Expanding the Phenotype of Mitochondrial Disease – What Every Genetic Counselor Needs to Know

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BACKGROUND

- Mitochondrial disease is typically understood by healthcare providers as a disease of severe neuromuscular manifestations and brain abnormalities, or recognized as various syndromes.
- It is an extremely pleiomorphic condition which can present in almost any system of the body; therefore providers unfamiliar with the disease may not recognize mild or moderately affected patients
- Recent controversies involving several cases in the news have brought mitochondrial disease into the public spotlight due the diagnosis brought into question as possible medical child abuse. One such controversy involved patient Justina Pelletier, who was diagnosed with mitochondrial disease by one doctor but thought to have a psychiatric disorder instead by others.
- This trend highlights a potential lack of awareness and understanding of the medical community and the general public regarding the full spectrum of mitochondrial disorders. This study focuses on patients who do not have the well-known severe phenotypes or syndromes.

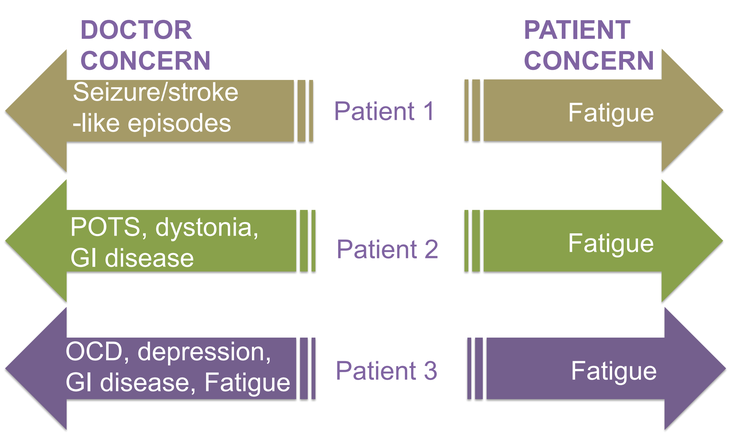
METHODS

Three subjects from different medical centers with longstanding diagnoses of mitochondrial disease were interviewed regarding their experiences in the emergency room, symptoms, and the effects on their daily lives. A literature search was performed to compile a comprehensive list of lesser known mitochondrial symptoms.

Subject Demographics:

- Patient 1: 20 year old male. Diagnosed by muscle biopsy on more affected sib, biochemical testing, DNA (NGS) testing.
- Patient 2: 13 year old female. Diagnosed by muscle biopsy (complex I, III, IV, V deficiency), biochemical testing, DNA (NGS) testing. Her mother was interviewed for this study.
- Patient 3: 24 year old female. Diagnosed by muscle biopsy on more affected sib, biochemical testing, DNA (NGS) testing.

Figure 1. Primary concern of doctors vs. Most debilitating symptom per patient



This poster is presented by Holly Hornung, MS, LCGC.

"When I go to an emergency room that is not familiar with me or mitochondrial disease…"

Every time I go in to an unfamiliar hospital it is stressful. The problem always starts with the paramedics, not listening and saying I can't possibly have what I have, so by the time I get to the hospital everyone is already on edge. Then doctors and nurses alike do one of two things, they either decide they have heard something about some form of mito and they don't need to listen to us, or they say we can't have wrong what is wrong and don't listen to us. Very rarely will a doctor actually consult [my treating physician] about the situation. This causes a great amount of anxiety for me, and in some cases has made my hospital stay much longer than needed because treatment was very delayed. – Patient 1

It's scary when [the doctors or staff] don't understand mitochondrial disease because they don't know how to take care of your child, but it goes beyond that. It's scary because the more knowledge you have and the more you fight for your child, the more at risk you are for alerting the staff [for medical child abuse] and being red flagged for having your child taken away. We often get asked by the doctors in the ER, "Who says she has mito? What makes you think this?" When it's not frightening, it's frustrating, it's exhausting. In the ER when we go in, the [patient's treating specialist] has already called in orders to get an IV started and the tests that need to be run, but because of egos [of the ER physicians], they don't want to follow that. We've had the IV withheld for 2 hours, she can't fast for that long. By the time they order it she's too dehydrated to get an IV in or she's deteriorating. Having mitochondrial disease is like driving a Ferrari with a bad engine. Your body looks good on the outside but inside you feel like crap."
– Mother of Patient 2

During the majority of emergency visits, I was disappointed with the lack of physician knowledge regarding mitochondrial disorders. Most [doctors] were not familiar with my disorder and failed to incorporate it into my care. It created instantaneous friction between my parents, myself, and my physician when we should have all worked as a team. One incident stood out in which a physician admitted that he was not familiar with my disease and asked what he could do for me, acknowledging that I was more knowledgeable on the subject. – Patient 3

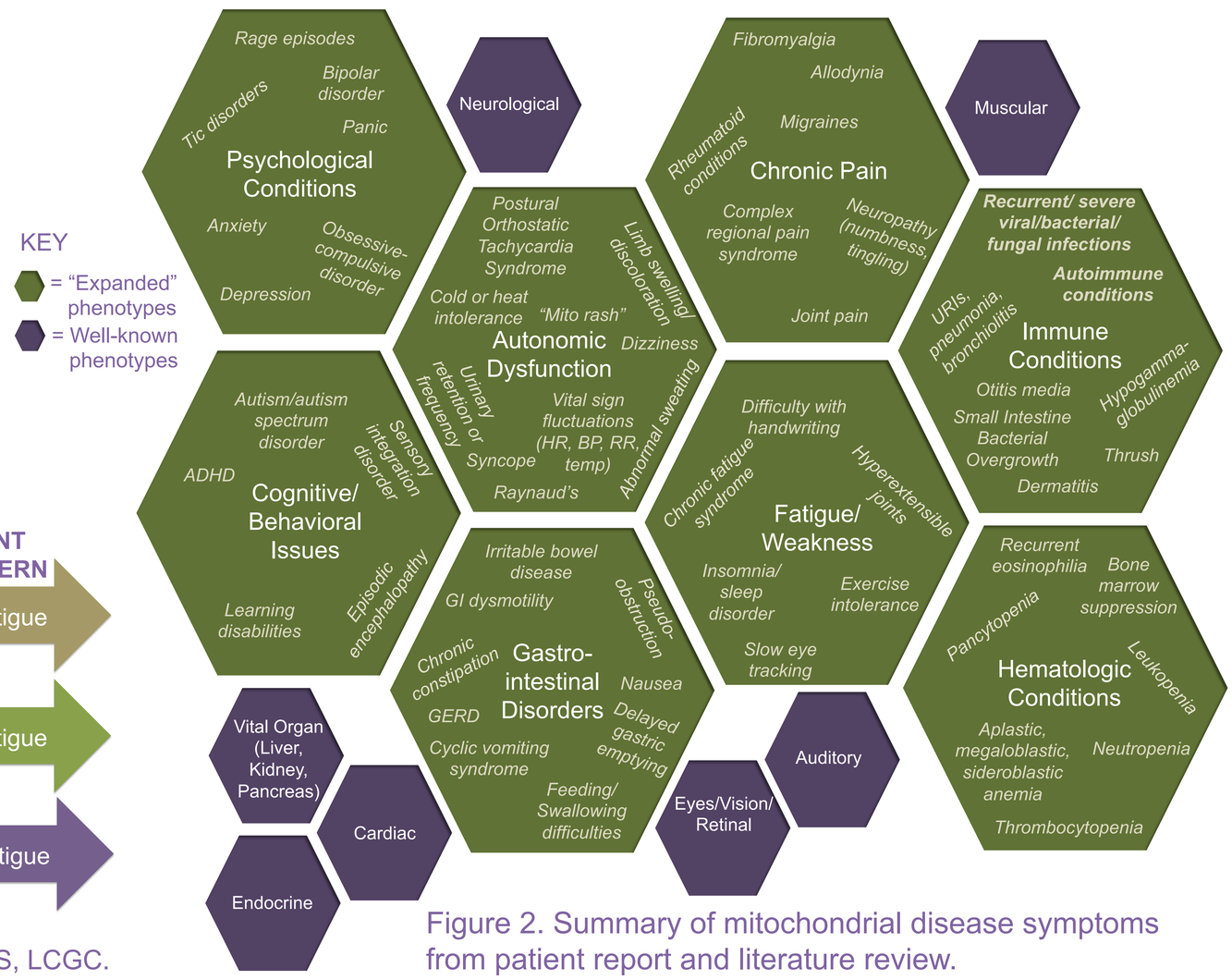


Figure 2. Summary of mitochondrial disease symptoms from patient report and literature review.

DISCUSSION

Mitochondrial disease is complicated to diagnose and difficult to understand or accept due to the following:

1) *EPISODIC*: Manifestations may come and go dependent on energy demand, even lab abnormalities, so many patients may show seemingly normal phenotypes and biochemical lab values if tested when not stressed or ill.
2) *SUBJECTIVE*: Many symptoms are not measurable by standardized methods and rely on the report of the patient. Due to their subjective nature, these symptoms are often perceived as being made up, when in fact are debilitating and disabling.
3) *PLEIOMORPHIC*: Presenting symptoms may be disparate and/or common diseases and may not be recognized as mitochondrial symptoms in the absence of the right context. The patient may present with new symptoms at any age and symptoms may change with age.
4) *"NORMAL APPEARANCE"*: Most mild and moderately affected patients are non-dysmorphic and of normal intellect.

CONCLUSIONS

- Mitochondrial disease is a common disorder (1/4000-1/1000) that is not well recognized, particularly the milder phenotypes.
- Withholding treatment from a patient in an emergent situation can have disastrous consequences; trust of the diagnosis of mitochondrial disease and acceptance and incorporation of the necessary interventions should be established upfront.
- Genetics professionals should take the lead in guiding more appropriate diagnoses and educating fellow providers and the general public, as they are adept in recognizing and understanding complex disease.

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