Deafblindness and Diagnosis Reflections on the role of genetics

Arvid Heiberg

Senior consultant, professor (em)

Dept. of Medical Genetics- Oslo university hospital

My background

- Consultant in medical genetics- long experience with psycho-social aspects of genetic disorders
- Visual and hearing impairment not highly regarded in medicine- «little action», so far.

Homage to Else Marie

- Not very long cooperation, compared to her enormous expertice, but…
- «Among the blind, the one-eyed is king»- and Else- Marie is therefore a «Super-Queen»
- Ekstensive experience. Deep understanding and knowledge.
- «Well-beeing of the user»
- «Else- Marie has given guidance»

Diagnosis

- Dia- greek: «through»
- Gnosis- greek: «knowledge»
- «Conditions with some common traits»
- ICD-10 No identity of «Deafblindness», nor Ushers syndrome
- But the conditions do exist-medical reality!
- ICD-11 to be implemented soon (for many years)

Diagnosis

- Phenotype, symptoms and signs obtained by medical history and physical examination
- Genotype- obtained by laboratory techniques
- Sometimes easy- often difficult, time and procedure as well as cost consuming.

What purpose?

What is in an accurate diagnosis

- Etiology-Why did it happen?
- Phenotype: What disorder is it-Information?
- Prognosis: What is going to happen-
- Complications- how to follow and what to be aware of?
- Can it be treated/cured?
- Will it happen again?-implications for the extended familiy

Diagnosis of DB

- Either descriptive: «Nordic»:
- Combination of visual and hearing impairment which restricts»full participation in society.i.e. social life,communication, information aand movement»
- Causal: Rubeola or due to spesific genes i.e

- Congenital: «Before language development»
- Acquired: Later onset, but may be genetic- Usher types 2-3.
- Additional comorbidities? A lot of syndromes described- most very rare!

Heterogenous group

- Some have a purely descriptive diagnosis, functional in some- room for judgement
- A question of «fairness»-equal judgement?
- But a genetic cause feels more definitive-i.e Usher
- But are the functions sufficiently reduced?
- Some disorders are progressive, others stationary.
- We recognize USHER as DB, but not others?

Recent developments in medical genetics

- From descriptive to etiologic entities: i.e. Usher 1, 2, and 3 to various genes.
- Availabilities of genetic tests has increased exponentially: more genes for lower price.
- Gene panels: UNN in Tromsø has a long tradition for providing such panels, but the other departments in Oslo, Bergen and Trondheim are coming up. Skien?

Some results from the Norwegian register

- About equal gender distribution
- 20 % congenital/ 80% acquiried- age differences- diagnostic delay mostly in acquired group- 4 versus 13 years
- Coverage in former Register:146/362 persons- 40 % only
- 53% of the 362 have a Usher diagnosis- no of genetically verified unknown.
- Age limit for onset of DB: 67 y for identification in NTT

unpublished results

What is in an accurate genetic diagnosis

- Etiology
- Phenotype: What disorder is it-Information?
- Prognosis: What is going to happen- sometimes
- Complications- how to follow and what to be aware of?
- Can it be treated/cured?- rarely, but hope
- Will it happen again?-implications for the extended familiy

Early diagnosis possible?

- Long diagnostic delays in general
- Newborn screening for hearing (electroacoustic): Implemented
- Gene panels for severe hearing deficits provides accurate diagnosis and possibilities for better follow up and secondary prevention
- Causal treatment increasingly coming up- genetherapy for deaf mice and PR 65, LHON.

Some ethical questions

- Is an early diagnosis beneficial if little impairment and no treatment
- Should NBS be included to gene panels for visual and hearing impairments?
- Preconceptional screening
- Gene testing in relatives

A few figures:

- NKBD serving approx. 356 subjects.
- NTT during 2010- 2021: 154 Cases
- NKDB:Congenital:105 (30%)
  - Acquired: 251(70%)
  - But a high number under surveillance(39 and 65,resp)
- Increasing number of genetic causes identified during this period and in general.

Usher syndrome largest group

- Usher type 1: 49
- Usher type 2: 69
- Usher type 3: 4
- Usher unspesified: 7
- Usher in total 129 or 52% of acquired or 36% of total
- (Genetically confirmed unknown)

Syndromes

- A large number of syndromes/disorders represented-some with DB as a known complication, some where this must be very rare-i.e:Down syndrome- 3 cases.
- Many single cases- very few others in Norway
- A large number of «unknowns» worth rediagnosis?- and also some «knowns»
- An evaluation of 154 NTT cases from last 11 years is underway. Next seminar!