Evaluation Of Bleeding Disorders /AAP Baton Rouge

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Evaluation and approach to management of a bleeding child

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Objectives

• Describe the physiologic process of blood clotting
• Summarize the importance of accurate history, through P/E and basic clinical lab test in making a diagnosis
• List common and severe bleeding disorders in Children
• Formulate plans for referral and continued care

• No conflict of Interest
Disclosure

• Nothing to disclose in relation to this presentation at this time
Coagulation

• Vessel wall
• Platelets
• Coagulation cascade
• Fibrin clot
• Fibrinolysis
Bleeding Vs. Thrombosis

Bleeding
- ↓ Procoagulant factors (e.g. F II, V, VII, VIII, IX, X, XI, XII)
- Thrombocytopenia
- Vessel wall damage
- ↑ Fibrinolytic potential (↑ tPA or plasminogen or ↓ inhibitors)

Thrombosis
- ↑ Procoagulant factors (e.g. F II, V, VII, VIII, IX, X, XI, XII)
- ↓ Natural anticoagulants (AT, Protein C, S)
- Thrombocytosis
- Vasculitis
- ↓ Fibrinolytic potential
Abnormal Bleeding

History

• Spontaneous Vs Induced
• Congenital Vs Acquired
• Nature and site of bleeding
• Circumcision, dental extraction
• Epistaxis, Menorrhagia
Abnormal Bleeding

• Hemarthrosis, hematoma - FVIII, IX

• Petechial, mucosal bleeds
  • Platelets
  • Vascular
  • Aspirin
Family History

X-Linked Recessive -
  FVIII, IX
VWD - auto dominant
Females with
  Hemophilia – Turner’s,
Lyon’s Hypothesis,
Testicular Feminization,
Carrier and patient
  having a baby!
Physical Examination

- Pallor
- Organomegaly
- Adenopathy
- Hemarthrosis
- I.C. Hge
Laboratory

Screening Tests
• CBC, Smear
• Platelet count
• B.T- not popular
• PFA
• P.T., P.T.T,
Lab - confirmatory

- Prolonged PTT work up –

Dilution or mixing studies

Lupus anticoagulant

DRVVT, PNP

Self limited, no risk of bleeding

?Hypercoagulable
Lab - confirmatory

- Factor assays - VIII, IX
- Platelet aggregation - VWD
- Fibrinogen, FSP, smear
  - D-Dimer -DIC
- vW Antigen, vW activity
  - Ristocetin Co-Factor
- vW Multimer
- Genetic study
- Bone Marrow
- Call your friendly Peds Hematologist
Case Studies

• Family H/O maternal uncles, easy bleeders
• Hemarthrosis
• Normal CBC, Platelets, PT
• Increased PTT
• Dx – Factor 8 or 9 deficiency
Case Study

• Boy 16 yrs old, Bleeding following T &A

• Increased PTT, Normal CBC, Plts, PT

• DX-? VWD, Mild Factor 8 deficiency
14 year old white female h/o antipyretics

Mucosal bleeding

Normal PT, PTT

High BT, Normal CBC

Further tests? Diagnosis?
Case Study

• 6 yr old white female
• Acute onset of Petechia, Purpura
• H/O viral infection
• Normal CBC, platelet - low
• Mega thrombocytes +
• ? Bone marrow needed - DX ?
D/D Bleeding

- Leukemia, malignancies
- DIC - Sepsis
- HSP
- EBV - Thrombocytopenia
- Vasculitis - SLE
- Drugs
- Aplastic or Hypoplastic
D/D Bleeding disorders

• ITP
• TTP
• HUS
• Storage Disorders
• Hemangiomas – Kasabach-Merritt
• Child Abuse
Retinal hemorrhages:

- Extraordinary force
- Unilateral or bilateral hemorrhages are present in 75-95% of abusive head trauma
- Common with birth trauma but resolve within 4 weeks
- Other causes of retinal hemorrhages include: hematologic abnormalities, central nervous system vascular malformations, infections, high-altitude mountain climbing, during normal deliveries of newborns, and as a complication of general anesthesia
Referred ?? bleeding disorder
Bleeding from gums, Pseudo paralysis
Hematuria, arthropathy
Toxic child in ER

- 2yr old with h/o fever for 1 day
- Toxic, hypotensive
- Hb 5 gms, platelets 21000
- Review smear
GI Bleed - less common
Fever, Lymphadenopathy, Pharyngitis, abnormal smear!
Beware of fever with bone pain!

- 8 yr old AA female
- Fever x 2 weeks
- Joint pain
- Bleeding from gums
- Easy bruising
• Fever
• Bone pain and joint pain
• Weight loss
• 14 yr old AA male
CASE 4

A 12 years old boy with progressive pallor, bruising ,no HSM

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>5.6 g%</td>
</tr>
<tr>
<td>TLC</td>
<td>2600</td>
</tr>
<tr>
<td>DLC</td>
<td>N34, L56, E5,M5</td>
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<tr>
<td>Platelet count</td>
<td>30,000 /cu.mm</td>
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<tr>
<td>MCV</td>
<td>114</td>
</tr>
<tr>
<td>MCH</td>
<td>28.4</td>
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<tr>
<td>MCHC</td>
<td>33.1</td>
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<tr>
<td>RBC count</td>
<td>1.7 million/cu.mm.</td>
</tr>
<tr>
<td>RDW-CV</td>
<td>21.5</td>
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Bone marrow- pt with pancytopenia
NEWER CBC PARAMETER

• Immature platelet fraction
• Immature granulocytes
• Immature reticulocyte fraction
• Red cell fragments/ Schistocytes
• Reticulocyte hemoglobin
Mean Platelet Volume (MPV)

- Normal MPV - 7 to 11 fL
- Platelets newly released - larger in size
- Platelets decrease in size with aging

- High MPV
  - Rapid turnover of platelets (ITP, TTP)
  - Bernard Soulier syndrome
  - MYH9- related thrombocytopenias [May-Hegglin anomaly, Sebastian platelet syndrome, Fechtner syndrome and Epstein syndrome]

- Low MPV
  - Wiskott Aldrich syndrome
  - X linked thrombocytopenia
Immature Platelet Fraction (IPF)

- Quantified by flow cytometry using any fluorescent dye that binds RNA
- Newly released, larger and more reactive
- Reflects the rate of thrombopoiesis
- Usual reference range: 1 – 7%
Immature Platelet Fraction (IPF)

**Low IPF → Decreased Production**
- Aplastic anemia
- Leukemia
- Marrow suppression
- Drugs

**High IPF → Increased Destruction / Regeneration after suppression**
- Immune Thrombocytopenia (ITP)
- Thrombotic Thrombocytopenic Purpura (TTP)
- Disseminated intravascular coagulation (DIC) – Drugs
CASE 5

A 3 years old boy presented with recurrent history of epsitaxis, gum bleeds and petechial spots since past 1 year.

H/O recurrent respiratory tract infections, skin infections present.

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<tr>
<td>DLC</td>
<td>N44, L46, E5,M5</td>
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<tr>
<td>Platelet count</td>
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<tr>
<td>MCV</td>
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<tr>
<td>MCH</td>
<td>29.4</td>
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<tr>
<td>MCHC</td>
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<tr>
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<tr>
<td>RDW-CV</td>
<td>14.5</td>
</tr>
<tr>
<td>MPV</td>
<td>5.6 fL</td>
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Recurrent infections and cancer

- 2 yr WM, h/o recurrent pneumonia, persistent skin rash and lymphadenopathy. Platelets 40,000.

- Small platelet size MPV

- A male sibling died of septicemia 4 years ago. Skin tests for mumps, Candida and PPD are negative
CASE 6

A 7 years old boy admitted with Dengue Hemorrhagic fever
Afebrile, Hemodynamically stable
No bleeding complaints currently

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<td>DLC</td>
<td>N34, L56, E5,M5</td>
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<tr>
<td>Platelet count</td>
<td>10,000 /cu.mm</td>
</tr>
<tr>
<td>IPF (Immature platelet fraction)</td>
<td>24% (Ref: 1 - 7)</td>
</tr>
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Will you transfuse the child?
Immature Platelet Fraction (IPF)

- During regeneration phase, IPF rises 1–2 days prior to the platelet count rise.
Platelets

- Psuedothrombocytopenia
- Small platelets /low plts - Hyoplastic and aplastic BM
  - Wiskott Aldrich Syndrome
  - X linked thrombocytopenia
  - THC 2 ( ANK RD26)
- Familial Plt disorder with predisposition to AML ( FPD/AML)
Platelets

• Large Platelets
  ITP, Auto immune
  BS, Grey plt syndrome
Type 2 B vWD
May Hegglin anomaly
Di George syndrome, Epstein Syndrome
Sebastian Syndrome, Jacobsen Syndrome
Familial Mediterranea<wbr/>n macrothrombocytopenia
H/O Nose bleeding, bleeding after extractions

• Large Platelets, decreased numbers
Fragmented Red Cells (Schistocytes)

Seen in

- microangiopathies (eg, TTP, HUS, DIC)
- cardiovascular disorders (eg, prosthetic valve and endocarditis)
- Serial counting in TTP may correlate with changes in serum LDH levels
- normal reference range for the schistocyte count is as 0.03–0.58%
Regression, Hepatosplenomegaly and Pancytopenia
Neonatal Thrombocytopenia

- Maternal ITP, Autoimmune disorders
- Alloimmune
- Sepsis, DIC
- IU Viral Infections, HIV
- Drugs
- TAR Syndrome
- Congenital leukemia
Neonatal Alloimmune Thrombocytopenia

- Healthy mother and infant
- Normal CBC except for platelets
- Self limited
- Risk of IU IC hemorrhage
- Maternal platelets (PLA 1 Negative)
- IV Ig . ? Antenatal treatment
Neonatal Thrombocytopenia

- TAR Syndrome
- Cavernous Hemangiomas – Kassabach Merritt Syndrome
- Wiskott Aldrich Syndrome
- Sepsis with DIC
- Maternal ITP, SLE, Drugs
- Alloimmune
- I.U.Infections,
- Placental infarcts
Clinical Case

• LBW, premie at 30 weeks, Looks ill
• Jaundice
• Anemia
• Purpura and Petichiae
• Hepatosplenomegaly
• Platelets – 40,000
Fever, Hepatosplenomegaly
Thrombocytopenia and bleeding in SICK neonates – 1 and 2
Case of a breast fed bleeding infant

• 7 day old infant born at 34 weeks
• Delivered at home in Bogalusa!!
• Baby Friendly mom- totally breast fed
• Generalized petichiae , Melena and GI bleed
• Transferred to you at 7 pm on a Friday afternoon!!
Hemorrhagic Disease Of New Born

- Classic
  - Primarily Breast fed infants
  - Bleeding 2-10 days of life
  - Generalized ecchymosis, GI Hge, Pulmonary Hge
  - I C Hge - Uncommon
Vit K Deficiency

- High risk in Premies and SGW
- Poor IU storage
- Poor Liver function and stores
- Gut flora – poor synthesis
- Decreased intake
- Breast Milk – poor source
DIC

- Sick Infant – Sepsis, Hypoxia, Hypotension
- NEC
- Death of a Twin in utero
- Kassabach Merritt
- Non immune Hydrops
- Neonatal Neoplasms
• Diagnosis – CBC, DIC Platelet, Smear, FSP, D-dimers, Fibrinogen PT, PTT, TT

• Treat Primary cause
• Supportive Care
• Transfusions as needed
• FFP, Platelets, PRBC
Congenital anomalies

- TAR Syndrome
- Trisomy 13
- Trisomy 18
- Trisomy 21
- Fanconi’s anemia
- Ivy Mark Syndrome
Cutaneous nodules, hepatosplenomegaly – smear
Healthy Newborn male with bleeding after circumcision

- First born male, Routine circumcision
- Profuse delayed bleeding
- Family H/O of bleeding in maternal uncle
- Prolonged PTT, Normal PT
Hereditary Bleeding Disorders

• Hemophilia A or B
• Factor XIII Def – delayed bleeding from Umbilical stump
• Von Willebrand Disease- 1% of all Caucasians have VwD
• Report of Unusual cases – X, VII,XIII
Tooth Extraction

- Treat before (50% or greater, depending on extent of procedure)
- Consider DDAVP for mild hemophiliac
- Epsilon amino caproic acid (Amicar) or tranexamic acid after
CNS Bleeds (Head trauma)

- Most common cause of fatal bleeding
- May occur in delayed fashion
- Treat even minor head trauma in general
- 100% replacement, before diagnostic procedures
- CT or MRI may be helpful
- When in doubt, or if any sign of objective head trauma (abrasion or external hematoma), treat
Philosophy of Care

• Normalization of life style and prevention of disability
• Rx still “on-demand” in most cases, but prophylactic treatment should be considered
• Home therapy whenever possible
References /Reading material

- Text Book Of Peds Hematology – Nathan
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- Neonatal Hematology – Christensen
- PCNA Oct 2010 ,57(5) 1085
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