A quick reference guide for rare disease: supporting rare disease management in general practice

INTRODUCTION

A rare disease is defined as any life-limiting or chronically debilitating disease affecting <1 person in 2000, with many rare diseases affecting <1 person per 100 000. There are approximately 8000 rare diseases, with recent analysis suggesting a conservative prevalence of 3.5–5.9%. Over the last decade, tremendous advances have been made in rare disease identification, treatment, and support. This has been largely driven by an increasingly vehement consolidated patient voice and an EU directive (2009) that all member states required a rare disease plan/strategy by 2013. In 2013, the UK strategy for rare disease was published, followed by the launch of rare disease implementation plans for the devolved nations (Scotland in 2014; Northern Ireland in 2015; Wales in 2017).

DIFFICULTIES WITH DIAGNOSIS

Rare diseases have major unmet medical needs. Healthcare professionals and rare disease charities often hear tragic stories of patients with rare life-threatening diseases where responsible doctors have been unable to help as they have never heard of the condition, nor seen a similar case presentation, nor found relevant knowledge and expertise online. More than 80% of individuals report difficulty in accessing relevant information and >70% of GPs struggle to identify or manage rare diseases. A long diagnostic odyssey is common, with patients often feeling misunderstood, isolated, vulnerable, receiving incorrect diagnoses, and feeling marginalised in decision making. The average time to receive an accurate rare disease diagnosis is 5 years, with half of patients with rare disease receiving at least one misdiagnosis. Even with a diagnosis, more than half of rare diseases do not have a dedicated support group. As a result, rare disease patients and families often feel self-advocacy is essential so they become experts in their own conditions, conducting extensive research and travelling worldwide to speak to professional experts and attend relevant conferences.

RESOURCES FOR GPs

Despite GPs having considerable expertise managing multisystem disease and (often uniquely) having oversight of long-term patient healthcare records, few have the resources to thoroughly research rare diseases and many report becoming overwhelmed as patients attend with detailed reports about rare conditions. Doctors often seek information on the internet, but it is difficult to know what information is trustworthy and where to direct patients for further support. Approximately 80% of rare diseases have a genetic cause, with others including rare cancers, autoimmune diseases, and toxic and infectious diseases; the molecular basis is known for one-third of these rare genetic conditions, so referral to a local genetics service is advised. Patients with a rare disease often present to their GP with unusual symptoms or signs that are difficult to diagnose, multiple diagnoses that in combination seem unlikely, and/or multiple ‘umbrella’ diagnoses (Figure 1). Useful resources include:

- Orphanet (https://www.orpha.net) is an internationally recognised one-stop online portal for collating high-quality knowledge and information on rare disease diagnosis, care, and treatment. It contains rare disease literature, reviewed by medical experts, that any member of the public may search through, as well as information on orphan drugs, patient organisations, experts in particular conditions, research expert centres, and medical laboratories that provide diagnostic testing.
- Launched in March 2017, European
Could your patient have a rare disease?

1 in 17 people have a rare disease. That means rare disease affects 1% of the population. Rare diseases can be life-threatening and lead to premature death. Even if the disease is not to be lethal, it can be fatal for the quality of life.

Does your patient have a rare disease? A rare disease is a disease or health condition that affects fewer than 1 in 2000 people in the EU. The British government defines rare disease as a condition affecting fewer than 1 in 2000 people in the UK.

Some of the common symptoms of rare diseases are:
- Diagnoses of a rare disease in a child or young adult, in which patients can have intellectual disabilities and/or a physical disability.
- 10% of rare diseases have a genetic cause, leading to genetic sensitivity.
- 75% of rare diseases require highly specialisation treatment.
- 50% of all patients with a rare disease healthcare system.
- Newborn screening programmes for rare diseases.

Key rare disease facts

Information and support

For Diagnosis: www.rarediseases.org (aimed at clinicians and scientists)
www.undiscovered.org.uk (aimed at patients, open to patients)
www.mendelian.co (aimed at patients)

For Support:
www.nirdp.org.uk (Northern Ireland)
www.ird.org.uk (IRland)
www.rcgp.org.uk (Scotland)
www.crowdmed.com (USA)
www.mendelian.co (USA)
www.mendelian.co (Australia)

Additional Resources:
www.swan.org.uk (Syndromes Without A Name; www.undiscovered.org.uk)
www.rarechromo.org.uk (Rare Chromosome Conditions Network for families with undiagnosed conditions)
www.rcgp.org.uk (general practitioners to help improve diagnosis and treatment of rare diseases)

Figure 1. Rare disease diagnosis and management support.

REFERENCES


Mendelian (www.mendelian.co) helps doctors match phenotypes and genotypes. CrowdMed (www.crowdmed.com) is a patient-oriented resource where medical detectives have helped solve challenging cases and provided many diagnoses within the rare disease community.

THE FUTURE OF TREATMENT

‘Big data’ approaches offer significant potential to improve rare disease identification and visibility; however, this means that careful data entry to electronic health and social care systems is essential. One strategy to improve information standards and data retrieval is using enhanced coding nomenclature in information systems such as using an ORPHA number or updated 11th revision of the international classification of diseases (ICD-11) codes. Information systems still need upgrading to make using these codes simple and efficient.

An increasing number of medications and clinical trials are available to the rare disease community. Although designing an orphan drug may not be intuitively competitive for pharmaceutical companies, rare disease drugs often have a faster path to commercialisation and attractive regulatory incentives. The US Food and Drug Administration Office of Orphan Products Development currently has 4699 listed treatments approved for rare diseases (orphan drugs), while the UK clinical trial gateway collates information to help informed decision making. Scientific advances such as international registries and biorepositories for rare diseases, improved molecular characterisation through initiatives such as the UK 100 000 genomes project, genetic editing, induced pluripotent stem cells (iPSCs), and RNA interference (RNAi) technologies are paving the way for the development of accessible treatments for patients with a rare disease.

Funding

Ashleen Crowe: PhD studentship from the Department for the Economy, Northern Ireland. Medical Research Council – Northern Ireland Executive supports the Northern Ireland Genomic Medicine Centre though Belfast Health and Social Care Trust.

Provenance

Freely submitted; externally peer reviewed.