Genetic Counseling: Case Examples

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Case #1

- Case:
  - 30 year old female patient
  - Currently 8 months pregnant with male fetus
  - 2yo son with severe hemophilia A, no genotyping
  - Carrier status unknown
  - No complications or bleeding with first birth
  - No personal symptoms of bleeding or bruising

[Family tree diagram showing genetic inheritance of hemophilia A]
Case #1 (cont.)

- Genetic counseling considerations:
  - Carrier risk
    - Up to 98% chance mom is a carrier
    - Timing prohibitive to facilitate genotyping to further inform risk assessment
  - Lack of family history was leading parents to feel hemophilia was de novo in first son

- Plan:
  - Discussed her risk to be a carrier
    - 8 month factor VIII level drawn to assist with labor and delivery management plan
  - Discussed risk for current pregnancy to be affected
    - Provided cord blood kit
    - Reviewed birthing plan considerations
  - Discussed outcome of this pregnancy may further inform her carrier status
Case #1 (cont.)

- New case info:
  - 2nd son dx with severe hemophilia
  - Mom is obligate carrier

- New GC considerations:
  - Parents initially displayed shock and disbelief
  - Mom stated that learning she was a carrier was more difficult to deal with than learning that her sons had hemophilia

- New plan:
  - Genotype one of the sons at time of next blood draw
  - Facilitate communication and education to at-risk relatives
Case #2

- Case:
  - 16 year-old male referred to our clinic
  - Previous FVIII level drawn following pronounced bleeding after dental extraction
  - Additional labs drawn in interim
    - VWD R:Co (69%)
    - VWD antigen (32%)
  - Differential diagnosis:
    - Type 2N VWD
    - Mild hemophilia A + VWD type 1
  - Family history reported of hemophilia A
Case #2 (cont.)

- Genetic counseling considerations:
  - Diagnosis not definitive, so inheritance unclear
  - No records to confirm reported history of hemophilia A
  - Family from Columbia, ESL

- Plan:
  - VWD binding studies were ordered to r/o VWD2N
  - Hold off on more detailed information until diagnosis is clear
  - Introduce possibility of genetic testing to assist with diagnosis
  - Encourage them to discuss with family further and obtain any records available
Case #2 (cont.)

- New case info:
  - VWD binding studies came back normal (r/o VWD2N)
  - Diagnosis believed to be Hemophilia A with Type 1 VWD

- New genetic counseling considerations:
  - 2 separate bleeding disorders in the family
  - 2 separate patterns of inheritance
  - Large family structure
  - Father seemed to blame mother
    - resistant to accept possibility that he contributed
  - Relatives remain in Columbia

- New plan:
  - F8 genotyping
  - Participation in research study on VWD phenotype/genotype correlation
  - Facilitate communication and education to at-risk relatives
Case #3

- Case:
  - Newborn has excessive bleeding with circumcision
  - FVIII level drawn, < 0.01 = severe hemophilia A
  - At initial visit, mom reported she shared family history of hemophilia A to her MDs
  - External provided ordered a FVIII level (during pregnancy), which was normal; mom was told she was not a carrier
Case #3 (cont.)

- Genetic counseling considerations:
  - Mom frustrated that testing was unnecessary and gave false reassurance
  - Mom expressed guilt – saying she would not have circumcised her son without testing first if she knew he was at-risk
  - Maternal grandfather is a patient at our office but the mother is estranged from him

- Plan:
  - Baseline factor level in mom
  - Genetic testing in patient at next blood draw
  - Facilitate communication and education to at-risk relatives
Case #4

- Case:
  - Known hemophilia A carrier by genetic testing
  - Comes to office for baseline factor VIII level prior 2\textsuperscript{nd} pregnancy
  - Reports she is currently going through IVF, oocyte retrieval not yet performed
Case #4 (cont.)

- Genetic counseling considerations
  - Patient has limited contact/interaction with affected relative
  - What family planning options are available through her reproductive endocrinologist

- Plan:
  - Hematologist obtained factor level and reviewed recommendations for oocyte retrieval procedure
  - Facilitate education about natural history of hemophilia
  - Make patient aware of prenatal testing options
  - Make patient aware of pre-implantation genetic diagnosis (PGD) options
    - Gender selection vs. testing for known hemophilia mutation
Case #4 (cont.)

- **New case info:**
  - Reproductive endocrinologist able to coordinate PGD
  - Patient interested in PGD
  - Insufficient time to pursue PGD for current cycle

- **New genetic counseling considerations:**
  - Discuss family dynamic and potential reactions from her sister/nephew regarding her pursuit of PGD

- **New plan:**
  - Patient decided to stop current cycle to allow time for hemophilia-specific PGD option to be set-up
Case #5

- Case:
  - Genetic testing performed in carrier mother and her adult sister
  - Results revealed that they did not share the same father

- Question:
  - Should this information be disclosed to the family?
Case #5 (cont.)

- Outcome:
  - Information was not disclosed with the family
Case #6

Case:
- Male hemophilia patient seen at HTC passed away
- Deceased patient’s mother called HTC stating that deceased patient’s daughter was pregnant and was unsure whether she knew of her obligate carrier status
- Requested that the HTC reach out to her pregnant granddaughter to advise of her carrier status and risks

Question:
- Should the HTC contact the granddaughter to provide education about her carrier status?
Case #6 (cont.)

- Outcome:
  - HTC advised that she speak with her granddaughter and have her granddaughter contact the HTC
Case #7

• Case:
  • A genetic counselor was contacted by a mother of a hemophilia A patient
  • The GC had previously helped coordinate genetic testing for the woman’s affected 8 year old son – intron 22 inversion identified
  • Mother was now interested in pursuing genetic testing in her 15 and 17 year old daughters to determine carrier status
  • The mother indicated that she did not plan to tell her daughters that they are being tested

• Question:
  • Should the genetic counselor process with testing?
Case #7 (cont.)

- **Outcome:**
  - Discussed with patient concerns about daughters not knowing
  - Talked through several scenarios
    - e.g. when would you tell daughters?, how would they feel knowing you decided for them?
  - Mother’s ultimate underlying fear was being unable to protect her children; validation of this fear was provided.
  - Mother agreed that it would be in their best interest for them to actively participate in the decision for testing.
Case #8

- Case:
  - Couple is 8 months pregnant
    - Mother is obligate hemophilia A carrier
    - Father has severe hemophilia A
    - History of inhibitors on both sides of the
Case #8 (cont.)

- **Plan:**
  - Factor VIII level drawn in mom to assist with labor and delivery management plan
  - Reviewed risks to current pregnancy
    - 50% carrier, 50% homozygous hemophilia
    - Provided cord blood kit
    - Reviewed birthing plan considerations

- **Genetic counseling considerations:**
  - Any previous genotyping in either side of the family?
  - Father disengaged from conversation
Case #8 (cont.)

- New case info:
  - Cord blood kit VIII level = <1%
  - Both familial mutations identified previously via research studies

- New genetic counseling considerations:
  - Family and daughter may feel “different”
    - Consider outreach to another homozygous/compound heterozygous female
  - Review inheritance for compound heterozygous with family and daughter, as she gets older

- New plan:
  - Genotyping in daughter at next visit
  - Baseline level in mom at next visit
  - Outreach and education to other family members
Case #9

- **Case:**
  - 2-year-old female
  - History of seizures at birth, multiple small brain hematomas
  - Microarray testing ordered externally
    - 12p deletion
      - VWF gene
      - ANO2 gene (no clinical significance)
    - Xq deletion
      - MAMLD1 gene (risk for hypospadias)
  - Mother and maternal grandmother tested externally, both positive for 12p deletion
Case #9 (cont.)

- Genetic counseling considerations:
  - 2 genetic deletions of clinical significance
  - 2 different patterns of inheritance
  - Patient is young
  - Mother currently pregnant with male fetus

- Plan:
  - Recommend others with 12p deletion be evaluated at HTC
  - Discuss genetics with patient at future visit, as she becomes age-appropriate
  - Offered mom referral to prenatal genetic counseling
Discussion and Questions