INTRODUCTION

The GM2 gangliosidoses are a group of autosomal recessive lysosomal storage disorders that cause a progressive deterioration of nerve cells. Three disorders include: Tay-Sachs (TS) and Sandhoff disease (SD), caused by mutations in the HEXA and HEXB genes, respectively, leading to a deficiency of the hexosaminidase A (HEXA) enzyme in both diseases and hexosaminidase B (HEXB) in SD. Mutated enzymes are no longer able to break down GM2 gangliosides and other molecules, which all then accumulate in the neurons of the brain and spinal cord to toxic levels.

TS and SD are clinically indistinguishable and present as progressive loss of central nervous system function.1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22

Juvenile and adult forms are more variable in the age of onset and symptomatology range. Both display slower progression. However, whilst the adult form may never reach a full level of physical or mental retardation, both forms are fatal.

Juvenile TS and SD patients in order to serve as a research platform of real-world data for improving outcomes of patients suffering from Tay Sachs and Sandhoff diseases.

OBJECTIVES

The objective of the GM2DR was to gather information on multinational TS and SD patients in order to serve as a research platform of real-world data for epidemiological and translational research, and to contribute to a better understanding of the longitudinal progression of disease.

METHODS

Registry Design

The GM2DR was designed using a meticulous and collaborative multi stakeholder approach following an initiative of the United Kingdom (UK)-based CATS Foundation and the Spanish-based ACTAYS with the support of the European Tay-Sachs and Sandhoff Charities Consortium (ETSSC) member organizations.

RESULTS

— A high volume of data per patient was collected and, as a result, the GM2DR houses a rich data set containing information about TS and SD that can be made available for research.
— The registry went live on June 3, 2015, the first patient enrolled on that day.

Patients and eligibility criteria

— Patients (n=114; 85 TS and 29 SD) were identified through the ETSSC, via referrals at diagnosis centers, and through social media.
— Inclusion criteria were as follows:
— Diagnosed with TS or SD following the 2015/2016 assessment prior to 2015 but still alive at the time of enrollment.
— European national or domiciled in Europe.
— Patients (n=8) or their caregivers (n=106) provided informed consent.

Data collection and management

— Data is collected via a secure web-based platform and is managed by the Open App registry system. Data is protected and stored in the Open App registry system.

Data on sociodemographic and disease-related characteristics

Patients (n=114) were distributed over the following countries: Austria, Belgium, Cyprus, France, Germany, Hungary, Italy, Netherlands, Poland, Portugal, Sovereign States (Australia, Switzerland, Turkey, UK), as well as 4 ex-EU residents in the United States and Australia. See Figure 1.

There were 89 patients with the infantile form (n=114), 17 patients with the juvenile form (n=114), and 8 with the adult form (n=114). See Table 1.

There were also 2 patients residing in the United States and 1 patient in Australia.

— Amongst the most common form, the infantile one, on average, patients were diagnosed at 18.8 years old (ranging from 1 month to 71 years old). Among patients with the juvenile form, on average, they were diagnosed at 4.2 years old (ranging from 1 month to 17 years old). Around half (52%) were female (n=59; 44 TS and 15 SD).
— The registry included patients from the UK (n=28; 23 TS and 5 SD), Spain (n=18; n=27 TS and 4 SD), and Germany (n=14; n=10 TS and 4 SD). See Table 1.

— The majority resided in the UK (25%, n=28; 23 TS and 5 SD), Spain (18%, n=18; 27 TS and 4 SD), and Germany (14%, n=14; 10 TS and 4 SD). See Table 1.

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— Amongst the patients with the infantile form who were still alive (n=41), the mean age was 5.3 years old. See Figure 4. Among those with the infantile form for whom data was available, the average age of death was 4.2 years old. See Figure 5.

— As of April 2020, the complete dataset included 75% (n=85) of patients with TS and 25% (n=29) patients with SD. Around half (52%) were female (n=59; 44 TS and 15 SD).

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