Reviewer #1:

Q1: Specific Comments to Authors: The authors present a well-done work on a rare and complex clinical case. However, after the complete recovery of the patient (after such 6 months) what is the therapeutic proposal and the socio-professional lifestyle that the authors propose for this patient.

A1:

In terms of life: after 6 months, the muscle strength of the limbs will recover, and in the future, light physical labor can be carried out, such as company employees, etc., and normal life can be moderately exercised. The abundance of evidence suggests that exercise training is efficacious, well tolerated and safe; no studies report clinical adverse events or detrimental effects on muscle (serum creatine kinase levels), perceived fatigue or self-reported activities of daily living **[1-8]**. Our recently conducted systematic review and meta-analysis to determine the effect of exercise across a range of outcomes in patients with neuromuscular disorders, which includes mitochondrial disease, also supports these findings **[9]**.

Treatment: Other supplements including antioxidants (vitamin C, vitamin E and alpha-lipoic acid) and electron acceptors (CoQ10 or carthine) may remove ROS from cells, improving mitochondrial function. Supplements could also bypass a cellular defect (e.g. a deficiency in the activity of complexes I, II or III in the electron transport chain) **[10-12]**.

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2. Jeppesen TD, Schwartz M, Olsen DB, Wibrand F, Krag T, Dunø M, et al. Aerobic training is safe and improves exercise capacity in patients with mitochondrial myopathy. Brain. 2006;129:3402–3412.
3. Taivassalo T, De Stefano N, Argov Z, Matthews PM, Chen J, Genge A, et al. Effects of aerobic training in patients with mitochondrial myopathies. Neurology. 1998;50:1055–1060.
4. Taivassalo T, Gardner JL, Taylor RW, Schaefer AM, Newman J, Barron MJ, et al. Endurance training and detraining in mitochondrial myopathies due to single large-scale mtDNA deletions. Brain. 2006;129:3391–3401.
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9. 149. Stefanetti RJ, Blain A, Jimenez-Moreno C, Errington L, Ng YS, McFarland R, et al. Measuring the effects of exercise in neuromuscular disorders: a systematic review and meta-analyses. Wellcome Open Res [Internet]. 2020 [cited 2020 Nov 30];5. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7331112/ .

10. Hayashi G, Cortopassi G. Oxidative stress in inherited mitochondrial diseases. Free Radic Biol Med. 2015;88:10–17.
11. Parikh S, Saneto R, Falk MJ, Anselm I, Cohen BH, Haas R. A modern approach to the treatment of mitochondrial disease. Curr Treat Options Neurol. 2009;11:414–430.
12. Rajman L, Chwalek K, Sinclair DA. Therapeutic potential of NAD-boosting molecules: the in vivo evidence. Cell Metab. 2018;27:529–547.

Reviewer #2:
Conclusion: Minor revision
Q1: Please revise the following statements: “The third-party and the family history led towards the diagnosis of the underlying disease.” Avoid using words like “third party”. “But in a plateau,support, prevention and treatment are the main.” “Now completely normal.” “Therefore, the brain and muscles, most sensitive to energy supply, are particularly vulnerable.” “Exercise intolerance, paroxysmal muscle weakness, and muscle soreness are other denominations when mitochondrial myopathy is suspected as the underlying cause.” “Generally, the disease presents with a chronic course, with a few subjects suffer from severe mitochondrial myopathy, characterized by acute muscle pain, palpitation, dyspnea, limb weakness, and lactic acidosis.” “The sepsis patient, increased ROS generation, hormonal changes and altered mitochondrial gene transcription significantly affected mitochondrial function.” “The third-party and the family history with recurrent fatigue and weakness after exercise in the patient and established or suspected (mitochondrial) myopathy in other family members confirmed the clinical suspicion.” “Its diagnosis includes…” “…….and can also modulate immune”

A1: Thank you for your suggestion, we have revised your suggestion.

Q2: Chinese medicine (invigorating the spleen, supplementing qi, removing dampness, promoting blood circulation and removing blood stasis) is also effective. Please give reference **[1-5]**..

A2:

1.Du Q, Bian X L, Xu X L, et al. Role of mitochondrial permeability transition in human hepatocellular carcinoma HepG2 cell death induced by rhein [J]. Fitoterapia, 2013, 91: 68-73.

2.Yu J Q, Bao W, Lei J C. Emodin regulates apoptotic pathway in human liver cancer cells [J]. Phytother Res, 2013, 27(2): 251-257.

3.Cui Y, Lu P, Song G, et al. Involvement of PI3K/Akt, ERK and p38 signaling pathways in emodin-mediated extrinsic and intrinsic human hepatoblastoma cell apoptosis [J]. Food Chem Toxicol, 2016, 92: 26-37.

3.Zhang L, He D, Li K, et al. Emodin targets mitochondrial cyclophilin D to induce apoptosis in HepG2 cells [J]. Biomed Pharmacother, 2017, 90: 222-228

4.Chen JM, Yang TT, Cheng TS, Hsiao TF, Chang PM, Leu JY, Wang FS, Hsu SL, Huang CF, Lai JM. Modified Sijunzi decoction can alleviate cisplatin-induced toxicity and prolong the survival time of cachectic mice by recovering muscle atrophy. J Ethnopharmacol. 2019 Apr 6;233:47-55.

5.She M, Huang M, Zhang J, Yan Y, Zhou L, Zhang M, Yang Y, Wang D. Astragulus embranaceus (Fisch.)Bge-Dioscorea opposita Thunb herb pair ameliorates sarcopenia in senile type 2 diabetes mellitus through Rab5a/mTOR-mediated mitochondrial dysfunction. J Ethnopharmacol. 2023 Jun 7:116737.

Special note: We cite the latest literature [5] in the manuscript.

Q3:“in critical condition due to sepsis, with hyperlaccidaemia..” Please replace it with hyperlactatemia.

A3:I've made changes in the manuscript.

Q4: Full forms for many acronyms are missing eg MELAS. Full forms should be mentioned first with acronyms in the brackets.

A4:I've made changes in the manuscript.

Q5: Figure legends for figure 2 are very long. The detailed description of the figure should be given in the text, not in the legend.

A5:I've made changes in the manuscript.

Q6： Table 3 does not add anything new to the case report and hence may be omitted.

A6：Table 3 has be omitted in the manuscript.