TITLE: The Power in a Name: Teaching future doctors the value of providing a definitive diagnosis in the support of patients with rare disease

QUESTION

Living with a rare disease is a life-long learning experience in which patients become experts in their own disease. Use a case study to demonstrate what future doctors can learn from patients with rare diseases.

INTRODUCTION

In medical school, our understanding of disease begins with first identifying the condition; giving it a name, a definition, a classification. We see the value of diagnosis as a tool to providing the right treatment, and for most common diseases once we have found our answer, clear protocols and guidelines exist to aid this. The reality for sufferers of rare diseases, however, is less straightforward and the significance of a recognisable name for their condition goes beyond just medical need.

WHY DIAGNOSIS IS IMPORTANT IN RARE DISEASE

For conditions that go largely unrecognised, even within the medical community; where research is often in its early stages and effective treatment lacking, patients naturally become the experts in their own disease. For many rare diseases, patient groups exist for this exact purpose; offering a supportive community to share experiences and remain informed. Additionally, with a name to stand behind, the potential for patient-centred advocacy can lead the push for more awareness, funding and research to actively improve our understanding of less common conditions[(1)].

Consequently, when individuals are left without a diagnosis, they exist in a state of uncertainty. Unable to access these support groups, they rely entirely on medical professionals to understand their health, which can leave them feeling helpless, disconnected and left in the dark. This sentiment was especially true for Clare, the mother of identical twin girls Pip and Alix, who spent many years without answer before their diagnosis of the newly identified DDX3X Syndrome in 2015.

DDX3X SYNDROME

Before making contact with Clare, I had never heard of DDX3X syndrome, which is unsurprising as there are only around 250 known cases worldwide[2]. First reported in 2014, DDX3X syndrome is a genetic disorder, caused by a de novo (also known as spontaneous) mutation in the DDX3X gene, on the X chromosome of affected females[3]. The condition exists as a spectrum, presenting with a range of differing severities in different individuals, but all those affected will have some degree of intellectual disability or developmental delay. Other common features are communication difficulties, low muscle tone and neurological problems such as epilepsy[4]. As of now there is no specific treatment available for DDX3X patients, and they are managed according to their individual medical needs.

Initial research is still ongoing, but experts believe 1%–3% of cases of intellectual disability in females with no known cause could be due to a DDX3X mutation[4]. Despite the short amount of time since its discovery, there is an American DDX3X foundation dedicated to spreading awareness and registering affected individuals(2). In the UK, there is an active DDX3X Support Facebook group, of which Clare is an active member.

LIFE BEFORE DIAGNOSIS

Clare first suspected that Pip and Alix might have some form of developmental delay when they began to miss milestones. At age two neither of them could sit up without support while, on average, children achieve this between six and nine months of life[5]. The next period of their life, Clare describes as a "blur", filled with many doctors and specialists, but unfortunately no one could identify their underlying condition. As a result, their treatment was largely aimed at managing individual health needs as they arose, including speech problems, sensory issues and attention difficulties.

Without a diagnosis, it was challenging to get the care they desperately needed. Clare felt the label of ‘learning difficulties’ was too broad and ultimately meant different things to different people. It was a struggle to obtain the communication devices that allows Pip to convey basic phrases and the one-to-one support that helped them in the school often became " two for the price of one", Clare told me. " It was hard to get people to see that even though they were twins, Alix needs additional support to Pip, and a one size fits all approach suited neither of them".

During this period, Pip and Alix attended various different support groups for many more common and better understood conditions, such as cerebral palsy, as well as other physical disabilities, but they did not find one that resonated with them. "The people were lovely, but we didn't quite fit in or share the same experiences". It was not until they finally got a diagnosis, that things started to change.

GETTING ANSWERS

By the age of ten, Pip and Alix had attended appointments with 142 health professionals; after this age, Clare no longer kept count. In 2011, the twins were registered by one of their doctors to partake in the NHS funded "Deciphering Developmental Disorders" study, sending off a sample of saliva. The study aim was to recognise DNA mutations, in order to discover the genetic cause for developmental conditions, through the use of genome sequencing techniques to[(6)].

It was not until four years had passed that Clare received an update, "I had almost forgotten about it, to be honest," she stated. In a genetics appointment in 2015, at the age of 15, Pip and Alix finally received the diagnosis of DDX3X syndrome. It was then that Clare was handed a copy of the very first research paper to mention the condition, published only a month previously by the "The American Journal of Genetics"[(4)].

IMPACT OF DIAGNOSIS

I had thought the most life-changing part of getting a diagnosis would be access to better treatment, or in the absence of this, the opportunity to join clinical trials to receive new, more experimental treatment. In fact, for Pip and Alix, it has had limited effect on the medical care they receive. Speaking with Clare has shown me the value of diagnosis is more than changes in treatment regimes.

In Clare's experience, "people tend to listen more carefully and take what you say more seriously when you have a name for your condition". Soon after Pip and Alix's diagnosis, the American DDX3X foundation was formed. Reaching out to the foundation, and meeting with UK families, was a wonderful experience for Clare, and provided the opportunity to identify as part of a wider community.

Speaking to parents of other children with DDX3X syndrome, was also beneficial for Pip and Alix regarding treatment. Both twins had experienced from constipation for much of their lives, a fact which doctors had attributed as a consequence of their learning difficulties, assuring this would pass with time. In fact, relating to other girls with DDX3X showed others suffered from the same problem. This connection led to the twins undergoing gut transit studies, which discovered an intestinal problem was the underlying cause. After this revelation and receiving appropriate treatment, their symptoms improved.

Ultimately, receiving the diagnosis of DDX3X has mobilised a group of patients; allowing them to speak as one in advocating for their condition. With a name, they can raise awareness, encourage future research, raise funding and most importantly create a supportive community, for people just like them.

WHAT DOES THIS TEACH FUTURE DOCTORS?

Even in conditions like DDX3X, where no specific treatment exists and the presence of a diagnosis does little to change disease management, providing patients with a name for their condition is immensely beneficial. While this is not always feasible, and some patients may have a while to wait before medical science can give them the answers they desperately want, we can still help them. By encouraging patients to join support groups, in person or over the internet, can give them the support any patient with a lifelong condition should have access to it.

In a time of NHS funding cuts, patients often have to fight to ensure their condition is deemed a priority. For sufferers of rare diseases, this battle is only more challenging. The best doctors will strive to provide the best, most effective care possible, for their patients. What is just as important, however, is giving patients the chance to advocate for themselves and their condition. The first, and often the most challenging step; giving them a name to stand behind.

REFERENCE LIST

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