Lecture_7

Leukaemia

fourth year students

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Leukaemias

- are malignant disorders of the haematopoietic stem cell
- characterised by increased No. of dysfunctional WBCs in the bone marrow and/or peripheral blood
- The course of leukaemia may vary from a few days or weeks to many years, depending on the type

Epidemiology and etiology

- Males are affected > females
- The ratio being about
    - 3 : 2 in acute leukaemia(ALL, AML)
    - 2 : 1 in chronic lymphocytic leukaemia (CLL)
    - 1.3 : 1 in chronic myeloid leukaemia (CML)
- Acute leukaemia occurs at all ages. ALL peak incidence in children aged 1–5 years

Risk factors for leukaemia

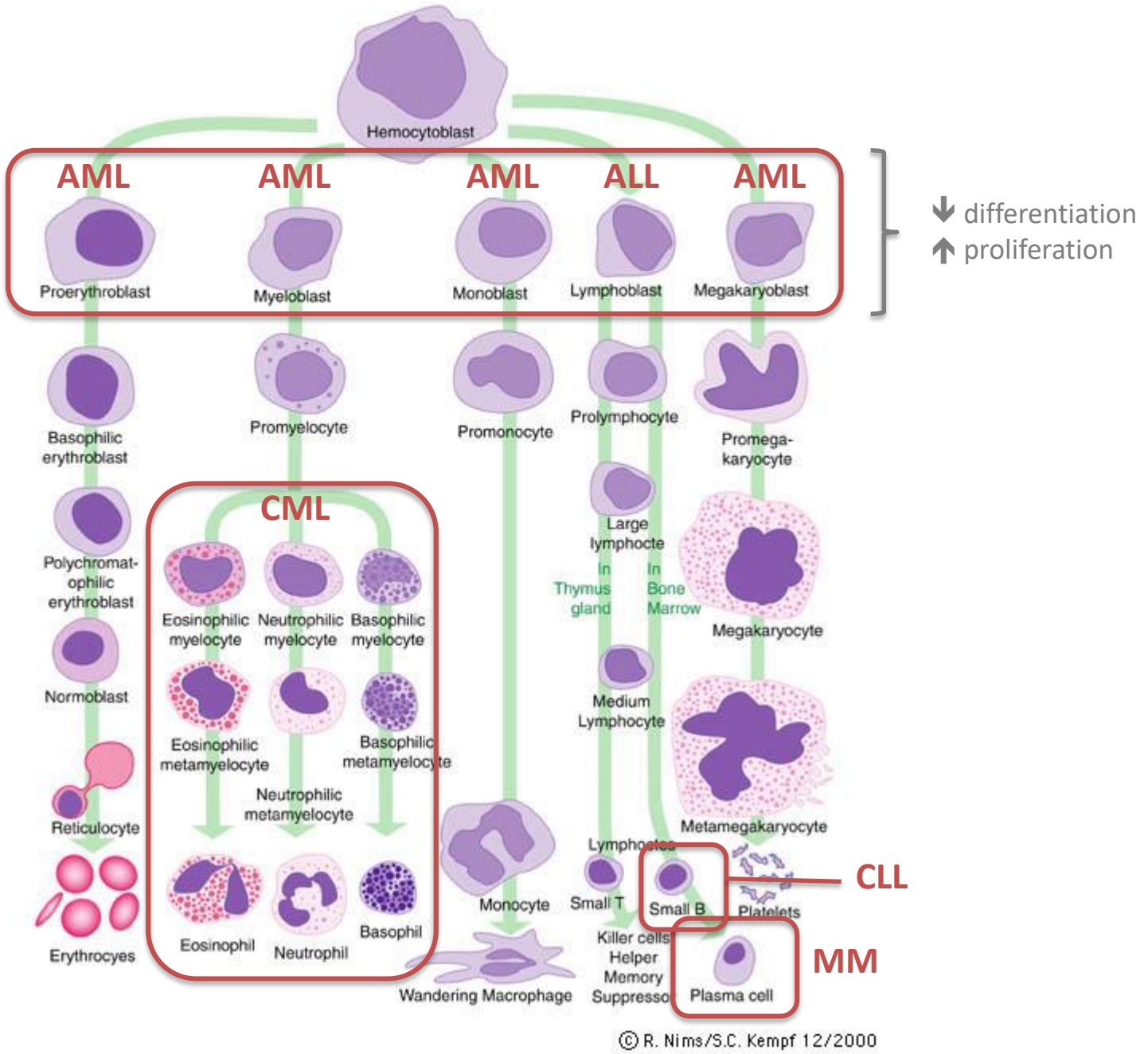
- **Ionising radiation**
  - After atomic bombing of Japanese cities (myeloid leukaemia)
  - Radiotherapy
  - Diagnostic X-rays of the fetus in pregnancy
- **Cytotoxic drugs**
  - Especially alkylating agents (myeloid leukaemia, usually after a latent period of several years)
  - Industrial exposure to benzene
- **Retroviruses**
  - Adult T-cell leukaemia/lymphoma (ATLL) caused by human T-cell, lymphotropic virus 1(HTLV-1), most prevalent in Japan, the Caribbean and some areas of Central and South America and Africa
- **Genetic**
  - Identical twin of patients with leukaemia
  - Down's syndrome and certain other genetic disorders
- **Immunological**
  - Immune deficiency states (e.g. hypogammaglobulinaemia)

Terminology and classification:

Leukaemias are traditionally classified into four main groups:

1) • acute lymphoblastic leukaemia (ALL)
2) • acute myeloid leukaemia (AML)
3) • chronic lymphocytic leukaemia (CLL)
4) • chronic myeloid leukaemia (CML)

Hematopoiesis



Acute leukaemia

- There is a failure of cell maturation
- leads to an accumulation of primitive cells that take up more and more marrow space at the expense of the normal haematopoietic elements
- Eventually, this proliferation spills into the blood
- Acute myeloid leukaemia (AML) is about 4 times more common than acute lymphoblastic leukaemia (ALL) in adults

Clinical presentations of acute leukemia

Chief complaint	Reason
“Abnormal labs”	cytopenias, circulating blasts, sometimes bone marrow Bx
Malaise	pancytopenia, especially anemia and neutropenia
Infection	dysfunctional immune system
Bleeding	thrombocytopenia, DIC
Organ failure	leukostasis, tumor lysis syndrome, hypoxia

Investigations

- **CBC:**
  - anaemia with a normal or raised MCV.
  - WBCs may vary from as low as 1 × 109/L to as high as 500 × 109/L or more. In the majority of patients, the count is below 100 × 109/L.
  - Severe thrombocytopenia is common
  - Blast cells in the blood film but sometimes may be absent
- **A bone marrow examination will confirm the diagnosis**
  - BM is usually hypercellular, with leukaemic blast cells (>20% of the cells)
  - The presence of Auer rods in the cytoplasm of blast cells indicates a myeloblastic type
- **Classification and prognosis are determined by**
  - immunophenotyping and chromosome and molecular analysis

Management

1. Supportive therapy

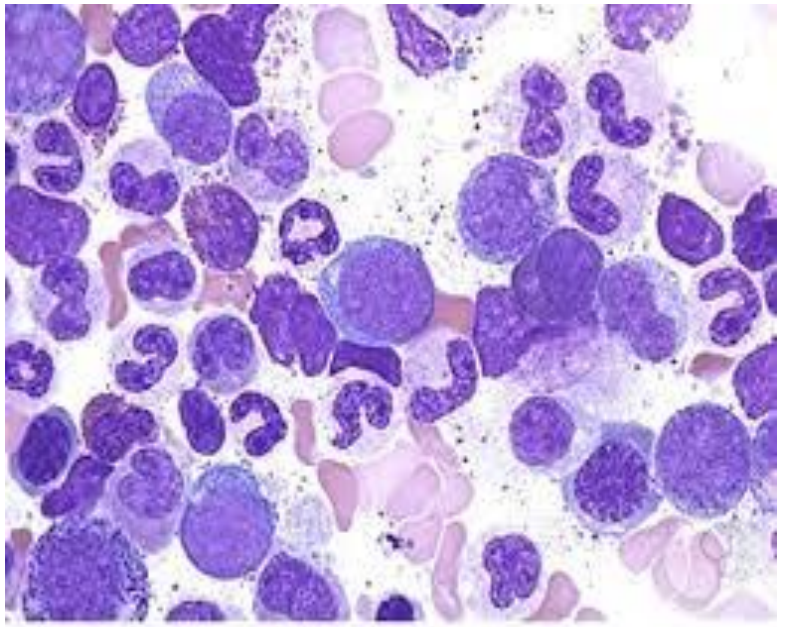
- Anaemia is treated with red cell concentrate transfusions
- Thrombocytopenic bleeding requires platelet transfusions to maintain the platelet count above 10 × 109/L
- Infection Fever (> 38°C) lasting over 1 hour in a neutropenic patient indicates sepsis. Parenteral broad-spectrum antibiotic therapy is essential
- Metabolic problems required Frequent monitoring of fluid balance and renal, hepatic and haemostatic function is necessary
- Psychological problems Psychological support is a key aspect of care

2) Specific treatment

- cytotoxic drug
  - The aim of treatment is to destroy the leukaemic clone of cells without destroying the residual normal stem cell
- Hematopoietic stem cell transplantation

Chronic myeloid leukaemia (CML)

- is a stem cell disorder resulting in proliferation of all haematopoietic lineages but predominantly in the granulocytic series.
- Maturation of cells proceeds fairly normally. The disease occurs chiefly between the ages of 30-80
- accounts for 20% of all leukaemias.



Clinical features

1. about 25% are asymptomatic at diagnosis
2. lethargy, weight loss,
3. gout and sweating
4. Splenomegaly is present in 90%; in about 10%, the enlargement is massive, extending to over 15 cm below the costal margin
5. Hepatomegaly occurs in 50%
6. Lymphadenopathy is unusual
7. With treatment, Median survival comparable to normal population

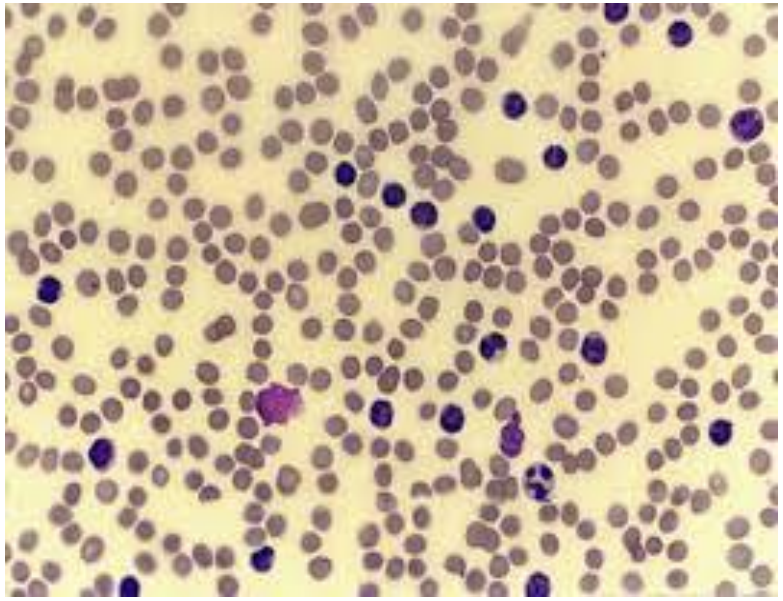
Treatment

1. Supportive
2. specific

- Targeted therapy, Tyrosine kinase inhibitors (TKIs) for the treatment of CML These specifically inhibit BCR ABL tyrosine kinase activity.

  Imatinib, nilotinib and dasatinib

Chronic lymphocytic leukaemia (CLL)



- is the most common leukaemia
- accounting for 30% of cases
- The male-to-female ratio is 2 : 1 and the median age at presentation is 65–70 years

- In this disease, B lymphocytes, which would normally respond to antigens by transformation and antibody formation, fail to do so

Clinical features

- The onset is usually insidious
- 70% of patients, diagnosis is made incidentally on a routine FBC. Presenting
- problems may be anaemia, infections, painless lymphadenopathy,
- and systemic symptoms such as night sweats or weight loss;
- these more often occur later in the course of the disease.

Investigations

- The diagnosis is based findings of a mature lymphocytosis (> 5 × 109/L) with characteristic morphology and cell surface markers. Immunophenotyping reveals the lymphocytes

23.50 Staging of chronic lymphocytic leukaemia

Clinical stage A (60% patients)

- No anaemia or thrombocytopenia and fewer than three areas of lymphoid enlargement

Clinical stage B (30% patients)

- No anaemia or thrombocytopenia, with three or more involved areas of lymphoid enlargement

Clinical stage C (10% patients)

- Anaemia and/or thrombocytopenia, regardless of the number of areas of lymphoid enlargement

Management

- No specific treatment is required for most clinical stage A patients, unless progression occurs
- Life expectancy is usually normal in older patients
- Treatment is required only if there is evidence of
    - bone marrow failure
    - massive or progressive lymphadenopathy or splenomegaly
    - systemic symptoms such as weight loss or night sweats, a rapidly increasing lymphocyte count, autoimmune haemolytic anaemia or thrombocytopenia

Thank you for your attention