Common Hematology disorders
血液腫瘤科
滕傑林

Anemia

Anemia: Hb<12 g/dL in women and <14 g/dL in men

PE findings that aid in diagnosis include lymphoadenopathy, hepatic or splenic enlargement, jaundice, tenderness, neurological symptoms, and blood in feces

Lab evaluation

- Hb and Hct: Hb might be normal in acute blood loss because not having enough time to restore plasma volume
- Reticulocyte count: reflex the BM response to anemia
- MCV
- Peripheral blood smear
- Additional testing: such as G6PD...

Anemias associated with decreased RBC production

Iron-deficiency anemia (IDA)

- Etiology: blood loss (menstruation, feces, occult GI tract malignancy, consumption of clay...)
- Lab results
  - MCV: usually normal in early IDA
  - Hct<30%: hypochromatic microcytic
  - Serum Ferritin level: <10 ng/ml in women; <20 ng/ml in men
  - Serum iron: < 50 ug/dL; TIBC: >420 ug/dL
  - Bone marrow biopsy: absent staining for iron is the definitive test for iron deficiency

Therapy

- Oral ferrous sulfate, 325 mg PO TID, taken between meals
- Parental iron therapy
  - Most patients require 1000-2000 mg iron to correct the deficit
### Anemias associated with decreased RBC production

#### Thalassemias
- **Alpha-thalassemia**
  - Normally, 4 α-globin genes
  - Def. 3 genes: HbH
  - Def. 4 genes: hydrops fetalis
- **Beta-thalassemia**
  - Normally, 2 β-globin genes
  - Def. 1 gene: Thalassemia minor (trait)
  - Def. 2 genes: Thalassemia intermedia
  - Def. 2 genes severely: Thalassemia major (Cooley’s anemia)

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#### Treatment
- Transfusion
- Splenectomy
  - Not performed for patient younger than 6 y/o
  - Immunization against Pneumococcus, H.I, and Neisseria meningitis
- Iron chelating therapy: Deferoxamine 50-100mg/Kg/D
- BMT

#### MDS
- Refractory anemia
- Refractory anemia with ringed sideroblast
- Refractory anemia with excess blasts
- Refractory anemia with excess blasts in transformation
- CMMoL

#### Vitamin B12 deficiency
- Pernicious anemia
- Gastricctomy
- Pancreatic insufficiency
- GI bacterial overgrowth
- Intestinal parasites

#### Megaloblastic anemia: MCV>100
- Folic acid deficiency
  - Decreased intake (alcoholism)
  - Malabsorption
  - Increased utilization (hemolytic anemia, pregnancy)
  - Drugs

#### Lab results
- Besides macrocytic anemia, leucopenia and thrombocytopenia may occur
- PB: anisocytosis, polikilocytosis, hypersegmented neutrophil (> 5 segments)
- LDH, indirect Bil elevated (ineffective erythropoiesis)
**Anemias associated with decreased RBC production**

- Lab exams
  - Serum vitamin B12 and folate level
  - BM biopsy: for R/O MDS and hematologic malignancy
- Therapy
  - Folic acid 1mg PO QD until corrected
  - Vitamin B12 1 mg IM QD for 7 days→weekly

**Anemias associated with increased RBC production or destruction**

- Bleeding
- Hemolytic anemia
  - Intravascular hemolysis
    - S/Ss: fever, chills, backache
    - Severely Decreased hematoglobin
    - Positive Coomb’s test
  - Extravascular hemolysis
    - RBC destruction in the RE system, primarily the spleen
    - Jaundice, splenomegaly (+)

**Anemias associated with increased RBC loss or destruction**

- Sickle cell disease
- G6PD deficiency
  - Lab results:
    - PB smear: bite cells, RBC inclusion (Heinz bodies)
    - Tx: hydration, RBC transfusion
- Autoimmune hemolytic anemia (AIHA)
  - Warm antibody AIHA: IgG
  - Cold antibody AIHA: IgM

**Anemias associated with increased RBC loss or destruction**

- Drug-induced hemolytic anemia
- Microangiopathic hemolytic anemia
  - DIC
  - Thrombocytopenic purpura
  - Hemolytic-uremic syndrome
  - PB: fragment RBC
Lymphoma

Dividing into 2 types:
- Non-Hodgkin's lymphoma
- Hodgkin's lymphoma: RS cell (+)

Lymphoma

HD
- Usually presents with cervical LN and spreads in a predictable manner along LN group
- Stage I A and IIA: R/T alone, unless mediastinum mass over 1/3 of chest
- Stage IIIA: either R/T or C/T
- Stage IV: C/T
- If B symptoms noted-> C/T

Lymphoma

NHL: Classified as low, intermediate, and high grade
- Low grade lymphoma:
  - Often involves BM at diagnosis
  - Tx: watch and wait until S/Ss
  - R/T: some benefit for stage I/II
  - Anti CD20 "Rituximab": 50% response to follicular lymphoma

Intermediate grade lymphoma
- Can be cured by C/T (CHOP is the most common) with CR rate: 80%
- Prognosis index
  - LDH
  - Stage III/IV
  - Age > 60 y/o
  - More than one extranodal site
  - Poor performance status

High grade lymphoma (Burkitt's, lymphoblastic)
- High frequency of CNS and BM involvement
- Combined C/T (usually CHOP) with CNS prophylaxis
- Prevention of tumor lysis syndrome
  - Hydration
  - Allopurinal 300-600mg QD
Acute Leukemia

- Two groups
  - Acute myeloid leukemia (AML)
  - Acute lymphocytic leukemia (ALL)
- Def: abnormal blasts in bone marrow (usually > 20-30%)
- Classification: AML: M0-M7; ALL: L1-L3, by morphology

aml

80% of adults with leukemia
50-80% CR with induction C/T with Cytosar + Idarubicin (7+3 or 5+2)
Consolidation C/T: high dose Cytosar based
Cure rate: 30-40%
High risk patients: Allogenic PBSCT in first remission

Acute Leukemia

- All
  - Only 25% of leukemia patients over 15 y/o
  - Tx
    - multiple chemotherapeutic agents for induction and consolidation for 6 months
    - At least 18 months low dose C/T (MTX+6-MP) for maintain therapy
    - 30-40% cured
    - Allogenic PBSCT for poor prognostic patients in 1st remission

Acute Leukemia

- Special consideration: AML, M3 (APL)
  - Tx with all-trans retinoic acid as induction: 90% in CR
  - C/T for maintain therapy: 75% cure

Acute Leukemia

- Chronic myeloid leukemia (CML)
- Chronic lymphocytic leukemia (CLL)

Chronic Leukemia

- S/Ss: leukocytosis, usually with splenomegaly
- Dx confirmed by Philadelphia Chromosome t(9,22)-> bcr-abl gene
### Chronic Leukemia

- **Tx**
  - Hydrea for leukocytosis
  - Glivec (bcr-abl tyrosine kinase inhibitor)
    - Magic bullet
    - Increase differentiation and maturation of CML cells
    - May be used in all three phases (Chronic phase, accelerated phase, blast crisis)
  - Allogenic PBSCT is the only way to cure the disease

### Chronic Leukemia

- **CLL**
  - Usually in western people
  - S/Ss Tx
  - Tx principle: Wait and See
  - Fludarabine may help

### Multiple Myeloma

- Malignant plasma cell disorder
- Accompanied by a serum or urine paraprotein
- **S/Ss**
  - Hypercalcemia, anemia, bone pain, renal failure, infection

### Multiple Myeloma

- **Exams:**
  - Skull and long bone X-ray
  - BM exams
  - Serum and urine protein electrophoresis
  - B2-microglobulin
  - IgG, IgA, IgM, Kappa, lamda

### Multiple Myeloma

- **Tx:**
  - MP (melphalan + prednisolone), PO
  - VAD (Vincristine/Doxorubicin/Decadron), IV
  - Thalidomide, PO
  - PBSCT
  - S/Ss Tx, such as pamidronate, 90mg IV/month, decreases skeletal complications
Platelet Disorder

- Thrombocytopenia: plt<150,000/ul
  - Under production
  - Increased destruction

Platelet Disorder

- Under production
  - Viral suppression
  - Marrow infiltration (myelophthisis)
  - Drug induced (ethanol is the most famous)
  - Vit B12 and folic acid deficiency

Platelet Disorder

- Increased destruction
  - Immune thrombocytopenia
    - ITP (immune thrombocytopenic purpura)
      - Dx: isolated thrombocytopenia
      - Possible causes: SLE, HIV infection, hyperthyroidism, APS....
      - Tx: Steroid, IVIG, splenectomy

Platelet Disorder

- Thrombotic thrombocytopenic purpura (TTP)
  - Pathophysiology: plt aggregation in the microcirculation
  - S/Ss: thrombocytopenia, microangiopathic hemolytic anemia, fever, deteriorated renal function, conscious change, fragment RBC
  - Tx:
    - Plasma exchange
    - Steroid
    - Anti-platlet agents

Platelet Disorder

- Platelet transfusion is contraindication!!
Platelet Disorder

- Thrombocytosis: Plt>500,000
  - Reactive
  - Splenectomy
  - IDA
  - Chronic infection
  - Malignancy

- Essential thrombocythemia: MPD
  - Dx:
    - No reactive cause
    - Philadelphia chromosome negative (R/O CML)
  - Tx
    - Aspirin
    - Hydrea

Platelet Disorder

- Essential thrombocythemia: MPD
  - Dx:
    - No reactive cause
    - Philadelphia chromosome negative (R/O CML)
  - Tx
    - Aspirin
    - Hydrea
### ABO 血型

#### Genotype

<table>
<thead>
<tr>
<th>ABO Type</th>
<th>Phenotype</th>
<th>RBC surface Ag</th>
<th>Secretor ABO/H product</th>
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</thead>
<tbody>
<tr>
<td>H/H Se/-</td>
<td>ABH secretor</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>H/H se/se</td>
<td>ABH-non secretor</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>A/A Se/-</td>
<td>Parabombay</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>A/A se/se</td>
<td>Bombay</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

#### 规则抗体

- Anti-A, anti-B
- 在不具有该带原者的血浆中出现，称为"这些抗体会由肠内菌刺激产生。

#### 后天性的 ABO 血型变化

- Acquired B
  - 因肠阻塞等疾病导致细菌酵素 deacetylase 进入血液中而造成。
- Weakened A or B
  - 某些疾病时（以白血病最常见），导致 RBC AB Ag 减弱。

#### ABO 亚型

- ABO 型
  - RBC 携 anti-A or anti-B 易见，没有规则的 ++ 反应时，可能系亚型。
- Caucasian: A2 most often
- Taiwanese: B3 most often

- 孟买血型
  - RBC and sera 皆无 ABH Ag-> 有强效的 anti-H
  - 亚孟买血型：国人属第三型（分泌型），anti-H 低 (1/8000)

#### 输血前检查

- ABO, Rh(D) 血型检查
  - Saline phase, 室温下进行
  - Forward typing (Cell typing)
  - Reward typing (Serum typing)

- 不规则抗休筛检
  - Indirect Coombs Test
  - 2-3 名 O 型带者之 RBC 便见反应

- 交叉试验
  - 病人血清与血品进行反应

#### 血液成品介绍

<table>
<thead>
<tr>
<th>抗凝剂种类</th>
<th>RBC 保存期限</th>
</tr>
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<tbody>
<tr>
<td>ACD</td>
<td>21 days</td>
</tr>
<tr>
<td>CPD</td>
<td>21 days</td>
</tr>
<tr>
<td>CPDA-1 (CPD+ adenine)</td>
<td>35 days</td>
</tr>
<tr>
<td>CPD + SAGM</td>
<td>35 days</td>
</tr>
</tbody>
</table>
血品保存與使用

<table>
<thead>
<tr>
<th></th>
<th>RBC</th>
<th>Platelet</th>
<th>Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>存放條件</td>
<td>1-6℃</td>
<td>20-24℃</td>
<td>-18℃</td>
</tr>
<tr>
<td>輸血安全要求</td>
<td>ABO compatible</td>
<td>ABO alternative</td>
<td>ABO compatible</td>
</tr>
</tbody>
</table>

**FFP**: one year

**Cryoprecipitate**: 5 years

**Shelf Life**

- Plasma (FFP & Cryoprecipitate)
- Platelet
- RBC (PRBC & Whole Blood)

**Frozen Plasma**

- Fresh Frozen Plasma (FFP)
  - 收集的全血在8小時內即進行分離
  - 不穩定因子（Factor V/VIII）較充足
- Traditional Frozen Plasma
  - 收集的全血在8小時後才進行分離
  - 不穩定因子（Factor V/VIII）較少
- 冷凍上清品（Cryoprecipitate）
  - 含有豐富的
    - Factor VIII
    - Factor V
    - vWF
    - Fibrinogen
    - Factor XIII

血小板輸血

- **Platelet Surface Antigen**
  - Tissue antigen
    - HLA
    - ABO
    - P
    - Z
    - Lewis
  - Specific Antigen: Glycoprotein
    - HPA (Human Platelet Antigen)
    - HPA-1 to HPA-13, increasing

血小板輸血

- **Platelet Transfusion Refractory**
  - 因反覆輸注血小板，產生 HLA and plt-specific Ab
  - 一般認為，anti-HLA Ab 較重要
- **Corrected Count Increment (CCI)**
  - [(輸血後血小板數目-輸血前血小板數目) x BSA] / (輸注之血小板數10^11)
  - 1U 分離血小板，約有 3x10^{11} 血小板
  - 輸後
    - 輸血後一小時之 CCI 應大於 7500-10000 (Preferred)
    - 輸血後 18-24 小時之 CCI 應大於 5000

Thank you for your attention