The Long Road to Diagnosis: A Journey of Resilience

During my first year of medical school, I remember sitting in class when one of my hematology lecturers put up a slide entitled "Types of Bleeding Disorders". On that slide, he listed numerous diseases including Immune Thrombocytopenia (ITP). I remember a feeling of excitement that my medical school class was finally going to learn about my rare autoimmune platelet disorder. To my disappointment, the next slide quickly moved on to another subject. That was it. The disease I had been living with since I was 12 years old simply got an honorable mention on one slide. As a medical student, I was relieved that I was not expected to know all 7,000 rare diseases that exist. However, as a patient, I could not help but feel let down, that somehow my disease was not common enough to be taught more extensively to a class of future doctors. I have spent 14 years of my life teaching everyone around me what it means to have ITP, including on some occasions, to health professionals. My path to becoming a doctor was heavily inspired by my diagnosis and the personal challenges I have experienced from living my life around a platelet count. My diagnosis is also the reason why I became a passionate advocate with the Platelet Disorder Support Association (PDSA) to raise public awareness and much needed funds to support other patients with ITP. Nevertheless, I quickly realized that there remains a large gap in medical students' understanding of rare diseases and the unique challenges that rare patients face. Even as a rare patient, I was eager to participate in the Global Genes patient match program, to experience rare disease from a different perspective and to continue to broaden my own biases.

When I first started to get to know Elizabeth[1], I felt instantly connected to her. Like me, she is 26 years old, and grew up in Quebec just a few hours away. Although we had lived very different lives, the many hours that we spent messaging and talking to each other over the last few

[1] All names have been changed to protect the privacy of the patient and her husband in compliance with HIPAA.

months revealed that we could relate to one another on multiple levels. I learned that Elizabeth has been dealing with adversity since the day she entered this world. She was born two months premature and had to remain in an incubator until she was strong enough to leave the hospital. The doctors suspected there was something wrong with her considering she was very hypermobile, had fragile gums, veins and skin that bruised easily and multiple gastrointestinal problems. As a child, Elizabeth was investigated for many different diseases, but most tests at that time could not explain her multiple, seemingly disconnected symptoms. It was not until almost a decade later that one of her doctors suggested the possibility of the Ehlers-Danlos Syndromes (EDS) that things started to make a bit more sense. EDS is a group of inherited connective tissue disorders that result in defective collagen production or function and thus can affect the body on a multi-systemic level. Unfortunately, Elizabeth's mother had died suddenly at 36 from complications during a liver transplant which is now suspected to be related to an undiagnosed rarer form of EDS. At 9 years old the devastating loss of her mother put a serious strain on her family situation and her diagnostic journey was put on hold.

Elizabeth explained to me that she did her best to live a normal life despite the daily struggles of constant musculoskeletal pain, insomnia, fatigue, migraines and easy bruising. She used her hyper flexibility to her advantage and became an excellent belly dancer. Although she was much shorter than her peers, and could not participate in sports due to the risk of injury, Elizabeth loved to read and write. She later pursued a university degree in classical studies. She even went on a trip to England where she unexpectedly fell in love with her now husband.

It was not until April 2015, when Elizabeth experienced an accident at work, that her life seemed to take a turn for the worse. The trauma from her severe back sprain seemed to be the triggering event for the subsequent worsening of all her symptoms. Over the last couple of years

her mobility has decreased significantly to the point where even walking is a daily challenge. She now relies on her mobility scooter or wheelchair to go outside. She also has more frequent dislocations and subluxations that contribute to her long-term joint degeneration and pain. Most recently, Elizabeth described how her lungs felt like they were on fire from aspiration due to her worsened acid reflux. Unfortunately, her deteriorating health state forced her to put her degree on hold and she could no longer work. She expressed to me how grateful she is for her husband James, who has committed to taking care of her full time. She does not know what she would do without his support, especially since she does not get much help from her family. However, the psychological stress on their relationship has not been easy.

A few months after her accident, Elizabeth decided it was time to put an end to her diagnostic odyssey. She had been bounced around between so many specialists over the years with no consistent follow up, and wanted to confirm whether her past physicians' suspicions about EDS were correct. In September of 2015, she was put on a waiting list to see a geneticist to help confirm her EDS and which subtype she may have (there are 13). Almost three years later, Elizabeth is still waiting to get her answers. Although EDS is not curable, it is treatable. A confirmed diagnosis would allow for better treatment management, follow-up and vigilance for specific known complications. Furthermore, an official diagnosis would allow her to finally benefit from financial assistance from the government, which she is currently not eligible for. Considering she cannot work, paying the bills has been extremely difficult. More importantly, Elizabeth would have some peace of mind of finally knowing with certainty what has been causing her life-long health issues.

Elizabeth's story and her long diagnostic journey is not an uncommon occurrence amongst the rare disease community. It is estimated that it can take an average of 8 years for a rare disease patient to get an accurate diagnosis. I cannot begin to imagine what it must have been like for her

to live 26 years in complete uncertainty of her health status. Although my own diagnosis of ITP was one of exclusion, I do not think I fully appreciated how lucky I was that it only took a few days to confirm what I had. Although receiving a diagnosis is never pleasant, it brings about a sense of relief to know why you had those symptoms in the first place, to know what to expect in the future and to be able to seek out the appropriate resources and support groups to deal with your disease. A diagnosis gives you back a sense of power over your health so that you can learn about your disease and become your own best advocate. Without a diagnosis, none of this is possible and can be extremely detrimental to a person's physical, mental and emotional wellbeing.

Hearing about Elizabeth's frustrating hospital experiences have made me realize how much more complex it can be when you have a rare disease that can potentially affect any organ system in the body. I find it difficult enough to keep up with my hematologist appointments, so I can appreciate how much more exhausting it must be to also need to see a rheumatologist, a gastroenterologist and an endocrinologist. This can make coordinating care enormously tough, especially if these specialists do not communicate with each other. Unfortunately, this is the reality that Elizabeth must face on a regular basis. Every time she sees a new specialist, she must repeat her health history and convince her doctors that her new type of pain is not simply from anxiety.

Like many rare disease patients, Elizabeth has become an expert in her own health. She knows which symptoms are part of her baseline and which ones are considered new or worrisome. In anticipation of her confirmed diagnosis, Elizabeth has already spent hundreds of hours reading and learning all she can about EDS. She even has a few friends with EDS thanks to Facebook support groups. Nevertheless, she still experiences a lot of uncertainty every time a new symptom appears because it is not always clear whether that symptom is an "expected" part of EDS, or something else. It is even less reassuring when she often shows up to the emergency department

and no one has heard of EDS before. Elizabeth explained to me how disheartened she feels when the doctors who are supposed to be advocating for her do not believe her or minimize symptoms they do not understand. It is okay if physicians do not have all the answers, but we must be willing to listen to our patients and work as a team to figure out the right solutions.

An unconfirmed diagnosis, lack of awareness, and discordance amongst her numerous doctors, are the biggest factors inhibiting Elizabeth from having a good quality of life despite her illness. These are just some of the issues that I hoped to tackle when a few of my colleagues and I founded our medical school's first Rare Disease Interest Group (rareDIG). In just this past year, we have organized multiple events to help prepare future physicians for the reality of rare disease and to foster positive, open-minded attitudes about helping rare patients. Our "Patient Perspective Series" events allowed medical students to learn directly from the daily experiences of rare patients and how to build trusting therapeutic relationships with them. Our Rare Disease Day event in February featured inspiring talks from leaders in the rare disease community. The event brought together over 100 attendees from different health professions, patients and their families, to raise awareness and exchange innovative ideas. Our journal club event taught medical students how to navigate the often-scarce literature that is available on rare diseases. I think we have made great progress in bringing rare disease challenges into the spotlight. We are only just beginning, however, to figure out how to provide medical professionals with concrete tools that could effectively shorten the diagnostic odyssey, that patients like Elizabeth, have been on for too long.

In medical school, we are taught so many 'approaches' to common presenting complaints. These algorithms help us to know which questions to ask on history, what to look for on physical exam, and which tests to order to confirm our diagnosis. Elizabeth's story made me realize that we do not have an approach for the undiagnosed patient. What if the usual tests come back normal

and the patient's symptoms have no obvious connection? Where do we go from there? This is likely the point where most rare patients experience a dead end in their diagnostic work-up. To change this, I plan to organize workshops for medical students that provide an approach to the rare or undiagnosed patient. If we are not going to learn all 7,000 rare diseases then we need to learn how to recognize important constellations of symptoms or identifying features that could point us towards specific groups of diseases, like connective tissue disorders. We would partner with geneticists to teach us these basic skills and then learn how and when it is appropriate to refer our patients to them. Having this foundation early on would allow physicians to put rare patients in contact with the right specialists in a timely fashion. Furthermore, rareDIG has just started to collaborate with research groups in Toronto that are working on creating applications for physicians and medical trainees to annotate symptoms that we see in rare patients. This information can then be compiled in databases and shared around the world. This would allow us to better characterize rare diseases like EDS and constantly update their often-changing symptom profiles. The more we understand about how a disease presents, the easier it will be to diagnosis it.

I am humbled and grateful to Elizabeth for letting me into her world and opening my eyes to aspects of rare disease, that even as a rare patient, I never truly appreciated before. We look forward to keeping in touch and I hope to involve her in one of our future rareDIG events, so that other medical students can learn from the important lessons that have come out of her story. It takes a certain kind of resilience to not give up on a diagnostic journey as long as hers. I think the value of having an accurate diagnosis, no matter how rare, can often be overlooked by physicians. Yet, it is the most important first step in the long healing process. I hope all future and present physicians take it upon themselves to continue looking for answers for their patients, even if at first those answers are hard to find.