A sickle in a “pickle”!

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A couple of definitions!

- **Sickle Cell Disease** - an autosomal recessive genetic blood disorder characterized by red blood cells that assume an abnormal, rigid, sickle shape. The abnormal hgb mutation leads to various risks and complications.

- **“In a pickle”** - In a quandry or some other difficult position!
History

- African American female with **sickle cell anemia**

- Family history: Positive for sickle cell trait in mother, father and 3 brothers

- 2 other reports state “Sickle cell disease with *hemoglobin SS, beta thalassemia zero*”
Sickle beta Thalassemia zero
Hgb S/β^0

- **Hemoglobinopathy** producing one of the most severe forms of sickle cell disease
- Clinically *indistinguishable* from homozygous inheritance of sickle globin gene *(Hgb SS)*
- Compound heterozygous state of inheritance producing both abnormal *qualitative and quantitative* effects on β-globin synthesis
  - Complete absence of β-chain production
  - Hgb produced is almost entirely Hgb S
Our Patient’s family

Mother with sickle trait

Father with thalassemia trait

Our patient
Background Information

- First record, Community Blood Center received a sample from **CMH in 1999**. (She was **14 years old**)
- **Cardiomegaly** with history of ventricular ectopy
- Cholecystectomy at age 14
- Patient typed as **B+, Positive Ab Screen**
CBC’S TESTING

- Refering Hospital reported Patient had received 2 units on 11-21-99.
- Patient came into ER with 3.4 g Hgb.
- Patient typed as group B, Rh positive.
- DAT testing
  - +mf poly, IgG, C’ and saline control.

- Insufficient red cells to make and eluate.
  - Asked for more sample.
Initial testing all cells strongly positive at 4C, 22C, LISS 37C, IAT including I-, Vel-, PP1Pk- (Tja-).

- Auto control: strongly reactive @ 4C, negative at 22C and LISS 37C, wk reactivity IAT.

- Ficin Panel looks like anti-D, -C, -E.

- Phenotype with Hypotonic washed cells: E-, C-, c+, e+; K-; Fy(a-b-); Jk(a+b+); M-, N+, S+, s+.
### CBC TESTING CONT.

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Conclusions

- Antibodies present: anti-D, anti-C, anti-E, anti-Fy\(^a\), cold autoantibody.
- Since patient is D positive and her plasma contains anti-D it is uncertain if anti-D is autoantibody or alloantibody.
- If anti-D is alloantibody, patient’s red cell may lack D epitopes.
- Recommend transfusing D-C-E-Fy(a-) units. Frequency of 1%.
- 5 D-C-E-Fy(a-) units sent to Hospital.
More Sample from Hospital

- Additional sample 2 days later.
- DAT: Poly (+)mf, IgG (+)mf, C’ neg.
- Ether eluate prepared: Anti-M detected.
- Anti-M in eluate may not correspond to any clinical significance in tx therapy.
- Given complex serology of patient recommend D-, C-, E-, Fy(a-), M- units.
  - Incidence of these units is 0.22%.
More Sample from Hosp. cont.

- 3 weeks later more sample to investigate D status of patient.
- Hypotonic wash to get autologous cells.
- Test patient cells with multiple anti-D specific for certain epitopes of D antigen.
- Pt. reactive with all anti-D reagents.
  - Indicates pt red cells have normal expression of D or are category D$^{\text{III}}$.
  - D$^{\text{III}}$ cells carry all 9 epitopes of D known at that time.
D Investigation goes on….

- Patient serum tested with known partial D cells that are C-E-Fy(a-)M-
- Pt. serum reacted with 1 D$^\text{VI}$ cell and 1 of 2 D$^{	ext{III}_a}$ cells.
- Significance of this is uncertain.
- Sent sample to New York Blood Center for further testing.
New York Blood Center’s Report

- Confirmed anti-D, C, E, Fy\(^{a}\), M in pt. serum. Also contains autoantibody.
- Pt. serum nonreactive with 3 of 4 M+ D\(^{IIIa}\) cells tested by prewarm technique.
- Pt. cells reactive with 2 anti-DAK.
  - DAK is novel low incidence ag associated with D\(^{IIIa}\) phenotype.
- Pt. cells are partial D phenotype D\(^{IIIa}\) and has made alloanti-D.
- NY doing molecular analysis on sample.
Genomic DNA isolated.

Both RHD and RHCE were amplified.

PCR-RFLP analysis showed pt. cells are homozygous for mutation in exon 4 of RHD gene that correlates with D$^{\text{IIIa}}$ phenotype.
More Transfusion History: CMH

- 8-7-00: Sent 3 D-, C-, E-, Fy(a-), M-units
- 2001-2003???: Was she transfused somewhere else??
- 1-2-04, sent 4 prbc’s: D-, C-, E-, Fy(a-)
  (M not showing with prewarming)
- 1-15-04: this time M- units sent, since prewarming did not circumvent the reactivity
- 6-12-05: sent 3 prbc’s: D-, C-, E-, Fy(a-), M- units
It is now 2006… she is 21 years old and a patient at SLH

- Policy at SLH for “newly discovered” sickle cell patients
  - ...Alloimmunization and delayed hemolytic transfusion reactions can be reduced by phenotyping the patient and giving selected Ag negative units
  - Determine the patient’s phenotype in regards to E, C, K and Fy^a
  - Units must be Sickledex negative
  - Thanks to CBC’s record keeping, she is a “known” problem
21 yrs old, 14 wks. pregnant, presents to our ER complaining of chest pain

- WBC: 17.2 TH/UL, HGB: 5.6 g/dL
- Normal chest x-ray
- Plan to infuse 3 units prbc’s as “exchange”
- Transfused with antigen/sickledex/CMV negative, crossmatch compatible blood
One week later... (10-23-06)

- Admitted directly from our ER to MICU
- Weakness, nausea/vomiting, systemic pain
- Fetus- normal heart tones
- WBC: 26.2 TH/UL, HGB: 3.1 g/dL
- Urinalysis: Large RBCs and WBCs
- Plan to infuse 4 units prbc’s as “exchange”
  (given over 11 hours)
- Transfused with antigen/sickledex /CMV
  negative crossmatch compatible blood
Outcome of 10-23:

- Hgb increased: **3.1 g/dL to 7.9 g/dL**
- In <36 hours, hgb was **5.4 g/dL**
- Taken to OR: D/C for fetal demise
- Order for **4 units of blood**
- *Incompatible* x-matches with ag neg units
- DAT- IgG positive
- *Sent to CBC* for possible DHTR workup
Community Blood Center’s report:

- Warm wash pt. rbc’s to get ABO & Rh type and valid DAT results.
- DAT: poly +, IgG (+), C’ 2+, sal ct. 0.
- Ether Eluate: anti-Fy3 and anti-V; positive with all ficin treated cells.
- Plasma: anti-Fy3, anti-V, cold autoaby. Did not test for previous alloantibodies.
- Serologic evidence of delayed transfusion rxn due to anti-Fy3 and anti-V.
Transfusion Requirements

- Pt. must now get D-C-E-Fy(a-b-)M-V-units.
- Very Rare.
- Sufficient time should be allowed to obtain blood from Rare Donor program.
The “pickle” has begun!!

- After DHTR- rapid decline in her condition
- 10-23 thru 10-25: **5 units blood** given.
  - 4 D-C-E-K-Fy(a-)M-,CMV-; 1 D-C-E-K-Fy(a-b-)
    due to urgent need for blood.
- Hgb consistently dropped: **2.2 g/dL** on 11/1
- **Hyperhemolysis** suspected!
- HPT below linearity
- **LD:** **4502 IU/L**
- Survived this crisis.... But wait!
## 2007-2008

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<td>SLHx3</td>
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<td>Pain crisis PICC line for transfusions</td>
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<td>R ax. DVT, coumadin therapy</td>
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The “pickle” remains stable...

- 11-09-08: back to SLH, **6.0 hgb**, no transfusions, coumadin therapy
- 10/2009: **6.0 hgb**, *erythropoietin* given
- 11/2009: **7.0 hgb**, treated for pneumonia
- 5/2010: painful crisis, UTI stable hgb, no transfusions
- 7/2010: Diffuse skeletal pain, stable hgb, no transfusions
Interesting comments from the patient’s chart

“Delayed hyperhemolytic transfusion reaction with numerous alloantibodies. Avoid transfusions at all costs.”

“Her hemoglobin was at 6 and close to her baseline. Do not transfuse at this time”

“Tolerates hgb down to approximately 3 g/dL well.”
Her history has GROWN!!

- **Sickle cell disease**
- Autosplenectomy
- Narcotic dependence
- Hypertension
- SVC thrombus
- Sepsis
- Respiratory failure
- Dysphagia
- Left hemiparesis
- Fevers
- Malnutrition
- Leukocytosis
- Antiphospholipid Ab syndrome
- **Severe anemia**
The “pickle” begins to get ugly!

- 9/2010: *Intracerebral hemorrhage*, left side weakness, OR, admitting **hgb 8.3**.
- 10/02/2010: **hgb drops to 5.2**
- **3 units blood transfused** between 10-2 and 10-18.
- Critical condition: “pickle” to obtain blood
- Just in time for the AABB national meeting
We are Beginning to Dislike Pickles

- Can the pt. make more antibodies??? But of course!
- Another work up by CBC and more samples sent to NY.
- Now the patient has made anti-Le^a, anti-Le^b and has additional reactivity with some antigen matched Le(a-b-) cells.
- TX recommendations are: D-C-E-Fy(a-b-)
  M-V-Le(a-) nonreactive with pt’s plasma.
Pickles are a Pain…

- Compatible blood is extremely hard to find. Only 2 units available in the country and at least 2 patient’s needing the same type of units.

- Record of one more unit given 1/19/2011.
  - D-C-E-K-Fy(a-b-)M-V-Le(a-b-) from New York.

- Heard nothing again until 4-14-11

- Came in with acute chest pain and hgb of 4.3
Acute Chest Syndrome:

- **Definition:** a noninfectious vasoocclusive crisis of the pulmonary vasculature commonly seen in patients with *sickle cell anemia*

- **Cause:** often initiated by a lung infection, and the resulting inflammation and loss of oxygen tension leads to *sickling of the red cells* and further vasoocclusion

- **Prognosis:** it may result in death, and it is one of the most common causes of death for sickle cell patients
St. Luke's Hospital
4401 Wornall Road
Kansas City, MO 64111
ProVue SN 057-0003559

Results by sample

Date: 4/14/2011 2:17:40 PM
Batches: 100
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<td>4+</td>
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<td>2+</td>
<td>Pos</td>
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Unit transfused on 4-15-11

I’m the “MIRACLE” UNIT!!!
Really, I am!
Outcome

- The unit was found quickly; “local”
- Our patient tolerated the unit quite well
- Hgb went from 4.3 to 6.3
- After 2 days her hgb was 7.1! Amazing!
- According to her patient chart, discharged on day 4 with a hgb of 6.5!
- “The patient’s vital signs are good, the crisis is over and she appears quite cheerful”!
Future Outlook for Our Patient!!

- Local Donor Available
- Will she build *more* antibodies?
- How will her disease progress?
- When will we see her again?
- Once a *pickle*, always a *pickle*!

- Thank You!!