Familial Amyloidosis

What Does it Mean for Your Family?

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The Journey

Familial Amyloidosis

- Imaging
- Transplant
- Blood work
- Biopsies

Meeting with Doctors
Testing
Diagnosis
Treatment
Familial Amyloidosis

How do I tell my family?  
How will they react?

How did I get this?

What does Val30Met mean?

Who in my family is at risk?

How will they react?
Roadmap

• **HOW and WHY**
  • Genetics of Familial Amyloidosis

• **WHO’S at RISK**
  • Describe how Familial Amyloidosis passed on

• **COMMUNICATION**

• **GENETIC TESTING**
Genetics – Back to the Basics

- Our bodies are made of millions of cells
Cells and DNA
DNA and Genes

- GENES are made up of special sequences of DNA
- Genes code for the proteins in our body that do the work

- GAT CCT GCA TAC GAT

AA1 AA2 AA3 AA4 AA5
Mutations

• DNA changes result in changes in protein

• THE CAT ATE THE RAT

• THE CAT ATE THE MAT

• THE CAT ATE THE RRT
Example: Pigment
Genetics of Familial Amyloidosis

- Transthyretin (TTR)

- Carries thyroid hormone and retinol

- Soluble – able to be dissolved
DNA Changes can Lead to FA

How did I get FA?

FREE TETRAMER

FOLDED PROTEIN

Functional TTR Structures

*Amyloid fibrils can be caused by a variety of amorphous aggregates

http://www.thaos.net
Genetics of FA

• We all have 2 copies of all of our genes, including TTR, GSN, APOA1

• Dominant Inheritance
  • A mutation in 1 of the 2 copies is enough to cause condition
What’s in a Name

DNA

140 148

GTG GCC GTG CAT GTG

Protein

AA28 AA29 AA30 AA31 AA32

Valine (Val or V)

GTG GCC GTG CAT GTG

AA28 AA29 AA30 AA31 AA32

Methionine (Met or M)

What does Val30Met mean? (c.148G>A)
What’s in a Name

• Over 100 different mutations
• Specific code change may provide information about symptoms
  • T60A – Heart & autonomic nerves
  • V30M – Peripheral and autonomic Neuropathy
  • V122I – Cardiac
• Same mutation exist in a given family
FA is a Family Condition

Who in the family is at risk?

All the kids have a 50% chance of inheriting the gene with the mutation.
Genetic Testing for Family Members

- No mutation found
- Did not inherit mutation
- Further evaluations not needed

- Mutation identified
- Inherited mutation from father
- Seek care with physician and team
- Continue with regular evaluations
Who else is at risk?

- All first degree relatives of person with FA
  - Children
  - Parents
  - Brothers and Sisters

- Symptoms of FA are variable
  - Age
  - Symptoms
  - Severity
Should a person with FA have genetic testing?

• Part of diagnostic work-up
• Important in understanding cause of Amyloidosis (inherited or not)
• May provide information about what to expect medically
• Will impact treatment and eligibility to clinical trials
• Necessary to determine prior to genetic testing other family members
Family Communication

- Understand the condition yourself
  - Educational info from providers
  - Patient support groups

- Think through how your family members will respond
  - Each will respond differently
  - Each has their own coping mechanism
  - How have they handled other information in the past

How do I tell my family? How will they react?
Family Communication

• Familial Amyloidosis
  • Wild Type (AA)

• Open the conversation

• Family members will ask questions that are important to them

• You don’t have to have all the answers

• Will need more than one discussion
Genetic Testing for Family Members

Benefits

- “I felt like I needed to know so I could follow through with my doctor if needed, rather than being worried and having a bunch of tests I may not need if I was tested negative”

Limitations

- “Yesterday I knew I might be at risk, today I know I am. I wonder if I would have thought about it less if I hadn’t had the test”

Should my kids have testing, when?
Genetic Testing for family members

• When is the right time for testing?
  • “right time” and “right way”

• Adult onset
  • Testing of young children is not advised

• Individual choice; informed decision
  • Take into consideration how information will be used now – will change over time

Should my kids have testing, when?
Making informed decisions about pre-symptomatic testing

• How will I use the information?
• How will I react if my test confirms that I am at risk?
• How will I feel if I am not at risk?
• How will my family react if some of us are found to be at risk and some are not?
• Am I able to handle the medical and psychological impact of a positive result?
• Is now the right time?
Testing Logistics

- Blood Draw or Cheek Swab
- Only looking at FA related genes
- Cost ~ $800-$1000 (TTR)
- Family specific testing ~ $400-500
- Results 2-3 weeks
- Set up appropriate time for results
Insurance Concerns

- Will my insurance cover it?
  - Possibly

- Will my health insurance raise my rates or deny coverage?

- Will my employer discriminate against me?
  - No – Protected by Federal Law (GINA)
  - Note: Life insurance not covered by this law
Summary

• FA is inherited and can be passed on to the next generation
• Take the time to understand the condition
• Communicate with Family and Support Systems
• Genetic testing is an option for family members
• Work with professionals who understand FA
• Learning and understanding never ends