Speech by Manuela Lotze (patient)
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Rare disease or only rarely treated?

Since we encountered a few inconsistencies in the diagnosis and non-treatment of Fabry disease, we had to investigate the correlations more intensively than we thought as non-professionals. We noticed that there are still many unanswered questions:

- Mutations that occur more frequently in the population are already ruled out at the time of diagnosis.
- Although all organs can be affected, the 'recognized symptoms' are limited to a few organ systems.
- Biomarkers are not reliable. Even in men, a genetic defect cannot be ruled out despite normal Lyso Gb3 or alphagalactosidase values, so a genetic test must always be carried out. But it won't.
- The therapy is only prescribed in the case of proven organ damage, although this should actually be prevented.
- Why more women than men are affected. In the Centogene database, for example, there are 3 times as many women as men. However, a mutation is considered benign as long as men do not have more severe symptoms than women.
- Why some men have no symptoms.
- Which, apart from the deposition of Gb3, also leads to cell damage, such as cell stress due to the breakdown of misfolded enzymes...

There are over 1000 different mutations. Some of these are found more frequently in the population and the full range of phenotypes has been observed within these mutations. Everything has been described, from the so-called classic type to the late-onset with involvement of only one organ to the symptom-free man. There is therefore a wide range of variants within a mutation, from symptom-free to severely affected. Two of these common mutations are D313Y and A143T.

These are increasingly being excluded from diagnosis and therapy. In other countries they are already considered benign. In Germany, the D313Y was no longer reported by at least one laboratory, patients received a negative result although a mutation in the GLA gene was found in the laboratory.

It annoyed us that patients are not treated despite a proven genetic defect and massive complaints.

It is also incomprehensible to us how a mutation that has been recognized as pathogenic can suddenly be classified as benign, although severely affected patients are being treated at the same time.

We have looked intensively at the studies on these mutations and have come to the following conclusion:

- There is no robust study that can prove that the mutations D313Y and A143T are benign.
- Many studies point to a 2003 study on double mutations, which concluded that symptomatic D313Y carriers must have a second mutation in the GLA gene. There is no recent scientific data for this thesis.
- Studies that prove that the mutations cause illness are apparently ignored.

Why people are so stubbornly interested in excluding these mutations is a mystery to us. We were told it was a political decision. For us, politics means power and money. A possible explanation could be that the pharmaceutical industry does not want to lose the status of the rare disease. The average therapy costs are €250,000/year and patient. A disease is considered rare if it affects no more than 5 in 10,000 people. That is the equivalent of 1 in 2000. The number of undetected Fabry patients is estimated to be very high. It is now assumed that in many patients the disease is not recognized during their lifetime and that premature death is attributed to other diseases.

There are many misdiagnoses such as multiple sclerosis, rheumatic diseases and much more. All known differential and misdiagnoses can be found at d313y.org or a143t.org.

Somatization disorder is also one of the most common misdiagnoses. You do not get the psychosomatic diagnosis, as might be expected, after all possible organic causes have been ruled out, but when you as a patient consult several doctors and question the diagnosis, the treatment or the medical system. Once it is on record, doctors are advised not to carry out any further investigations in order not to confirm the patient in the assumption of an organic cause.

Therefore we would like to contribute to the clarification with our side, so that some of the rare ones again are not categorized as psychosomatic and are only treated symptomatically, although a causal therapy is available.

Pain is our daily companion. There is hardly any satisfactory pain therapy. We can't imagine how many suicides there are among those who are not fortunate enough to find support from their families and friends.

We wish us:

- That the diagnosis "psychosomatic" is not made so lightly, because with this diagnosis one is doomed and it is difficult to find a doctor who looks for other causes.
- That no mutation is excluded from treatment and diagnosis, but that each case is considered individually.
- That the laboratory that sent the patient a negative genetic finding, although a GLA variant was found, corrects these findings and informs the patients or their doctors about it.
- That the therapy is not only prescribed when organ damage has been proven, but based on the symptoms with the aim of preventing organ damage.
- More information about the connections between neurological symptoms.
- That other organ involvements are researched: thyroid gland, connective tissue, joints...
- That the cost of therapy will be reduced to invalidate the claim of the placebo effect that is supposedly created by receiving such an expensive drug.
- More support for patients in social matters, such as through the use of Fabry pilots.
- Easier access to therapies of the remedy regulation such as physical therapy, lymphatic drainage, ergotherapy or foot care.
- Better networking between patients, because ultimately we all want a life worth living for ourselves and our families.