## Collaboration in Medicine: a Case Study into how teamwork was used to produce a successful treatment plan for rare diseases.

When treating a patient diagnosed with a rare disease, a healthcare provider must understand that their patient is an expert in their condition (1), especially due to the rarity of the diagnosis and little patient data to help guide their management plans. Therefore, patient testimonies are crucial to assisting doctors to receive a holistic view of how rare diseases affect their quality of life and helping other newly diagnosed patients understand what a typical prognosis of their condition can look like. Often, the journey to receiving a rare disease diagnosis is a diagnosis of exclusion, which means that many patients will anxiously be tested for many differential diagnoses, and undergo numerous scans, referrals, blood tests etc., until their diagnosis is reached. Constant handovers between different healthcare teams and specialists until a diagnosis has been narrowed down can become an emotionally taxing and fearful ordeal for patients (2). This essay uses a case study to explore how collaboration within healthcare and charities/organisations can support and empower patients to navigate their illness and ensure a better quality of life.

### Generalised Lymphatic Anomaly (GLA)

Generalised Lymphatic Anomaly (GLA), previously called Lymphangiomatosis, falls under 'Complex Lymphatic Anomalies' (CLA), where it involves non-typical lymphatic system activity. This is alongside Gorham Stout Disease (GSD), Kaposiform Lymphangiomatosis (KLA) and Central Conducting Lymphatic Anomaly (CCLA), which all fall under CLA (3).

CLA's can show a focal or generalised infiltration of the lymphatic system. It can be characterised by a range of excess pericardial or pleural effusions and can present with bone pathologies as well, such as osteolysis (4). In other forms of CLA such as GSD or KLA, there are risks of significant haemorrhages, CSF leakages or spinal cord lesions, which can progress to severe neurological symptoms such as paralysis (5).

GLA is believed to be a condition triggered by a congenital error in lymphatic system development during the 20th week of gestation (6), although this is still unclear. GLA may also triggered by a mechanical obstruction of the lymph system associated with lymphedema (7). It has been associated with mutations in the phosphoinositide 3-kinase pathway (PI3K) in lymphatic malformation, and somatic NRAS mutations in lymphatic endothelium (8).

The general prognosis of GLA is poor, especially if diagnosed within childhood or adolescence. In comparison, KLA tends to have more of an aggressive onset and requires early diagnosis due to higher mortality rates (9).

### Case Study

In this case study, I had the opportunity to speak with Kelly, a mother of two whose 17-year-old daughter Cate had been diagnosed with GLA in her teenage years. Cate grew up with little to no serious medical issues and enjoyed attending school and a highly active lifestyle.

A few years prior, Cate was driven to her local children's hospital to receive an X-Ray after an incident where she had tripped in her backyard and fallen on her shoulder. Her radiologist observed that her shoulder was perfectly fine but noticed an alarming amount of right lung pleural effusion in the corner of her X-Ray. Now, Cate was immediately admitted for something completely unrelated to her initial complaint and was advised to receive a thoracostomy done on her right lung, which showed 1300Cc or mL of effusion drained. GLA is a rare cause of pleural effusion, due to the systemic spread of lymph duct lesions that is observed in GLA that can lead to fluid accumulation in the pleural, pericardial and mediastinal spaces (10).

Cate being admitted to a children's cancer ward and rigorously tested for cancer had made her admission fraught and nerve-wracking. The constant rounds of medical students who observed Cate as the doctors discussed possible aetiologies of her condition had only raised the family's anxiety further. A bone biopsy was taken on her sternum, confirming a sternal lesion at which point the onco-haematologist started to suspect GLA. The incidental discovery of asymptomatic pleural effusion by the radiologist was integral to Cate's journey to being diagnosed, which reflects the insidious onset of GLA. Despite it being commonly a congenital disorder (thought to be spurred by a malformation of the lymphatic system in utero), the quiet onset symptoms can present in childhood, adolescence or in adulthood too (11). Unusually, Cate had reported feeling fine in the days leading up to her hospital admission, only mentioning in hindsight that she had experienced very slight shortness of breath a few isolated times but had thought it to be benign. After having a pleurodesis procedure done, Cate's pleural effusion finally stopped.

From Kelly's perspective, she appreciated Cate's current doctors' stark honesty in acknowledging their inexperience in treating Cate's condition, and the need for her to liaise with other expert doctors in this field. Upon news of her diagnosis, Cate's doctor recommended that she meet with Dr Denise Adams at Children's Hospital Philadelphia, an expert in lymphatic abnormalities in children and adolescents. Upon flying to Philadelphia, Dr Adams had arranged for Cate to have a full MRL, where her entire lymphatic system was mapped. The MRL would soon become a regular monitoring procedure for Cate for the foreseeable future.

Cate was administered Sirolimus, a transplant drug that proved to be successful in regulating her lymphatic system, as shown in recent studies covering GLA and GSD treatment (12). Cate responded well to Sirolimus and started to reduce the frequency with which she would come in for checkups. Now, Cate attends checkups every 6 months where she has an MRL done and is reviewed for any pain, exertional dyspnoea, coughing or any notable lung auscultation findings. After three normal MRLs and checkups off medication, Cate has shown great improvement.

Remarkably, Cate showed great strength during her diagnosis and despite her condition, adhered strictly to her treatment plan and continued to do what she loved. She still strives to attend school and partake in her hobbies and active lifestyle and sees herself as an independent, normal teenager not defined by her condition.

<u>Organisations for Rare Diseases</u>

Another striking example from Kelly & Cate's story was the importance of healthcare organisations or charities that seek to uplift those who are living with rare conditions. Lymphangiomatosis and Gorham's Disease Alliance (LGDA) is a charity founded by Jana Sheets, a woman who was diagnosed with GLA but struggled to find other patients to connect with other the uncertainty and lack of research and information surrounding her GLA condition. Jana, on her website before passing in 2010, said something that had struck me. She said that in hindsight, she wished her childhood diagnosis had been cancer, as it would at least have had doctors "interested in the diagnosis and actively researching it" (13).

LGDA supported Kelly and put her in contact with a seventy-year-old woman called Eva who had been living with GLA for almost her entire life. Just hearing about Eva's existence, as an elderly woman who had successfully managed her GLA on the same Sirolimus regimen, and lived a fulfilling life greatly reassured Kelly, as her initial impression of GLA was that every person who was diagnosed would show poor prognosis and early mortality.

Doctor-patient Relationships

From my research on LGDA's work, and hearing from Kelly and Cate's firsthand experience when navigating Cate's diagnosis, I was reminded of the challenges surrounding diagnosing rare diseases. It was challenging for the healthcare team as well, as they had to seek other expert's opinion as there was no gold standard, concrete treatment plan for GLA like there would be for other more commonly diagnosed conditions.

From a patient's perspective, I learnt about the uncertainty and insecurity regarding the prognosis of a rare condition, or the impact it may have on lifestyle. With little information or patient stories readily available on the internet and around us, it is more important than ever to have healthcare professionals and organisations advocate and support you. This essay focuses on healthcare professionals, but I wanted to mention LGDA as an organisation for rare disorders, especially as I believe more hospitals or healthcare institutes should work closely with charities and organisations like the LGDA to provide further support to patients who are seeking a community.

Kelly and Cate's story helped remind me of the importance of shifting from a paternalistic to a mutually understanding doctor-patient relationship in healthcare systems worldwide, especially when managing a rare condition shrouded by uncertainty and insecurity. Overall, Cate's treatment was successful, and they had a positive experience with their multidisciplinary clinical team. Both Cate and her family were treated as equal partners in their healthcare team and felt that their input was highly valued in deciding the best management plan that would align with Cate's values as a patient. The importance of showing empathy and forming a good rapport with a patient is essential to help them trust in the healthcare provider and encourage successfully adhering to a management plan which can greatly improve their quality of life when living with chronic, rare conditions.

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