

## ***What is Leigh Syndrome? If you had MS, I could help you.***

I had the fortunate and unique opportunity to speak with F (pseudonym), a 30-year-old female who suffers from maternally inherited mitochondrial disease. Officially, Leigh-like syndrome. She described the way in which having the condition affects her life, and how her engagement with the health service has affected her.

Leigh Syndrome (LS), also known as subacute necrotizing encephalopathy, is a rare and inherited condition. Usually, signs of the disease become apparent in early infancy, with a loss of motor skills, vomiting or seizures (1). LS ultimately results from defective production of mitochondrial energy. This can be caused by deficiencies or mutations in any of the mitochondrial respiratory chain complexes, but complex I and IV tend to be the most common (2). There are two inheritance patterns for LS: mitochondrial inheritance and nuclear gene-encoded, the latter of which may be autosomal recessive or X-linked. In F's case, the mode of inheritance followed the rarer mitochondrial pattern only occurring in around 20% of cases (1). Unfortunately, there are almost limitless gene mutations at multiple locations which result in mitochondrial diseases like LS, many of which are not yet clearly understood. F explained that her mutation is m.3697 causing Leigh-like syndrome, and that she has complex 1. 'm.3697' represents the mutated allele in a coding gene which is at the MT-ND1 position. This mutation is not only associated with LS but also MELAS and LDYT (3). Discussing her family history, F was very open in telling me about her and her family's experience of sadly losing her brother to the same condition at only 19 months old, just one month after diagnosis.

What I found poignant, was that when she first developed difficulty walking at aged 7, the consultant who also treated her brother told her she was "attention seeking". This dismissal resulted in a delay in diagnosis and consequentially a delay in treatment. At aged 11, F visited a local GP who suggested seeing a specialist at Alder Hey Children's Hospital, given her family history. Here, she was subjected to numerous tests including MRI, kidney scans and eye examinations. F described how some investigations had significant long-term effects for her.

A lumbar puncture induced headaches lasting 10 years and a muscle biopsy performed left her unable to walk:

*“I walked into the hospital and came out in a wheelchair”.*

F recalled how being restricted to a wheelchair stopped her from riding her bike and left her feeling excluded from socialising with her peers. These adverse experiences of engaging with healthcare practitioners at a young age immediately undermines trust in the profession. First experiences of the health service set the tone for a patient’s trust in doctors, and a lack of understanding of symptomology discourages patient’s from seeking out the support they need in future.

On average, patients with rare diseases wait four years before finally receiving a definitive diagnosis which allows them to access treatment (4). F did eventually receive a diagnosis at age 12 based upon brain imaging. The wait for this diagnosis can only have been exacerbated by the fact the family had already lost one child, thus seeing worrying symptoms in another must have been devastating. Because LS only rarely begins after infancy (1), F did not present with ‘typical’ symptoms thus was overlooked, despite her family history. Furthermore, fears and uncertainty surrounding inheritance of mitochondrial disease exist. Establishing correct molecular diagnoses for rare genetic disease is essential for women and couples making reproductive decisions (4). For females with maternally inherited LS, the likelihood of passing on a form of the disease to their offspring is high. This is something that F is aware that she will have to contend with.

F is also registered as severely sighted, however, her experiences of visits to ophthalmologists and eye examinations have not always been positive. When she was just 23, she experienced an abrupt reduction in her vision following a chest infection which she described as:

*“like a power cut to the eyes”*

At the time, she visited an ophthalmologist to test her vision who bluntly told her:

*“If you believe in miracles get hoping. There’s nothing I can do.”*

It shocked me to discover that anyone would converse so abruptly, demonstrating such a lack of empathy, with a patient who has experienced such a life-changing health event. In a study conducted by Royal Blind, questionnaires and interviews were conducted to establish the impact of visual impairment on mental health. Of the 378 respondents, 320 (85%) indicated that their emotional well-being had been challenged by their visual impairment (5). Sight loss inherently causes great changes to way of life for patients which consequentially has a detrimental impact on psychosocial wellbeing. F had only recently achieved a lifetime dream of driving, but her sight loss meant she was unable to take her test. She now only has pixelated vision, is unable to read or watch TV. Patient’s should feel fully supported in navigating these changes by their clinician regardless of ability to actually improve sight.

Adequately co-ordinated care is equally essential. Often, patients must travel to see specialists at great cost financially and inducing a deterioration in health by repeated long journeys. On average, a patient with a rare disease must travel at least two hours for appointments regarding their condition (4). It is challenge enough when these appointments are necessary. Yet, as F told me, she has had experiences of being told she needn’t have made the effort. On one occasion she attended an appointment at the eye hospital, for which she had to pay for trains and hotel stays, only to be told she had wasted the trip. Effective communication between healthcare professionals to ensure appointments are of benefit, and enhanced integration of services would improve the rare disease experience for patients like F. Intrinsically, the nature of rare disease means not every hospital will house the specialists or facilities required for the management of rare conditions. Most rare disease patients will need to see more than one specialist, on average attending at least three clinics (4). F, for example, has contact with neurology, ophthalmology, speech therapy and mitochondrial specialists; to name a few. Currently, in the UK, there are three centres for the delivery of services to patients with rare mitochondrial diseases. These are in London, Newcastle and Oxford and are part of the NHS Highly Specialised Services (HSS) for rare mitochondrial disorders created in April 2007 (6). Although there are other mitochondrial specialists at other centres (6), the likely dispersal of required specialists into many separate centres creates barriers to accessing healthcare for many rare disease patients.

Optimising technology usage can reduce the limitations induced by many rare diseases. F suffers dystonia which she describes as feeling like her muscles are “pulling against each other”. She cannot walk unaided, using a frame indoors and a wheelchair outside. However, she can drive her power chair, which offers her independence. For example, she travels alone to Liverpool to learn Braille. Similarly, her synaptic talking phone gives her additional independence. Audio books and audio description allow for enjoyment of the arts even with increasing sight loss. Atrophy of muscles in the throat have led to a deterioration in speech which, understandably, has affected F’s confidence when speaking on the phone or at events. However, she actively uses social media to remain connected to others through both the Leigh Network and other UK and International mitochondrial groups.

F’s desire to ensure her diagnosis does not prevent her from pursuing her own independence and from helping those with similar conditions has been inspiring. She founded Leigh Network in 2010. The group supports families affected by mitochondrial disease. F is involved in fundraising as well as organising monthly online meetings for the families which, in turn, offers her reassurance. I was saddened to learn of F’s overall negative experience of engaging with the health service; noting only three doctors whom she felt had made her experience a positive one.

Overall, there must be a shift towards a better understanding of the every-day challenges faced by rare disease patients. The perception must change from one of medical ignorance to genuine interest and awareness. A neurologist once asked F:

*“What is Leigh syndrome? If you had MS, I could help you.”*

Although we cannot all be masters of every subspeciality and every rare disorder that comes with it; a generally more compassionate approach when it comes to rare disease goes a long way. Patients are experts of their own condition. It is our job to learn from them and provide the best possible coordinated care while we continue to endeavour to uncover improved treatments and potential cures.

**Acknowledgements:**

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**Abbreviations:**

LS- Leigh Syndrome

MELAS- Mitochondrial Myopathy, Encephalopathy, Lactic acidosis, and Stroke-Like Episodes

LDYT- Leber Optic Atrophy and Dystonia

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