of neurological dysfunction such as cerebellar ataxia, impaired intellectual and cognitive function, sensorineural hearing loss and neuropathy, various endocrine abnormalities, nephropathy, and dental anomalies. Case Report: Female patient, 62 years old, with heart disease using a bicameral pacemaker, type II diabetic, sedentary, with KSS, was admitted in Goiânia, Goiás on 05/06/2024 after desaturation and decreased level of consciousness, being diagnosed with pneumonia in the emergency room. She was intubated and maintained on mechanical ventilation until May 16th and then a tracheostomy (TQT) was performed. After the TQT, the patient was already in the infirmary bed (with TQT in a tent) where the patient's pulmonary investigation was continued with bronchoscopy under light sedation (midazolam, propofol and fentanyl). After the procedure, the patient was kept in the post-anesthesia recovery room for approximately sixty minutes and taken to the infirmary bed. Approximately six hours after bronchoscopy, the patient began to experience desaturation, cyanosis of the extremities and central region, and a lower level of consciousness. She was taken to the ICU and maintained on BIPAP support. Bronchoscopy result was negative. During her stay in the ICU, she was diagnosed with two bacterial pneumonias and one viral pneumonia due to Influenza A. The TQT was changed on 06/04/24 and 06/17/24. On 06/19/24, the patient underwent gastrostomy under light sedation using fentanyl 15 mcg, midazolam 3 mg, ketamine 5 mcg without complications and was subsequently sent to the ICU, where she remained without adverse events. Discussion: KSS is a rare mitochondrial disease that is difficult to diagnose early. Little is known about the behavior of the disease in the face of surgical procedures, which is why it is a challenge. In patients diagnosed with KSS, toxic mitochondrial medications should be avoided, such as propofol, aminoglycosides, linezolin, metformin and nucleoside analogues.

Keywords: Chronic Progressive external ophthalmoplegia, Kearns-sayre syndrome, Propofol.

INTRODUCTION

Kearns-Sayre syndrome (KSS) is a very rare multisystemic mitochondrial disease that occurs before the age of 20 and is characterized by a typical clinical triad: progressive external ophthalmoplegia with ptosis, pigmentary retinopathy, and cardiac conduction abnormalities, including heart block[1,2]. Other clinical manifestations may include muscle weakness, dysfunction such as cerebellar ataxia, impaired intellectual and cognitive function, sensorineural hearing loss, and neuropathy, along with various endocrine abnormalities, nephropathy, and dental anomalies[1,3,4].

Mitochondrial disorders result from mutations in mitochondrial DNA (mtDNA) or nuclear DNA (nDNA). Each human cell, except mature cells, contains between 500 to 6.000 mitochondria, and each mitochondrion contains one to fifteen copies of mitochondrial DNA[5,6]. The number of mtDNA copies differs significantly between cell types and tissues and depends on energy demands. During reproduction, only maternal mitochondria are inherited. Mitochondrial DNA is a double-stranded molecule of 16 kilobases that encodes 13 proteins essential for oxidation/phosphorylation, 22 types of tRNA, and 2 types of rRNA[7].

Chronic Progressive External Ophthalmoplegia (CPEO) is the most common manifestation of mitochondrial diseases and is characterized by progressive, symmetrical bilateral changes, ptosis, and reduced ocular motility. CPEO can be isolated or accompanied by a clinical picture characteristic of systemic involvement in mitochondrial dysfunction (CPEO plus syndrome). The global prevalence of CPEO is unknown; however, the incidence of CPEO is 1–2 per 100.000. In the UK cohort database, the estimated prevalence of CPEO recorded was 1 in 30.000[8].

In 90% of cases, Kearns-Sayre Syndrome (KSS) is caused by large-scale, spontaneous, heteroplasmic mitochondrial DNA (mtDNA) deletions that occur at the germline level during embryonic development, ranging from 1.1 to 10 kb[9,10]. Rarely, point mutations, single nucleotide deletions, mtDNA duplications, as well as exclusions or multiple mtDNA deletions and nuclear gene defects predisposing to multiple deletions are identified as causative of KSS[11,12]. The mtDNA rearrangements typically affect the coding of respiratory chain protein genes and a large number of various tRNAs. These rearrangements impair oxidative phosphorylation, resulting in reduced energy production in mitochondria and leading to dysfunction of many tissues, especially those with high energy demands[4,12].

Considering our experience in anesthetizing a patient with Kearns-Sayre Syndrome (KSS), the objective of this study is to gather data from the literature on KSS related to procedures performed by fellow anesthesiologists and their respective experiences, as well as the adverse effects of commonly used anesthetic drugs in the context of the patient's condition.

CASE REPORT

Female patient, 62 years old, with a history of heart disease and a bicameral pacemaker, type II diabetes, sedentary lifestyle, and Kearns-Sayre Syndrome, was admitted to a hospital in Goiânia on 05/06/2024 after desaturation and decreased level of consciousness. She was diagnosed with pneumonia in the emergency room. The patient was intubated and remained on mechanical ventilation until 05/16, at which point a tracheostomy was performed. The patient progressively improved with respiratory recovery and was discharged to the ward.

In the hospital room, the patient was under a tracheostomy with oxygen support via a tent, and the pulmonary investigation was ongoing with the performance of a bronchoscopy under light sedation (midazolam, propofol, and fentanyl). After the procedure, the patient was maintained in the post-anesthesia recovery room for about sixty minutes and then transferred back to the hospital room. About six hours after the bronchoscopy, the patient started showing desaturation, cyanosis of the extremities and centrally, and a decrease in the level of consciousness.

She was transferred back to the ICU and maintained on non-invasive ventilation support with two levels of pressure (Bilevel). The result of the bronchoscopy was negative. During her hospitalization in the ICU, she was

diagnosed with two bacterial pneumonias and one viral pneumonia caused by Influenza A. The tracheostomy was changed on 06/04/2024, and 06/17/2024.

During her hospitalization, 06/19/2024, the patient underwent a gastrostomy under light sedation using 15 mcg of fentanyl, 3 mg of midazolam, and 5 mcg of ketamine, without any complications. She was subsequently transferred to the ICU, where she remained without adverse events.

DISCUSSION

A 50-year-old female patient with uterine cancer undergoing radiotherapy developed radiation cystitis and ureLittle is still known about Kearns-Sayre Syndrome (KSS) in the context of surgical procedures, making it a challenge for anesthesiologists. In our case report, two different procedures were performed with different sedations. In the first procedure, for the bronchoscopy, the sedation used included fentanyl, propofol, and midazolam. In the second sedation, for the gastrostomy, fentanyl, midazolam, and ketamine in low doses were used.

Kearns-Sayre Syndrome (KSS) is a multisystem mitochondrial disease, and patients should be advised about medications that are toxic to the mitochondria, such as metformin, propofol, valproic acid, aminoglycosides, linezolid, and treatments with nucleoside analogs[13,14].

According to our case report, it is likely that the use of propofol during the first sedation led to central cyanosis, desaturation, and a decrease in the level of consciousness. Although the use of propofol is generally discouraged in patients with Kearns-Sayre Syndrome (KSS) due to mitochondrial dysfunction, Maddali et al. used propofol continuously for sedation in a 14-year-old patient undergoing permanent pacemaker implantation[15]. In that report, the patient did not experience complications from propofol use, unlike in our case.

The discouragement of using mitochondrial-toxic drugs is unanimous[4,11-14]. However, adverse effects such as propofol infusion syndrome are reported at very high concentrations, resulting in lactic acidosis[14].

Propofol can also disrupt the mitochondrial permeability transition pore, leading to a decrease in mitochondrial membrane potential and subsequent apoptosis. Additionally, the inhibition of free fatty acid uptake into the mitochondria may be a causal factor for propofol infusion syndrome. Therefore, it has been suggested that propofol may be toxic to mitochondria, and patients with mitochondrial disorders should not receive propofol in high doses for extended periods[16].

Thus, after reviewing the literature and the experiences of each author regarding anesthetic procedures, we cannot conclusively state that the complications in our patient during the first sedation were caused by propofol. However, based on the literature, we recognize that drugs causing mitochondrial damage should be avoided. Due to the lack of randomized clinical trials on Kearns-Sayre Syndrome (KSS), we maintain the recommendation to avoid drugs with unknown pharmacodynamic effects.

REFERENCES

1. Guo L, Wang X, Ji H. Clinical phenotype and genetic features of a pair of chinese twins with kearns-sayre syndrome. DNA Cell Biol [Internet]. 2020 Aug [Cited 2024 Oct 31];39(8):1449-47. doi: 10.1089/dna.2019.5010

2. Luca P, Alessia G, Camilla RM, Antonio N, Diego M, Federica D, Daria D, Rosalba C, Carlo DV, Daniela L. Spinal cord involvement in kearns--sayre syndrome: a neuroimaging study. Neuroradiology [Internet]. 2020 Oct [Cited 2024 Oct 31];62(10):1315-21. doi: 10.1007/s00234-020-02501-0

3. Gross-Jendroska M, Schatz H, McDonald HR, Johnson RN. Kearns-sayre syndrome: a case report and review. Eur J Ophthalmol [Internet]. 1992 Jan-Mar [Cited 2024 Oct 31];2(1):15-20. doi: 10.1177/112067219200200104

4. Maceluch JA, Niedziela M. The clinical diagnosis and molecular genetics of kearns-sayre syndrome: a complex mitochondrial encephalomyo-

pathy. Pediatr Endocrinol Rev. 2006 Dec-2007 Jan;4(2):117-37.

5. D'Erchia AM, Atlante A, Gadaleta G, Pavesi G, Chiara M, De Virgilio C, Manzari C, Mastropasqua F, Prazzoli GM, Picardi E, Gissi C, Horner D, Reyes A, Sbisà E, Tullo A, Pesole G. Tissue-specific mtDNA abundance from exome data and its correlation with mitochondrial transcription, mass and respiratory activity. Mitochondrion [Internet]. 2015 Jan [Cited 2024 Oct 31];20:13-21. doi: 10.1016/j.mito.2014.10.005

6. Satoh M, Kuroiwa T. Organization of multiple nucleoids and DNA molecules in mitochondria of a human cell. Exp Cell Res [Internet]. 1991 Sep [Cited 2024 Oct 31];196(1):137-40. doi: 10.1016/0014-4827(91)90467-9

7. Kierdaszuk B, Kaliszewska M, Rusecka J, Kosińska J, Bartnik E, Tońska K, Kamińska AM, Kostera-Pruszczyk A. Progressive external ophthalmoplegia in polish patients-from clinical evaluation to genetic confirmation. Genes (Basel) [Internet]. 2020 Dec 31 [Cited 2024 Oct 31];12(1):54. doi: 10.3390/genes12010054

8. Olson W, Engel WK, Walsh GO, Einaugler R. Oculocraniosomatic neuromuscular disease with "ragged-red" fibers. Arch Neurol [Internet]. 1972 Mar [Cited 2024 Oct 31];26(3):193-211. doi: 10.1001/archneur.1972.00490090019001

9. Kisilevsky E, Freund P, Margolin E. Mitochondrial disorders and the eye. Surv Ophthalmol [Internet]. 2020 May-Jun [Cited 2024 Oct 31];65(3):294-311. doi: 10.1016/j.survophthal.2019.11.001

10. Leal M, Dhoble C, Lee J, Lopez D, Menéndez LS. A rare case of kearns-sayre syndrome in a 17-year-old venezuelan male with bilateral ptosis as the initial presentation. Oxf Med Case Reports [Internet]. 2016 Mar 3 [Cited 2024 Oct 31];2016(3):34-6. doi: 10.1093/omcr/omw007

11. Pitceathly RD, Rahman S, Hanna MG. Single deletions in mitochondrial DNA-molecular mechanisms and disease phenotypes in clinical practice. Neuromuscul Disord [Internet]. 2012 Jul [Cited 2024 Oct 31];22(7):577-86. doi: 10.1016/j.nmd.2012.03.009

12. Yamashita S, Nishino I, Nonaka I, Goto YI. Genotype and phenotype analyses in 136 patients with single large-scale mitochondrial DNA deletions. J Hum Genet [Internet]. 2008 [Cited 2024 Oct 31];53(7):598. doi: 10.1007/s10038-008-0289-8

13. Hung KM, Chen PC, Hsieh HC, Calkins MJ. Mitochondrial defects arise from nucleoside/nucleotide reverse transcriptase inhibitors in neurons: potential contribution to HIV-associated neurocognitive disorders. Biochim Biophys Acta Mol Basis Dis [Internet]. 2017 Feb [Cited 2024 Oct 31];1863(2):406-13. doi: 10.1016/j.bbadis.2016.11.017

14.Orsucci D, Ienco EC, Siciliano G, Mancuso M. Mitochondrial disorders and drugs: what every physician should know. Drugs Context [Internet]. 2019 Jul 4 [Cited 2024 Oct 31];8:212588. doi: 10.7573/dic.212588

15. Maddali MM, Munasinghe TD, Al Aamri I, Al-Abri IA, Al-Adawi S. Propofol and kearns-sayre syndrome: an idiographic approach. Sultan Qaboos Univ Med J [Internet]. 2023 Dec [Cited 2024 Oct 31];23(Spec Iss):63-7. doi: 10.18295/squmj.12.2023.080

16. Finsterer J, Frank M. Propofol is mitochondrion-toxic and may unmask a mitochondrial disorder. J Child Neurol [Internet]. 2016 Nov [Cited 2024 Oct 31];31(13):1489-94. doi: 10.1177/0883073816661458

MATEUS FERREIRA DE SIQUEIRA E SILVA - http://lattes.cnpq.br/9487795557278238 - https://orcid.org/0000-0001-7977-484X

DIRCEU CASTRO PACHECO - http://lattes.cnpq.br/9259558054810108 - https://orcid.org/0009-0009-5316-482X

GUSTAVO SIQUEIRA ELMIRO - http://lattes.cnpq.br/4765163399934337 - https://orcid.org/0000-0003-2113-8757

GIULLIANO GARDENGHI - http://lattes.cnpq.br/1292197954351954 - https://orcid.org/0000-0002-8763-561X

MAILING ADDRESS:
GIULLIANO GARDENGHI
CLIANEST - Rua T-32, 279 - Setor Bueno, Goiânia - GO - Brasil
E-mail: coordenacao.cientifica@ceafi.edu.br

Library Review - Romulo Arantes
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MAILING ADDRESS:
LUIZ EDUARDO MARTINS FREIRE
Rua Grão Pará 570 - Santa Efigênia - apt 803 - Ed. Terezinha Isaira - Belo Horizonte- MG - Brazil
E-mail: luiz-motta@hotmail.com

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