PEDIATRIC ACUTE LYMPHOCYTIC LEUKEMIA
- EXCITING NEW DEVELOPMENTS

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Case Report: KM

• 4-year-old female
• 10/11/2011: nausea, abdominal pain, muscle aches, fatigue, no bone pain
KM

• 10/13 WMC
• Wbc 23,000, ANC 230, Hgb 3.9
• Platelets 12,000
• Differential segs 1%
• Blasts 63%
KM

• 10/13 sent to Children’s Hospital Colorado
• LDH 1968
• Bm-ALL, preB
Acute Lymphocytic Leukemia (ALL)

• 30% of malignancies in children <15
• 2,400 new cases of childhood ALL/year in USA
ALL

• Cancer of immature lymphocytes, clonal, cells proliferate, but don’t differentiate
ALL

• By definition, present throughout body at time of diagnosis
Garden Analogy

PLT

RBC

WBC

Normal Bone Marrow
Garden Analogy

Leukemic Bone Marrow
ALL – Presenting Signs

• Sometimes acutely, but usually insidiously
• Fever, infection
• Pallor
• Bruising
ALL – Presenting Signs

- Petechiae
- Bone pain or limp
ALL - Exam

• Pallor, bruising, petechiae
• Lymphadenopathy
• HSM in 30-50%
• Irritable, limp
CBC is a reflection of what is going on in the bone marrow.
When you evaluate a CBC

• Look at whole CBC, not isolated parts
• Be methodical in looking at CBC
CBC consists of 3 cell lines

1. WBC (ANC = % segs + % bands x total wbc)
2. RBC
3. Platelets
If one line down, more likely to be simple problem (ITP, Fe deficiency anemia)

If two lines down, worrisome for bone marrow problem

If three lines down, strongly consider bone marrow evaluation
ALL - Epidemiology

• Usually cause is unknown
• Associated with some genetic syndromes (ataxia-telangiectasia) or radiation exposure (Hiroshima)
Psychological Aspects at Diagnosis

1. ALL not an emergency, but it is to parents
2. Parents always ask why diagnosis not made earlier resulting in blame and guilt
3. Parents perseverate about cause, resulting in blame and guilt
4. Uncertainty is major stressor
ALL – Prognostic Markers
(resulting in different treatments)

• CNS involvement – worse prognosis
• Needs more aggressive therapy, usually radiation
Prognostic Markers

• <1 year = bad prognosis
• 1-10 years = best prognosis
• >10 years = not as good, but better than adults
Prognostic Markers

• High WBC at diagnosis – bad
• In general, the higher the WBC the worse the prognosis
• Cutoff for treatment purposes – 50,000, i.e. above that, need more aggressive therapy
Pediatric ALL Therapy 2012-2014

• Overall cure = 85-90%
• Low risk subsets = 95%
General Therapy Guidelines for ALL

• 2 years for girls, 3 years for boys
• Multi-drug, different phases
• Induction, consolidation, interim maintenance (usually high-dose methotrexate), delayed intensification, prolonged maintenance
Exciting New Developments

1. Prognostic Biologic Markers
   A. Cytogenetics
   B. Minimal Residual Disease

2. Children's Oncology Group (COG)

3. Knowledge of Late Effects
Exciting New Developments (cont.)

4. Improvements in Therapy of ALL in Down Syndrome
5. Twinning Programs in Developing Countries
6. Recent Advances in Gene Therapy
Prognostic Biologic Markers

Biologic features at diagnosis (cytogenetics) and at Day 29 (minimal residual disease) allow risk stratification and selective application of post Induction intensification strategies.
A. Cytogenetics – genetic pattern of leukemia cells

• Favorable – ETV6-RUNX1, double trisomies (4,10)
• Unfavorable – hypodiploidy, MLL rearrangement, Philadelphia chromosome
• Everything else
B. Minimal Residual Disease (MRD)

- End induction minimal disease burden
- Bone marrow sample at Day 29 of therapy
- Polymerase chain reaction, flow cytometry
- .01% cutoff very important prognostic factor
#2

Children’s Oncology Group (COG)

- pediatric cancer study group
- 200 hospitals in North America, Australia, Europe
- develop common therapeutic research trials
- collect specimens, pool data
COG Research Trials

• Therapeutic
• Supportive care
• Epidemiologic
• Biologic
• Quality of life
• Long-term follow-up
#3

Knowledge of Late Effects

• Learning
• Cardiac
• Fertility
• Second malignancies
Late Effects Summary

• Many ALL survivors are cured, normal intelligence, psychologically sound, work, have families – normal people.
• Subsets with long-term issues (e.g. cranial radiation)
• All are at some risk of second malignancies.
#4

Improvements in ALL Therapy for Down Syndrome

• 2-3% of ALL patients have Down syndrome
• increased risk of treatment mortality
• if treatment mortality is decreased, overall survival is excellent
Improvements in Therapy of ALL in Down Syndrome

• longer initial admission to prevent early death in induction from infection
• leucovorin rescue
• interrupted dose dexamethasone
• enhanced supportive care
#5 Twinning Programs in Developing Countries

• ALL still has less than 50% survival in some developing countries
• Multiple reasons include lack of medicines, poor access to care, delayed diagnosis, cost, lack of knowledge
• Internet allows easy transfer of information
• Twinning between US pediatric cancer program and program in developing countries
#6
Recent Advances in Gene Therapy (ASH 2013)

• Filter patient’s blood, remove T cells, add gene to T cells that target cancer cells, altered T cells reinfused into body

• Engineer patient’s own T cells to attack cancer

• 5/5 adults and 19/22 children went into remission. All heavily pretreated and resistant

• Results promising but very preliminary
KM

- 4-year-old, CNS-negative
- WBC 23,000
- Cytogenetics – TEL/AML
- MRD – 0%
- Best prognostic markers
KM Treatment

• 2 years chemotherapy
• 90-95% cure rate
Major Issue in Future

ALL in teenagers and young adults
QUESTIONS?
Contact the Center for Cancer and Blood Disorders (CCBD) at Children’s Hospital Colorado

• Hematology and Sickle Cell Clinic (720) 777-6672
• Bone Marrow Transplant (720) 777-6892
• Oncology (720) 777-6688
• Neuro-Oncology (720) 777-6772
• Experimental Therapeutics Program (720) 777-4159
• Helping Oncology Patients Excel (H.O.P.E.) Clinic (720) 777-5441
• Fertility Team Consults (720) 777-6686
• Wellness/Psychosocial Support (720) 777-8857

• One Call 24/7 Provider Dedicated Line (720) 777-3999 or (800) 525-4871

Thank you, Thomas Smith, MD
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