

CASE REPORT

Psychiatric care for a person with MELAS syndrome: A case report

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Abstract

This report provides information for future clinicians who may be involved in treating patients with mitochondrial disorders manifesting with psychiatric problems, as literature in treatment is limited. The interventions focus on both carefully crafted medication therapy and nondrug methods to manage the challenging behaviors in a medically infirmed person.

KEYWORDS

behavior therapy, case report, MELAS, multidisciplinary team, occupational therapy, psychiatric nursing, sensory deficit

1 | INTRODUCTION

This case report emphasizes the intervention journey targeting the psychiatric symptoms in a patient with MELAS. These interventions focus on both carefully crafted medication therapy and nondrug methods to manage the challenging behaviors in a medically infirmed person. This journey also showcases the beauty of harnessing a multidisciplinary team approach to assist this patient and his caregivers. It urges physicians to identify emotional care needs clearly in order to render early access to interventions. This report aims to provide information for future clinicians and therapists who may be involved in treating patients with mitochondrial disorders manifesting with psychiatric problems, as literature in treatment is limited.

The psychiatric and behavioral manifestations of mitochondrial diseases are varied.^{1,2} Studies have shown that psychiatric illnesses are common in patients with mitochondrial diseases.³⁻⁶ However, the treatment of psychiatric conditions in this population is not well established.^{7,8} Many psychotropics have detrimental effects on the mitochondria and hence may not be deemed suitable for use in these patients.⁹ Psychotherapeutic approaches and behavioral therapies could be more suitable; however, these modalities may be limited

by several disease factors such as cognitive impairment, physical impediment, and the unpredictable occurrences of behavior states.²

This case report described a patient with diagnosed MELAS (mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes) syndrome who at a later stage of his illness had developed psychological and behavioral disturbances.¹⁰ MELAS syndrome is caused by mutations in the mitochondrial DNA, most commonly MT-TL1. The narrative followed through the psychiatric evaluation, the inpatient therapy, and the many challenges faced in the treatment of this patient. Both of the patient's parents had provided explicit consent for the information to be published in the hope that the medical community would be better equipped to manage such patients.

2 | CASE HISTORY

The patient was a 26-year-old Chinese man named JWH,¹ and he was not diagnosed with MELAS syndrome at first. He had initially presented to the general pediatric unit at fourteen years of age for prolonged fever with an altered mental status.¹¹ An electroencephalogram (EEG) showed ongoing

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seizures. He was then diagnosed to suffer from an episode of viral encephalitis and treated appropriately. In the subsequent years, he had multiple readmissions for recurrent partial seizures, or cortical seizures affecting his visual tract, and even left-sided hemiparesis. A further workup was ordered, beginning with magnetic resonance imaging (MRI) and then spectroscopy (MRS) which revealed a duplex “lactate peak” alongside an elevated serum lactate of 3.6 mg/dL. JWH’s diagnosis was then revised to MELAS syndrome. His treatment commenced with intravenous Arginine with good clinical response. Over the course of the following twelve years after the diagnosis of MELAS, JWH’s effort tolerance gradually deteriorated due to the development of hypertrophic cardiomyopathy, sensorineural hearing loss, cortical blindness (secondary to bilateral occipital infarcts) with macular sparing, and progressive muscular weakness.

2.1 | Timeline and diagnostic assessment

An incident had occurred when he turned twenty-six years old. He became aggressive toward another player at a mini-golf course after a misunderstanding ensued between them. Angrily, he raised a golf club against her and caused injury. Security personnel separated them, and JWH was conveyed to a psychiatric hospital for evaluation. He became more irritable with frequent mood swings. He saw a psychiatrist for four months and Fluoxetine 20 milligrams daily was prescribed to curb the episodes. The SSRI² antidepressant caused him daytime sedation.¹² Although a switch to Sertraline was suggested, JWH and his parents did not wish to continue on medications. He was subsequently lost to follow up with that local psychiatric hospital and had stopped taking any psychotropics.

The following year after that index psychiatric assessment, JWH’s parents sought help from his pediatric neurologist for escalating aggression. He was found to have cognitive decline¹³ with worsening of neuropsychiatric symptoms over the fortnight, along with poorer intake and early satiety. He was observed to be talking and muttering to himself about having “a third eye.” He saw objects “wobbling around.” These were not visual hallucinations but a result of how he perceived and verbalized his deteriorating vision. He spoke irrelevantly at times. This was not a primary thought disorder but a result of his worsening hearing impairment. He slept poorly and talked to himself at night. He became increasingly irritable and displayed violence toward his parents when his needs were not met on time. At the time of assessment, his anger outbursts were untriggered and unpredictable. JWH’s mother had to hide behind a locked door after he tried to punch her.

JWH was referred to Psychiatry during that visit for worsening behavioral changes and escalating aggression

toward his parents. He was admitted to the pediatric high-dependency unit (HDU) from the clinic, while awaiting an urgent psychiatric review. JWH started manifesting challenging behaviors such as pacing up and down the HDU demanding to leave, repeatedly saying that the environment was not to his liking, “*it is so cold, (I) could freeze to death... the ceiling is full of germs,*” adding that no one could “fool” him. He required chemical restraint and was transferred to the psychiatric ward in view of his inability to restrain his emotions and hyperactivity. The impression from the Consultation-Liaison (CL) team was that of emotional and behavioral disturbances secondary to neurocognitive decline on a background of MELAS syndrome with significant medical complications.

Subsequent reassessments showed that JWH was prone to irritability and temper tantrums. He got frequently annoyed when he construed that circumstances and situations were not to his liking. His sensory impairments also worsened these behaviors. This led to more verbal and physical aggression toward staff and other patients in the psychiatric ward. He adamantly denied feeling depressed, yet often lamented about his poor health and unpleasant experiences in the hospital. He verbalized passive suicidal ideation but never demonstrated any attempts at self-harm. He did not report auditory hallucinations or paranoid ideations.

JWH’s parents saw his general function declining. He was unemployed for more than a year after a 3-year job as a cleaner. He would get into frequent arguments with customers and colleagues. His mother had cooked and cleaned for him as he could not do so himself anymore.

A mental-state examination revealed a small-built Chinese man who appeared older than his biological age, with features of under-nourishment and muscular atrophy. He had hearing and visual impairments and would often respond with a loud and threatening voice. He was verbally aggressive and confrontational. Objective test scores were attempted unsuccessfully due to his aggression and hyperactivity. He could not perform in the Montreal Cognitive Assessment due to his visual impairment. His cognitive symptoms appeared to correlate with the severity of the cerebral atrophy shown in his MRI.¹³

2.2 | Various therapeutic interventions

2.2.1 | Pharmacological treatment

Many classes of psychotropic medications are found in vitro to negatively affect mitochondrial function by inhibiting mitochondrial respiratory chain,^{9,10} and these include SSRIs,^{12,14,15} SNRIs,³ MAOIs,⁴ antipsychotics,¹⁶⁻¹⁸ and sodium-valproate¹⁹⁻²² although these agents have not been studied in a clinical setting. Therefore, prescribing psychotropics for symptom management becomes a challenge for

patients with mitochondrial disorders exhibiting psychiatric symptoms. JWH had previously used Fluoxetine and Sertraline (SSRIs), with minimal improvement in his mood state and impulse control. These medications made him excessively sedated during the day and exacerbated his irritability. The psychiatric team decided to proceed with a trial of Mirtazapine (NaSSA)⁵ in order to promote anxiolysis, in hopes of reducing his irritability. Additionally, the literature had not explicitly stated any ill-effects of mirtazapine on the mitochondria. The additional effects of improving his appetite and sleep were beneficial. At the same time, a trial of Pregabalin (GABA)⁶ was initiated for anxiolysis and preferred over prolonged reliance on benzodiazepine to contain the aggression. To reduce breakthrough agitation, very-low doses of Clonazepam were judiciously administered. The medications were well-tolerated in the ward's structured milieu albeit for unpredictable moments of daytime somnolence. Other agents were considered to retard agitation and offer anxiolysis. However, there were concerns on tolerance, dependence, rebound symptoms, and fall risk. Antihistamines such as hydroxyzine, beta-blockers such as propranolol were tried with little effect, and topiramate was considered.²²

2.2.2 | Non-pharmacological treatment

Attenuation of sensory deficits

One significant contributor to JWH's outbursts was his frequently misunderstood auditory cues due to his bilateral sensorineural hearing loss.²³ The team encouraged use of his hearing aids. The other sensory deficit was his cortical blindness with macular sparing. JWH would be startled and became hypervigilant when he was approached by staff or patients from his side. The team made efforts to educate everyone including his family members to directly approach him from his front, where his vision was *better*. Addressing JWH's sensory impairment allowed him to hear dialog and perceive the facial expressions of others more accurately. This reduced the incidence of interpersonal misunderstandings and the conflicts that often ensued.

Psychological and behavioral therapy

In the ward, it became apparent that there were psychological nuances to JWH's presentation. The anger and agitation were manifestations of his inner-psyche, made worse when he could not vocalize effectively or was misunderstood. JWH suffered from an inferiority complex. Culturally, being the only male child in a Chinese family meant that he had to have children to carry on the family name. He lamented over what his older sisters had achieved in life such as blissful marriage and freedom to choose their way of life. These milestones made JWH feel like "the sick child" his parents "left behind,"

unwanted and unloved. JWH's parents found him getting jealous and edgy during weddings of their extended family and friends. JWH behaved similarly if he saw his peers romantically partnered. In JWH's feeble attempts to conceal his muscular weakness (due to myopathy from MELAS), he would flex his biceps and even perform squats in front of ward staff to show that he was not a weakling. This display of "manhood," in his own words, sometimes escalated to physical aggression and became more pronounced when he faced persons taller in stature and bigger in physique than him. He would hurl insults loudly like "*small doctor!*" in his first attempt to belittle and frighten staff. JWH's use of aggression against other people may have been assimilated from his father's paternalistic parenting. JWH's parent-directed physical aggression may be related to his father's previous use of physical disciplinary measures.²⁴

The ward psychologist recommended a method building on acceptance and commitment therapy to build his acceptance toward his suffering by improving his avoidance toward difficult situations and taking on a different perspective.²⁵ However, delivery of psychotherapeutic material was limited by JWH's communication deficits, cognitive impairment, and his challenging behaviors with emotional upheaval. The therapist might be curtly shouted at to leave him. On days when JWH was in better form, he could engage in meaningful conversations with the psychologist albeit in a slowed and truncated manner. At the same time, his grief toward what his illness took from him made it exceptionally difficult to move toward acceptance and gaining the flexibility to work on other areas in his life that he can control. A similar difficulty was seen in JWH's parents, who had the expectation that medications alone would completely correct his behavioral problems and extinguish his aggression.

The advanced practice nurse (APN) attempted to moderate their expectations and provide psychoeducation^{26,27} on numerous episodes that psychotropics would have limited effect without parental and behavioral management. JWH's parents had also been taught how he had been "*nurtured over time*."²⁸ The phenotype or structure (such as genetic, epigenetic, anatomical, physiological, behavior, or mental profile) of a person at any given time is considered one's nature. Nurturing refers to a set of processes that generate, maintain, and transform one's nature. The pediatric neurology and adult medicine teams managing JWH understood the same concept. "*Nurtured over time*" described JWH's current "attitude" toward his parents. JWH would be cordial with ward patients and the nurses. The instance JWH's mother appeared in the ward, JWH would march to his bedside cabinet, drag out his bag of old clothes and fling it at his mother's feet shouting, "*What took you so long? Take this and wash!*" At other times, JWH had raised fists at his mother for not attending to his requests immediately. The staff had to intervene and invite JWH's mother to leave.

At the mother's departure, JWH then returned to his own routine in the ward such as sitting by his bedside table and quietly eating.

Individual cognitive psychotherapy was met with difficulty as JWH could not remember and retain well due to poor vision and cognitive decline, and he found it difficult to retain meaningful new information or perspectives presented to him. JWH had continued to ruminate over unpleasant experiences such as intensive care unit admissions and painful medical procedures. The team decided to focus on behavioral modifications and worked with his parents on the implementation of behavioral tactics and management, and successful transfer of this skillset back home. Therefore, the implementation of a simple reward-disincentivizing system was used. During episodes of aggression, the attending nurse would firmly, in an audible volume, instruct him to sit on the allocated chair beside his bed and his family members would be asked to leave the space momentarily. Over time, it was hoped that JWH would learn to appreciate his family's visitations more. The staff made it a point to treat JWH as an "equal" rather than an invalid. JWH also liked to be independent in his b-ADL⁷ as he resented being guarded and monitored.

Psychiatric nursing

Evidence for nursing-care specific for persons with MELAS was sparse.²⁹ The nurses adopted methods such as assisting JWH to adapt to new environments and recognizing his need for caregiver support. They made efforts to know JWH as a person, seeking to understand what he lived through, what makes him agitated, and what would make him calmer or friendlier. The ABC (antecedent, behavior, and consequences) template helped the nurses assess his behaviors and match the nursing interventions to suit JWH's needs appropriately. Charting JWH's behavioral patterns helped immensely with timely medication administration and behavior modification. By intervening to prevent the antecedent, communicating (at JWH's level of cognitive understanding) the potential consequences and redirecting him to other tasks or activities, the problem behavior can be reduced.³⁰

Nursing care revolved around his strong desire for independence. JWH would get upset if anyone attending to him "doubted" his independence. Examples of nursing-care plans individualized for JWH included encouraging his mobility (working with his unsteady gait) around his bedside and placing basic necessities near and around him, and not to offer assistance even if he was seen spilling his food while eating.

Mental health occupational therapy

The mental health occupational therapist (MHOT) used various activities and games to engage JWH. These included simple arithmetic manipulations, visual and sensory puzzles, and playing cards to name a few. His hearing and visual impairment hindered his ability to engage, thereby causing him

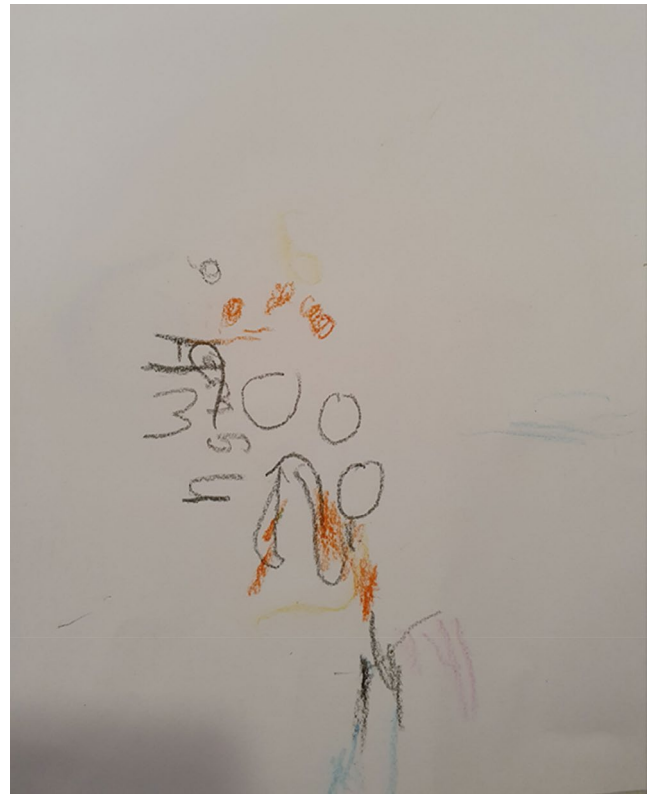


FIGURE 1 Patient's attempt at free-hand drawing of himself

frustration. He was averse to socialization and was not suited for group therapy: Cognitively complex activities were unsuitable for him. He enjoyed interactive games on a tablet (with a larger screen) that involved moving large, brightly colored shapes. This was to build his confidence and ability to enjoy games.

Two artworks of JWH were shown with his parents' permission to illustrate his attempt at drawing with pen and paper (Figure 1) and coloring with an iPad (Figure 2). In Figure 1, despite poor vision, he was trying to draw a picture of himself, showing him wearing his favorite yellow jacket (the yellow bits). In Figure 2, the therapist had used an iPad to guide him in picking colors to fill a picture, of which he dedicated this to his mother. Technological prompts and aids may be useful for patients with cognitive deficits and sensory problems.

2.3 | Follow-up and outcomes

JWH's temper eased with both pharmacological and non-pharmacological interventions. Following interventions, he appeared calmer and more uplifted. A lower dose of Mirtazapine was given in the morning instead of the night and ad-hoc as well, when observed to be angrier and talking with a louder voice. Medication therapy set the stage for de-escalation and distraction.



FIGURE 2 Patient's attempt with iPad-guided coloring

The goal toward the later part of his hospitalization was to empower his parents to care for him and manage his challenging behaviors. JWH began to initiate interest in MHOT activities and built rapport with the nursing team who could discern JWH's likes and dislikes. The parents were only marginally confident. At the last family conference, the family decided for JWH to be institutionalized. His mother, being the main carer, had lost confidence and become fearful of reliving the trauma of being battered by him. His mother was further upset by the observation that JWH continued to treat outsiders (staff and other patients) better than his own parents. His parents continued to feel powerless despite concurred improvement and trials of parent-child activity and home-leave.²⁴

Unfortunately, during JWH's prolonged hospitalization in the psychiatric ward, he developed a stroke-like episode and lactic acidosis. He was started on intravenous arginine and transferred to the HDU. He developed status epilepticus requiring multiple antiepileptics but eventually succumbed to his neurodegenerative illness. The family was hoping the experience that the team and JWH had together could be put together to help future sufferers with similar situations go through treatment successfully.

3 | DISCUSSION

To date, there is no clinical guideline or systematic review of treatment for this group of vulnerable patients.⁷ Although there are no supporting psychosocial interventions in MELAS

syndrome specifically, there continued to be a growing interest in such interventions as monotherapy with psychotropics were recognized to be limited and nontargeted.²⁹ The care for JWH would also not be possible without a multidisciplinary team approach and multiprong interventions from various professionals. There is importance in timing the medication and adjusting its frequency to match the behavioral occurrences to pre-empt and prevent the episodes. In JWH's case, mirtazapine timing was oddly used in the early morning but that had aided him greatly.

The team also realized that better outcomes may be more achievable with earlier referral for psychiatric and behavioral intervention in this group of patients. Patients with rare genetic diseases with young onset and protracted course may carry inherent risks of emotional and relationship problems, possible future violent behavior, substance misuse, and comorbid mental illnesses like depression. These might be mitigated by addressing childhood behavior problems early by adopting strategies targeted at removing ineffective parenting skills and helping parents build confidence and skillsets to handle difficult situations,³¹ before the problem behavior became too fixed and more difficult to treat. As caregivers live with the problem behavior longer, they can get traumatized or become too enmeshed or used to the problem behavior, making it more difficult for them to change and manage their child's problem behavior by the time they seek professional help.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

DYL: conceptualized the initial content and structure of the manuscript. DYL, RYC, and YSL: drafted the manuscript. RYC and YSL: revised and edited the manuscript substantively. All the authors: read and approved the final manuscript. DYL, CRY, and YSL were part of the psychiatric team who had assessed, managed the patient and collaborated with the parents in the care of the patient.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Written informed consent to publish this information was obtained from study participants. Informed consent for publication had been obtained patient's parents via institutional consent form. The manuscript contains no identifier or personal or clinical details that will compromise anonymity.

DATA AVAILABILITY STATEMENT

Not applicable. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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ENDNOTES

- ¹ JWH is a fictitious acronym and does not compromise anonymity.
- ² SSRI, Selective Serotonin Reuptake Inhibitor.
- ³ Serotonin-Noradrenaline Reuptake Inhibitor.
- ⁴ Mono-Amine Oxidase Inhibitor.
- ⁵ Noradrenaline & Specific Serotonergic Antidepressant.
- ⁶ Gamma-Amino-Butyric Acid.
- ⁷ Basic Activities Of Daily Living.

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