International Niemann-Pick Disease Registry: the characteristics of ASMD and NPC patients

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Introduction

- Niemann-Pick Diseases (NPD) are heterogeneous lysosomal storage disorders with low prevalence and poor understanding.
- Acid sphingomyelinase-deficiency disease (ASMD) and Niemann-Pick Type C (NPC) arise from mutations in the SMPD1 gene and NPC1 or NPC2 genes respectively.
- Incidences are estimated to be 0.5 per 100,000 births for ASMD and estimated ~ 1: 100,000 births for NPC (1).
- The International Niemann-Pick Disease Registry (INPDR), a not-for-profit organisation, has been running a well-established an Electronic Data Capture platform since 2014 for the systematic and uniform collection of NPD clinical data.

Aim

To investigate the clinical characteristics of ASMD and NPC patients enrolled into the INPDR

Results

Patient Demographics

- At the time of analysis, the median (range) age was 4.9 (N=1) for NPA, 26.9 (6.0-87.0) for NPB and 23.2 (2.2-74.3) for NPC.
- The median (range) age at diagnosis was 1.1 (0.3-2.9) years for NPA, 8.8 (0.8-62.7) years for NPB and 5.0 (0.0-68.1) years for NPC.
- No statistically significant sex differences in age at diagnosis and death were detected in NPC patients.
- SMPD1 mutations were confirmed in 20 ASMD patients.
- 97% of NPC patients were reported as having the NPC1 subtype
- Baseline characteristics are summarized in **Table 2**

	NPA (N=17)	NPB (N=41)	NPC (N=198)
Age at analysis, years Median (Range)	4.9 (N=1)	29.6 (6.0-87.0)	23.2 (2.2-74.3)
Age at diagnosis, years Median (Range)	1.1 (0.3-2.9)	8.8 (0.8-62.7)	5.0 (0.0-68.1)
Age at death, years Median (Range)	2.8 (0.5-4.8) (N=6)	11.7 (4.4-47.6) (N=3)	9.3 (0.1-42.4) (N=62)

Table 2 – baseline characteristics of patients enrolled into the INPDR

Limitations

- Retrospective and incomplete data and small sample sizes may have impacted statistics
- Patient data was from 6 countries, impacting the generalizability of results

Discussion

- Both ASMD and NPC present with a wide ranging heterogeneous clinical phenotype and age at diagnosis
- A disparity exists between NPB diagnosis age and symptoms first observed
- Whilst no statistical significance was detected, there appears to be a trend towards NPC females being diagnosed early and living longer than NPC males

Conclusion

- The analysis of NPD data from six countries has shown a heterogeneous phenotype in both ASMD and NPC.
- This work demonstrates the value of rare disease registries and the importance of patient-led registries in understanding the natural history of NPDs.

References

(1) - Kingma, S., Bodamer, O. and Wijburg, F. (2015). Epidemiology and diagnosis of lysosomal storage disorders; challenges of screening. Best Practice & Research Clinical Endocrinology & Metabolism, 29(2), pp.145-157.

Method

- Here we report the clinical characteristics of ASMD and NPC patients enrolled into the INPDR from 6 countries (United Kingdom, Ireland, Germany, Spain, Italy and Czech Republic)
- A data snapshot of the Registry data was taken in December 2018 to analyse the baseline clinical data of 256 patients (NPA:17, NPB:41 and NPC:198). The data points analysed are summarised in **Table 1**
- Descriptive analysis (median and range) was undertaken to describe the clinical data. Additionally inferential analysis was conducted to investigate if there are any sex differences between NPC patients.

ASMD	NPC
Age at analysis	Age at analysis
Age at diagnosis	Age at diagnosis
Age at death	Age at death
SMPD1 Mutation identified	NPC Subtype
Splenomegaly (%) and age first observed	NPC Clinical Form
Hepatomegaly (%) and age first observed	

Table 1 – list of assessments for analysis

ASMD Clinical Features

- Splenomegaly was reported in 96% of patients, with the median (range) age splenomegaly first observed at 3.5 (0.1-44.0) years
- Hepatomegaly was reported in 75% of patients, with the median (range) age Hepatomegaly first observed at 4.25 (0.1-44.0) years
- The summary of ASMD clinical features is found in **Table 3**

	NPA (N=3)	NPB (N=21)	Total (N=24)
Splenomegaly, %	100 (N=3)	95 (N=20)	96 (N=23)
Age first observed, years Median (Range)	0.2 (0.1-0.3)	4 (0.2-44.0)	3.5 (0.1-44.0)
Hepatomegaly, %	33 (N=1)	81 (N=17)	75 (N=18)
Age first observed, years Median (Range)	0.1	4.5 (0.2-44.0)	4.25 (0.1-44.0)

Table 3 – Clinical Features of ASMD patients

NPC Clinical Form

- The Early Infantile Neurological clinical form of NPC was most commonly reported (N=43), followed closely by the Late Infantile Neurological clinical form (N=42).
- The least commonly reported clinical form was Visceral symptoms only (2%).
- All clinical forms are summarised in **Figure 1**

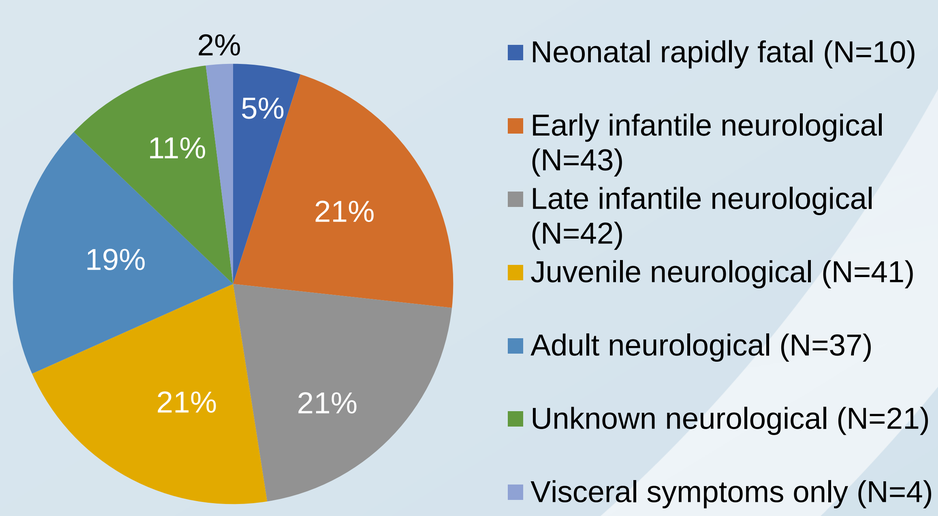

Figure 1 – Clinical Forms of NPC patients

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