Hematopoietic and Lymphoid Neoplasm Project
Acknowledgments

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Disease Presentations and Diagnostic Process

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Classification of Tumors

Objectives

Understand the basis of the WHO Classification

Understand the presentation and workup for hematopoietic and lymphoid neoplasms

Recognize provisional diagnoses
Objectives

Recognize the significance of immunophenotyping and genetic testing
Understand the terminology used in immunophenotyping and genetic testing
New Classifications of Hematopoietic and Lymphoid Neoplasms
2008 WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues

Basic principle: Classification for all neoplasms based on:

- Morphology and biologic features
- Genetic
- Immunophenotype
- Clinical features
Disease Definitions and Symptoms
Tumors Primary in Tissue

**Lymphoma**: Malignant tumor in lymph nodes or lymphoid tissue

**Myeloid sarcoma**: Solid tumor of immature white blood cells

**Plasma cell tumor (MM, extraosseous, osseous)**: Tumors comprised of plasma cells
Lymphoma Presentation

Not specific to disease
Swollen lymph nodes
Chest pain/breathing problems
Unexplained weight lost
Recurring fevers/night sweats
Rashes
Lower back pain
Sore LN after alcohol consumption
Leukemia
Presentation/Symptoms

Leukemia limited to BM involvement

Chronic leukemia
  Usually asymptomatic

Acute leukemia
  Symptomatic
  Symptoms vary with type of leukemia
Acute Leukemia Symptoms

Anemia
Shortage of red blood cells
Symptoms: SOB, tiredness, pallor

Leukopenia
Shortage of normal white blood cells; too few mature granulocytes
White blood cells do not protect against infection
Acute Leukemia Symptoms

Thrombocytopenia

Low blood platelets

Platelets control blood clotting by closing “holes” in damaged blood vessels

Symptoms: excessive bruising, bleeding, nosebleeds, and bleeding from gums
Initial Diagnostic Procedures
Lymphoma, Myeloid Sarcoma, Plasma Cell Tumor

Tissue biopsy

- Lymph node
- Organ
- Skin
- Bone
- Bone marrow
Leukemia

1. Blood counts (CBC; peripheral smear)
2. Bone marrow aspiration/biopsy
Provisional Diagnoses
Types of Diagnoses

NOS histology only
NOS with a “possible/probable” specific histology
Provisional Diagnoses

NOS histology only

NOS with a “possible/probable” specific histology
NOS Diagnosis

NOS histology

Provisional – awaiting test results

Only diagnosis available now

Use Appendix E to identify NOS
Example:
NOS DX Only Option Available

Chronic myeloproliferative neoplasm (MPN), NOS
Clinical, lab, and morphologic features + Does not meet criteria for specific MPN OR Features overlap two or more MPD categories
Initial stage
Late stage
Provisional Diagnoses

NOS histology only

NOS with a “possible/probable” specific histology
NOS with Probable Specific

1. MPN (9960/3), probably PV (9950/3)
Tests That Identify Specific Hematopoietic and Lymphoid Histologies
2008 WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues

Basic principle: Classification for all neoplasms based on:

- Morphology and biologic features
- Genetic
- Immunophenotype
- Clinical features
Genetic Testing

Laboratory studies of blood, bone marrow, or tissue to analyze DNA to identify chromosome abnormalities which diagnose specific neoplasms
Normal Chromosomes

46 in each cell

Each chromosome has a specific number

Example: (1;2)

Short arm “p” and a long arm “q”

Example: (p13;q22)
Genetic Abnormalities

1. Translocation: $t(1;2)$
2. Inversion: $inv16$
3. Deletion: -7 or 7-
4. Addition: +8 or 8+
Gene Translocation

Before translocation

Chromosome 20

Derivative Chromosome 20

After translocation

Chromosome 4

Derivative Chromosome 4

Courtesy: National Human Genome Research Institute
Gene Inversion

Diego Diez, Ph, Bioinformatics Center, Institute for Chemical Research, Kyoto University. Gokasho, Uji, Kyoto 611-0011 JAPAN diez@kuicr.kyoto-u.ac.jp
Gene Deletion

Before deletion

After deletion

Deleted area

Courtesy: National Human Genome Research Institute
Gene Addition

Genetic Testing

**FISH**: Identifies genetic changes and translocations.

**Polymerase chain reaction (PCR)**: Measures cancer cells that cannot be detected by FISH.

**Karyotyping**: To arrange and classify chromosomes based on number, size, shape, and other characteristics.
FISH to Identify NPM/ALK Fusion Gene

http://www.pathologyoutlines.com
Karyotype

http://www.pathologyoutlines.com

Chromosome 13 microdeletion Locus RB1
**Immunophenotyping**

Cells from blood, BM, tissue used to determine types of antigens or markers on surface of cell. Referred to as CD

**CD; cluster of differentiation:** Used to define the findings in immunophenotyping.
Additional Immunophenotyping

**Flow cytometry:** Cells from blood, BM, tissue are treated with antibodies and passed in front of a laser beam.

**Immunocytochemistry (IHC):** Shows specific antigens in cells from blood, BM, by using either fluorescent dyes or enzymes as markers.
Immunohistochemistry

http://www.pathologystudent.com/?tag=acute-myeloid-leukemia
Genetic Studies and Immunophenotyping

Cytogenetics: The study of the DNA to identify antigen receptors and translocations.
Genetic Testing/Cytogenetics

46,XY,del(5)(q15q33)

Identifying Definitive Diagnosis
Required to Identify Specific Histology

Use Hematopoietic DB to identify definitive diagnostic method(s)
<table>
<thead>
<tr>
<th>ICD-O-3 Code</th>
<th>Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>9866/3</td>
<td>Acute promyelocytic leukemia (AML with t(15;17)(q22;q12)) PML/RARA</td>
</tr>
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</table>

### Alternate Names
- APL
- Acute myeloid leukemia, PML/RAR-alpha
- Acute myeloid leukemia, t(15/17)(q22;q11-12)
- Acute promyelocytic leukemia

### Definitions
Acute myeloid leukemia in which abnormal promyelocytes predominate

### Definitive Diagnostic Methods
- Bone Marrow biopsy (and)
- Cytochemistry
An Additional Diagnostic Method
Types of Diagnoses

NOS histology only

NOS with a “possible/probable” specific histology

Diagnosis of exclusion (clinical)
Diagnosis of Exclusion (Clinical)

Tests are equivocal

Diagnosis based on equivocal tests and clinical presentation

Examples: myelodysplastic syndrome, unclassifiable; refractory thrombocytopenia
Myelodysplastic syndrome, unclassifiable

Alternate Names
MDS
Myelodysplastic syndrome, NOS
Preleukemia
Preleukemic syndrome

Definitions
Blood: Cytopenias, no blasts\nBone marrow: <5% blasts, dysplasia in granulocytes or megakaryocytes
Granulocytes or megakaryocytes (MDS, formerly known as "preleukemia") are a diverse collection of hematological conditions united by ineffective

Definitive Diagnostic Methods
Clinical diagnosis

Disease Genetics Data
No Genetics Data Found

Disease Immunophenotyping
No Disease Immunophenotyping Found
Get Information on Tests

Check with laboratory to get samples of tests
Ask HIM dept
  Where tests are filed
  How tests that arrive after MR is complete are filed
Follow-back with physician if tests have been ordered
Major Points

• Diagnostic/work-up process different
  • Genetic data and immunophenotyping
• Do NOT use ambiguous terminology
• Do NOT code to higher ICD-O-3 code
• Histology code updated to more specific
• Use Hematopoietic DB to identify Definitive Diagnostic Procedures
Conclusion

• The new hematopoietic and lymphoid neoplasm rules go into effect for cases diagnosed January 1, 2010, and after

• Email address for questions
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