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

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Background

- Niemann-Pick Diseases
  - Acid Sphingomyelinase Deficiency (Type A +B)
    - *SMPD 1*
  - Type C
    - *NPC1 or NPC2*
- Heterogeneous phenotypes, poorly characterised and low prevalence
  - ASMD – 0.4-0.6/100,000[1]
  - NPC - ~ 1/100,000[2]

Background

- International Niemann-Pick Disease Registry (INPDR)
- Global Electronic Data Collection platform
  - ASMD and NPC data forms
  - Paediatric and Adult data
- Not-for-profit status patient organisation
  - Robust and relevant operational and research governance in place

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

Methodology

- INPDR operating since September 2014
- Active in 7 countries
- INPDR data collection:
  - Baseline
  - Encounter/Follow-up
  - Retrospective
- Data snapshot of baseline data
  - August 2014 – December 2018
  - 6 countries

Methodology

- NPA (N=17), NPB (N=41) and NPC (N=198) patient records analysed
  - Minimum demographics data capture form completed
  - Missing data due to data incomplete data capture forms
- Descriptive analysis and inferential analysis undertaken

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 Demographics

	NPA (N=17)	NPB (N=41)	Total (N=58)
Age at analysis, years Median (Range)	4.9 (N=1)	29.6 (6.0-87.0)	29.5 (4.9-87.0)
Age at diagnosis, years Median (Range)	1.1 (0.3-2.9)	8.8 (0.8-62.7)	4.9 (0.3-62.7)
Age at death, years Median (Range)	2.8 (0.5-4.8)	11.7 (4.4-47.6)	4.1 (0.5-47.6)
SMPD1 mutation confirmed	3	17	20

ASMD Clinical Features

	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)
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)

NPC Demographics

	Male (N=99)	Female (N=99)	Total (N=198)	P-Value
Age at analysis, years Median (Range)	24.3 (2.5-74.3)	22.5 (2.2-69.7)	23.2 (2.2-74.3)	0.147
Age at diagnosis, years Median (Range)	5.6 (0.1-68.1)	5.0 (0.0-60.0)	5.0 (0.0-68.1)	0.271
Age at death, years Median (Range)	7.6 (0.3-33.7) (N=23)	11.1 (0.1-42.4) (N=39)	9.3 (0.1-42.4) (N=62)	0.103
NPC Subtype (%)				
i. NPC1 ii. NPC2 iii. Unknown	97 (98%) 2 (2%) 0	95 (96%) 1 (1%) 3 (3%)	192 (97%) 3 (1.5%) 3 (1.5%)	n/a

NPC Clinical Form

	Male (N=99)	Female (N=99)	Total (N=198)
Neonatal rapidly fatal, %	6 (N=6)	4 (N=4)	5 (N=10)
Early infantile neurological, %	18 (N=18)	25 (N=25)	22 (N=43)
Late infantile neurological, %	22 (N=22)	20 (N=20)	21 (N=42)
Juvenile neurological, %	21 (N=21)	20 (N=20)	21 (N=41)
Adult neurological, %	21 (N=21)	16 (N=16)	19 (N=37)
Unknown neurological, %	10 (N=10)	11 (N=11)	11 (N=21)
Visceral symptoms only, %	1 (N=1)	3 (N=3)	2 (N=4)

Limitations

- Incomplete data
- Small samples sizes may have impacted statistics
  - Low numbers of NPA records makes comparison to NPB problematic
- Retrospective data collection and analysis
  - Patient enrolment/ascertainment bias
- Patient data from 6 countries
  - Patients may not be representative of all NPD

Discussion

- Heterogeneous clinical phenotype in both ASMD and NPC
  - Wide hepatomegaly and splenomegaly onset age range observed in NPB
  - Varying distribution of NPC Clinical Forms
- Significant lag between age at splenomegaly and hepatomegaly onset and age at diagnosis in NPB
- Trend towards NPC females being diagnosed earlier and living longer compared to NPC males
  - Although no significant difference detected

Discussion

- INPDR can facilitate research into NPDs
- Proof of concept for patient-led registry
  - Model for other rare diseases
- Move from Industry owned product registries

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