Clinical spectrum of persons with HTAAD at TRS

Nina Riise, MD

HTAAD meeting

2016

Marfan and Marfan-like conditions at TRS

- 308 registered:
  - «Marfan syndrome»: 231
  - «Marfan like syndrome»: 77
- We don't know for sure what diagnoses these people have

TRS – overview

Diagnosis	Orphacode	Groups
Marfan	143 (5 dead)	
LDS1/TGFBR1		3
LDS2/TGFBR2		30
LDS3/SMAD3		5
LDS4/TGFB2		10
vEDS	25 (2 recently dead)	
HTAAD others		5-9

HTAAD - others

- 1 ACTA2
- 4 FBN2 – one with known aortic pathology
- 4 TNXB, 3 with aortic dilation
- We may have many more hiding among the 308 we have registered
- Our biggest group at TRS is «without diagnosis» - some may have HTAAD

- We need to meet more of them

Marfan - age

Age group	Number of people
0-19	13
20-39	50
40-59	59
60+	21

LDS (TGFB related group)- age

Age group	Number of people
0-19	8
20-39	22
40-59	16
60+	2

EDS vascular - age

Age group	Number of people
0-19	3
20-39	11
40-59	4
60+	5

Diagnosis

- Many people get their diagnosis as adults:
  - After a vascular incident
  - Meeting the right doctor
  - Doctor Google
  - After seeking medical advise because of their family history
  - Postponed genetic testing of children with HTAAD parents
  - Growing into the Ghent criteria

Life expectancy

- Shorter life expectancy than the general population
- Some of them grow old
- We may not know the mildest cases – more people than we know with these diagnoses may grow old
- Median age alive in the LDS/TGFB group is 37 years

Clinical spectrum in syndromic and non-syndromic HTAAD

- Clinical overlap between diagnoses
- Large variability within diagnostic groups
- Large variability within families
- Early cardiovascular episodes tend to coincide with syndromic features – but sometimes they don't
- Both men and women are alive in the older age groups
- Clinical impression: Sons may have a vascular incident before their mothers

Clinical criteria versus genes

- Very complicated issue
- Which diagnosis is right when clinical diagnostic criteria say one thing and the gene says something else?
- How many clinical, non-vascular findings must a person have before we use the term syndromic?
- « You don't have Marfan syndrome, but you should be followed as a Marfan patient»

Case 1: male first seen 40 years

- B dissection and aortic root dilation
- Pectus carinatum, flat feet, valgus, hypermobility, marfanoid facial features
- Dural ectasia
- Striae
- Aorta + 7 systemic points, Ghent 1+2 positive

Case 1

- FBN1-
- TGFB2+
- No hypertelorism, normal uvula
- Marfan or Loeys- Dietz syndrome?

Case 2: woman 49 years, Marfan

- Aortic root dilation, mitral valve prolapse, B dissection
- Lens surgery
- Dural ectasia
- Kyfoscoliosis, pectus excavatum, long limbs
- Genetic testing just to confirm the Marfan diagnosis

Case 2

- Lens surgery – for cataract. Glaucoma, amblyopia
- FBN1-
- FBN2+
- No contractures
- Normal ears
- Marfan syndrome, CCA or HTAAD?

Clinical implications

- How are we going to «label» these patients
- What are the implications for clinical follow up?
- What are the implications for research and statistics?
- How do we communicate these things to the patients?