FRIDAY the 13th

A SCARY STORY OF HEMATOLOGIC PROPORTIONS

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HMC ER page

“We have a 53 yo man with a spontaneous subdural bleed and 1 year history of nosebleeds treated with vitamin K and cauterization. His platelets are 120 and his INR is 1.2. Neurosurg wants you to decide what the transfusion thresholds should be.”
How do you respond?

- Hang up the phone and go to sleep
- “Keep the platelets above 100.”
- “Sounds scary, you should page Dr Gernsheimer.”
- “The INR is for monitoring warfarin effect, not assessing bleeding risk.”
- “What’s the PTT?”
More Information

- “The PTT is 56”
- “Also the protein is 10... that’s weird!”
- Epistaxis attributed to bike accident 6 months ago, but really ongoing x1 year
- PCP has been giving vitamin K for INR of 1.4
- He has been cauterized by ENT x2 without improvement.
- Subdural is stable, no surgical intervention planned overnight.
Differential

- Acquired factor deficiency
  - Factor X
- Acquired inhibitor
  - VIII or IX
- Acquired von Willebrand
  - Factor VIII deficiency
Friday the 13th 9AM

- No change in imaging, mental status
  - PT 16.2
  - 1:1 mix: 13.7
  - PTT 56
  - 1:1 mix: 35
  - Plts 96
  - Fibrinogen 133
  - D-dimer <0.27
  - Thrombin time 15
  - Protein 10.9

- Factors V, VII, VIII, IX, X, XI, VWF and activity pending
- SPEP and serum viscosity recommended
Peripheral Smear
Friday the 13th 4:30PM

- Factors
  - V: 38
  - VII: 80
  - VIII: 5
  - IX: 99
  - X: 45
  - XI: 46
  - VWF: 6
  - VW activity: 3

IgM kappa spike: 3.1

Serum viscosity: 6.0!
Fun Fact

- Friggatriskadekaphobia is the term for fear of Friday the 13th
  - Also called paraskavedekatriaphobia
- Triskaidekaphobia is fear of the #13.

Friday the 13th
Best Day Ever
Friday the 13th 5PM

- ICU attempts to place Mahurker in RIJ
  - Kcentra, plts, FFP, Amicar given
  - Hypotension develops
  - Hematoma forms
  - Pt intubated
- Mahurker ultimately placed in groin
- Plasma exchange initiated
  - 50% albumin, 50% FFP
Saturday the 14th

- AM labs:
  - PTT 56 -> 42
  - Protein 10.9 -> 7.5
  - PT 15.7 (INR 1.3), Plts 123
- Pt remains intubated for airway protection
- Febrile and hypotensive (on pressors)
- 3 units PRBCs given overnight
CT C/A/P

- “Lymphadenopathy of the chest, abdomen and pelvis, consistent with patient’s history of Waldenstrom’s macroglobulinemia”
- Splenomegaly 14.3cm
- Paratracheal soft tissue enhancement
Back to the labs...

- Factors
  - V: 38
  - VII: 80
  - VIII: 5
  - IX: 99
  - X: 45
  - XI: 46
  - VWF: 6
  - VW activity: 3
Acquired VWD

- Cardiovascular
  - Valvular disease, VAD, congenital HD
- MPNs
  - PV, ET, MF and CML
- Lymphoproliferative diseases
  - CLL, MGUS, Waldenstrom macroglobulinemia
- Immunologic
  - SLE, post-transplant
Pathogenesis

- Autoimmune clearance
  - Binding of paraproteins/inhibition of VWF
- Cellular
  - Binding to cell surfaces (platelets, myeloma cells)
- Mechanical
  - Shear stress -> increased proteolysis by ADAMTS13
- Decreased synthesis (?)
  - Severe hypothyroidism, drugs
Diagnosis

- VWF antigen, VWF activity, multimers, collagen binding capacity
- VWF:Rco/Ag ratio <0.6-0.7 suggests inhibitory antibodies or decrease in HMW multimers
- Neutralization assays and ELISAs may be used to detect inhibitory antibodies
  - Not widely available
  - Technically demanding
Treatment

- Treat the underlying disorder
  - 70% remission rate with chemotherapy (B cell lymphoma or multiple myeloma)

- Desmopressin
  - Low success rates

- IVIG
  - Useful in IgG antibody or paraprotein disease

- Supportive care for bleeds
  - Antifibrinolytics
Treatment

- Factor replacement
  - VWF containing FVIII concentrates
    - Humate P® 30-100 VWF Rco units/kg
    - Effective in 80% of cases
    - Half-life may be shortened

- Bypassing agents
  - Recombinant FVIIa
  - Off-label, few case reports
Fun Fact

- Fidel Castro and Butch Cassidy were born on Friday the 13th.
Sunday the 15th

- Hematoma stabilized, no new bleeding
- Hemodynamically improved
- Continued on antifibrinolytics
- Plasma exchange # 2 performed
- PT 18.1, PTT 41
- VW antigen 60
- VW activity 92
- Factor VIII 93
Plasmapheresis in AVWD

- Case reports
- Primarily used in lymphoproliferative disorders
- Mechanism: reduction of paraprotein leading to decreased VWF clearance
- Exchange with plasma + albumin to supplement decreased factors
Monday the 16th

- Pt remains stable, extubated
- Pt seen by optho for retinal hemorrhage
- Bone marrow biopsy performed
  - Inaspirable
- IgM: 3280
Bone marrow biopsy results

- The bone marrow is extensively infiltrated by a population of abnormal lymphocytes and plasma cells which in combination with the markedly elevated serum IgM, is most consistent with Waldenstrom macroglobulinemia/lymphoplasmacytic lymphoma
Biopsy
Wednesday the 18th

- PTT 37
- IgM 4470
- Viscosity 3.2
- Plasma exchange #3
- Pt started on modified BDR
  - Rituximab held
Fun Fact

- FDR would never host a dinner party with 13 guests in attendance.
- He would not travel on the 13th of any month.
Hospital Course Cont.

- No additional bleeding, good neuro recovery
- Tolerated modified BDR w/o incident
- 11/18/16: repeat TPE for PTT 37
  - line removed 2/2 fever
- 11/24/16: PTT 42, tunneled line placed
  - IVIG given (PTT 44->42)
  - Humate P given (VWF 11->20)
- 11/25/16: TPE (PTT 46->35)
  - Discharged
Patient Course Continued

- Readmitted 11/28 for TPE and C1D11 BDR
- Continued modified BDR at SCCA
  - Rituximab held for 1st 2 cycles
- Six more exchanges required due to PTT prolongation
  - Last 3/3/16
- BDR complicated by neutropenic fever
  - Transitioned to ibrutinib 5/2/16
Summary

- Acquired VWD is a known complication of a variety of conditions, including lymphoproliferative diseases.
- Treatment of the underlying disease, supportive care, IVIG and humate P are mainstays of therapy.
- In certain cases, plasmapheresis may be required
  - In the case of bleeding or prolonged PTT, partial replacement with FFP is required.
Fun Fact

- In Spanish-speaking nations, Tuesday the 13\textsuperscript{th} is considered unlucky.
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Questions?