Tan Tock Seng HOSPITAL

Medicine Review Course 2015

On Call:

Haematologic emergencies

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Objectives

Recognition & emergency management of:

1. Tumour lysis syndrome
2. Hyperleukocytosis

Case study

53 year old Chinese female,

Prolonged fever

Labs on admission

FBC – TW 2.5, Hb 9.7, Plt 101

K^+ 3.9, Cr 67

LFT - Alb 22, Bil 14, ALP 176

ALT 75 (↑), AST 156 (↑)

Case study

4 days later

FBC – TW 1.2, Hb 10.3, Plt 36

LFT - Alb 17, Bil 15, ALP 592

ALT 113, AST 415

LDH - >3800, Urate – 475,

Ca^{++} - 2.26

Bone marrow examination performed

Case study

4H after steroids given,

K^+ 5.0 (H 1+), Cr 142

LDH - >3800

Urate – 511

Ca^{++} - 2.17, PO_4 – 2.4

Rasburicase started

Case study

6H later

K^+ 5.7 (H 1+), Cr 212

LDH - >3800,

Urate – 235,

Ca^{++} – 2.19, PO_4 – 2.7

Patient collapsed and died

Tumour lysis

Table 1. Cairo-Bishop Definition of Laboratory Tumor Lysis Syndrome

Element	Value	Change From Baseline
Uric acid	≥ 476 μmol/L or 8 mg/dL	25% increase
Potassium	≥ 6.0 mmol/L or 6 mg/L	25% increase
Phosphorus	≥ 2.1 mmol/L for children or ≥ 1.45 mmol/L for adults	25% increase
Calcium	≤ 1.75 mmol/L	25% decrease

NOTE. Two or more laboratory changes within 3 days before or 7 days after cytotoxic therapy.

Patients with asymptomatic laboratory tumour lysis are at a high risk of clinical tumour lysis

Coiffier. JCO 2008,26,2767.

Tumour lysis

Clinical tumour lysis = Lab tumour lysis +

1. Renal impairment –
    a. single reading of Cr > 1.5 x ULN
    b. increase of Cr by >26 umol/L
    c. oliguria (< 0.5 ml/kg/hr x 6 hours)
2. Cardiac dysrhythmias
3. Seizures
4. Sudden death

Tumour lysis

Characteristic	Risk Factor
Tumor type	Burkitt's lymphoma Lymphoblastic lymphoma Diffuse large-cell lymphoma ALL Solid tumors with high proliferative rates and rapid response to therapy
Tumor burden/extent of disease	Bulky disease (>10 cm) Elevated LDH (> 2× ULN) Elevated WBC (>25,000/μL)
Renal function	Preexisting renal failure Oliguria
Baseline uric acid	Baseline serum/plasma uric acid > 450 μmol/L (7.5 mg/dL)
Effective and rapid cytoreductive therapy	Disease-specific therapy, varies according to tumor type

Coiffier. JCO 2008,26,2767.

Tumour lysis

Malignancy	Adult (n = 387) No.	%
Acute lymphoblastic leukemia	73	19
Acute myeloid leukemia	104	27
Chronic lymphocytic leukemia	37	10
Chronic myeloid leukemia	36	9
non-Hodgkin's lymphoma	109	28
Hodgkin's disease	6	1.6
Multiple myeloma	15	3.9
Other hematologic malignancies	3	0.7
Solid tumors	4	1

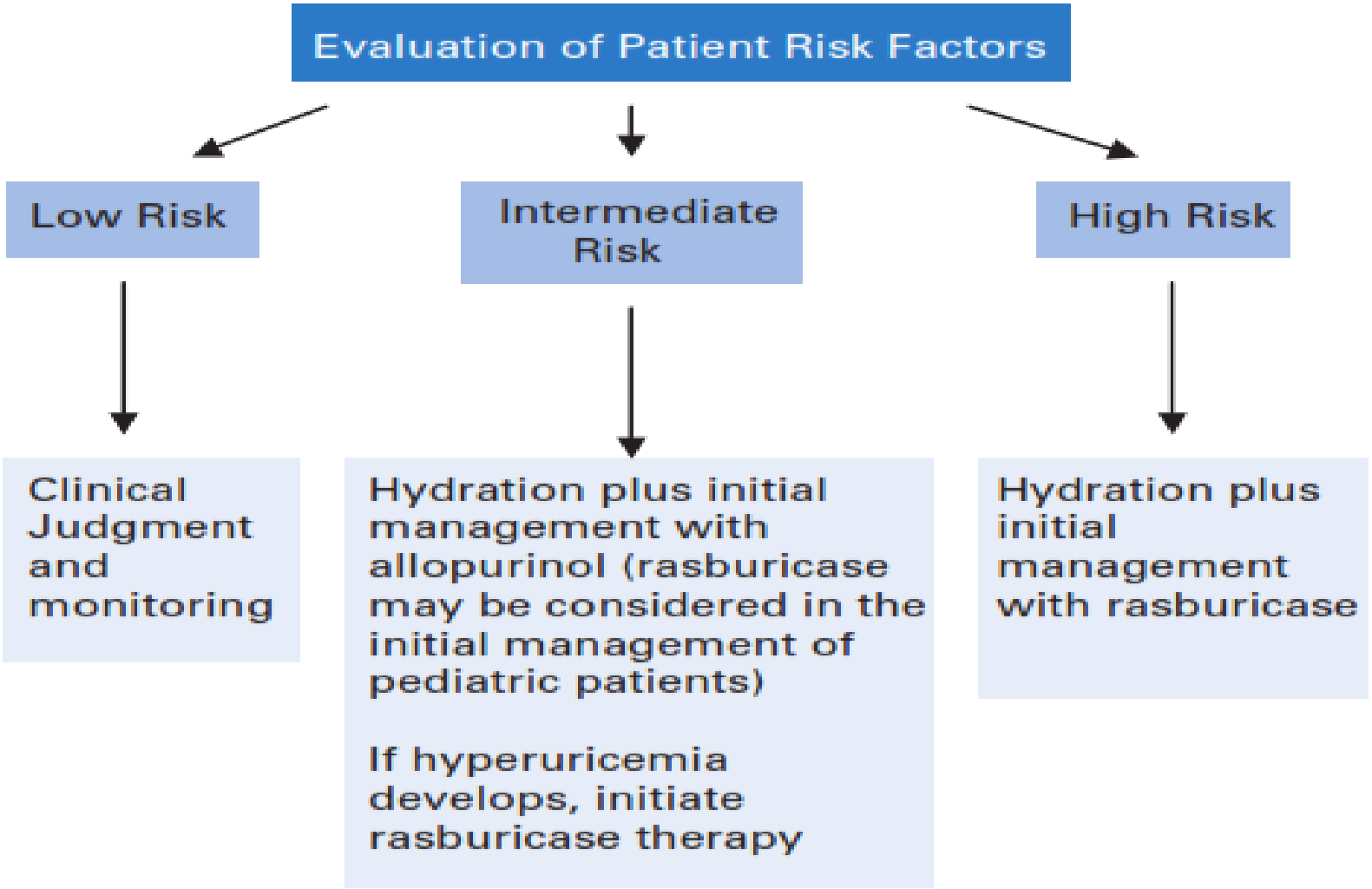
Coiffier. JCO 2008,26,2767.

Tumour lysis

Type of Cancer	Risk (of clinical tumour lysis) High	Intermediate
NHL	Burkitt's, lymphoblastic, B-ALL	DLBCL
ALL	WBC ≥ 100,000	WBC 50,000-100,000
AML	WBC ≥ 50,000, monoblastic	WBC 10,000-50,000

Coiffier. JCO 2008,26,2767.

Tumour lysis



Coiffier. JCO 2008,26,2767.

Tumour lysis

Management at appropriate facility and monitoring at appropriate frequency

1. Hydration – 3L/m^2/24H to achieve urine output of $\geq$ 2 ml/kg/hr
2. Allopurinol/ Rasburicase
3. Fluid and electrolyte management
4. Renal replacement therapy (continuous)

Tumour lysis - MCQ

The following are factors that contribute to the risk assessment of clinical tumour lysis except:

1. Renal impairment
2. Hypotension
3. Electrolytes and uric acid levels
4. Extensive marrow involvement by malignancy
5. Newly diagnosed or relapsed disease

Case study

35 year old Filipina,

Admitted for fever 1 week

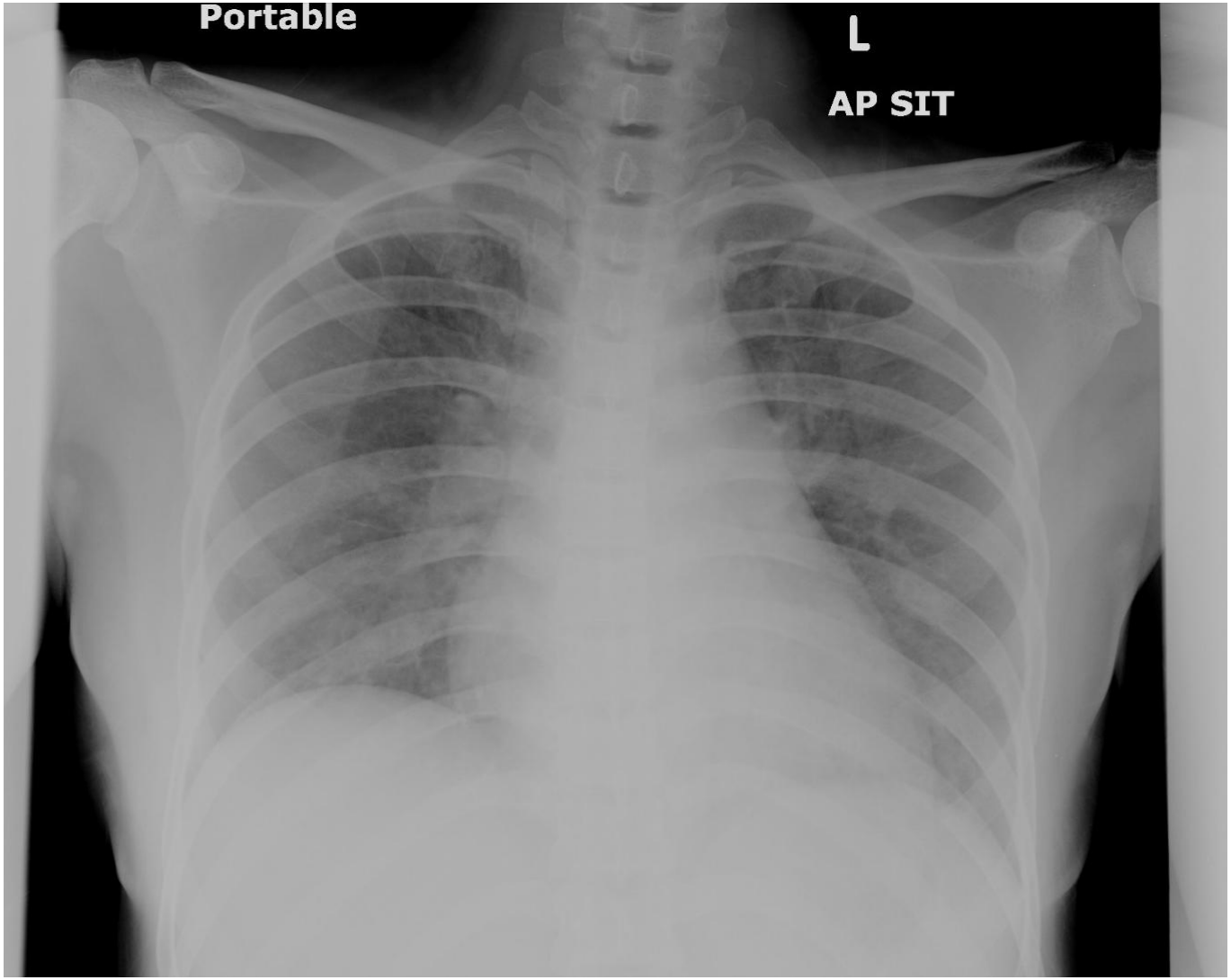
Labs on admission

FBC – TW 38.8, Hb 9.1, Plt 217

– 81% blasts

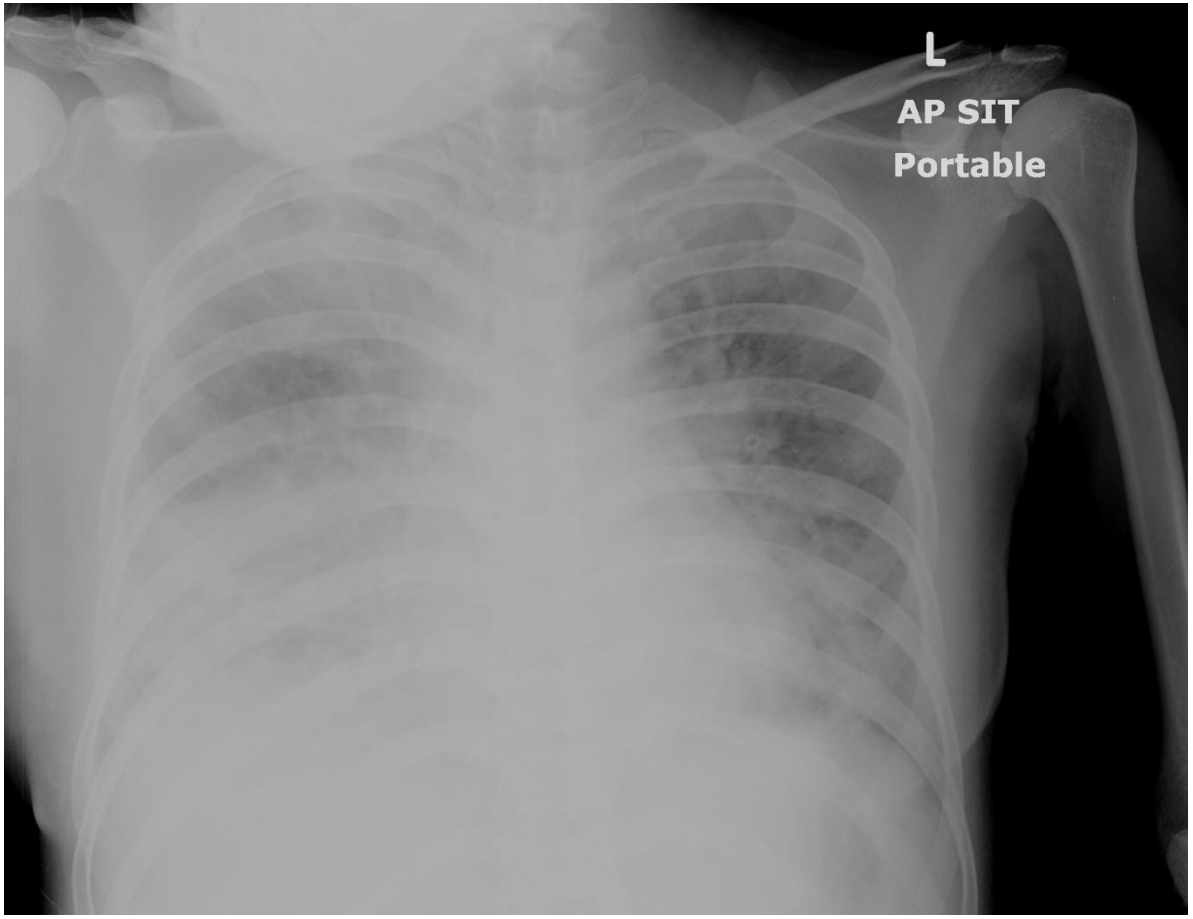
PBF – Acute Monoblastic Leukemia

Case study



Case study

4 days later



Hyperleukocytosis

WBC > 50-100 x 10^9/L

Main complication of Leukostasis

(esp acute leukemias)

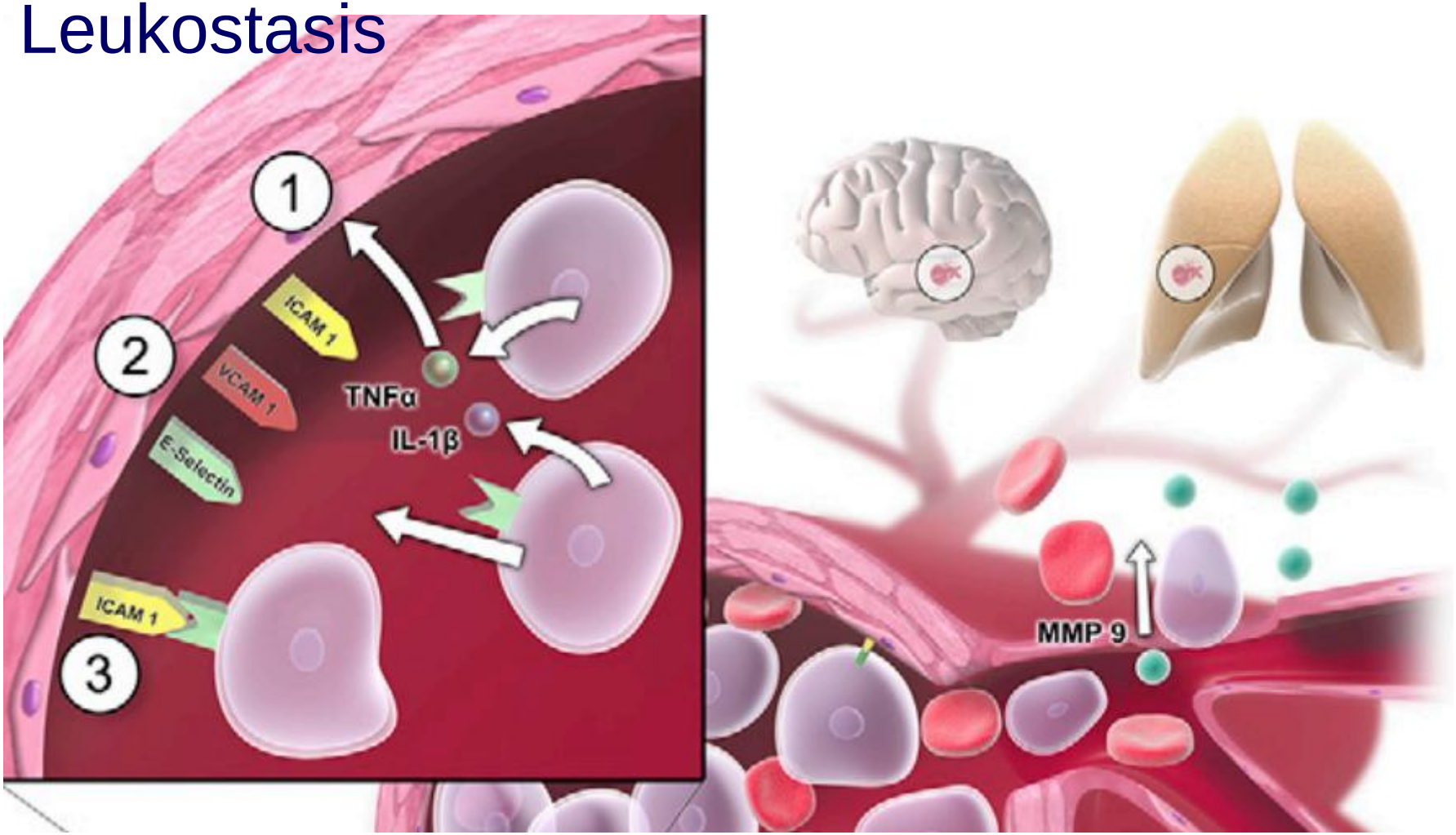
a. CNS vasculature
b. Pulmonary vasculature
c. Vessels of other organs – Renal, Cardiac

Leukostasis can happen at WBC <50 x 10^9/L

Especially for Acute Myeloid Leukemia (Monocytic/ monoblastic)

Hyperleukocytosis

Leukostasis



Rollig. Blood 2015,125,3246.

Hyperleukocytosis

Leukostasis

CNS

a. Blurred vision/ diplopia (acute)
b. Confusion/ Delirium
c. Somnolence
d. Intracranial haemorrhage
e. Severe tinnitus
f. Severe headache/ dizziness less specific

Hyperleukocytosis

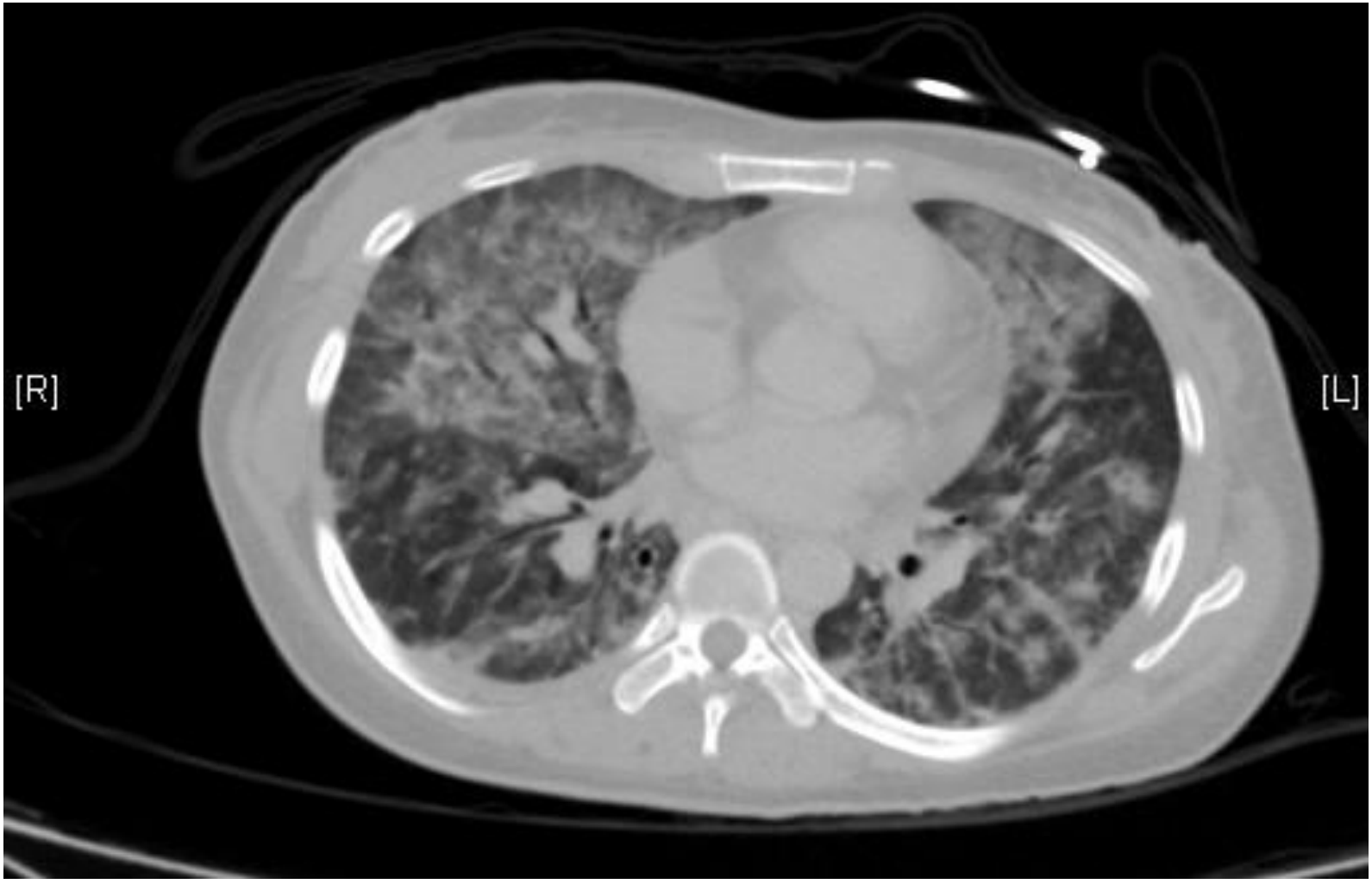
Leukostasis

Pulmonary

a. Dyspnoea at rest
b. O_2 required for maintenance of SpO_2

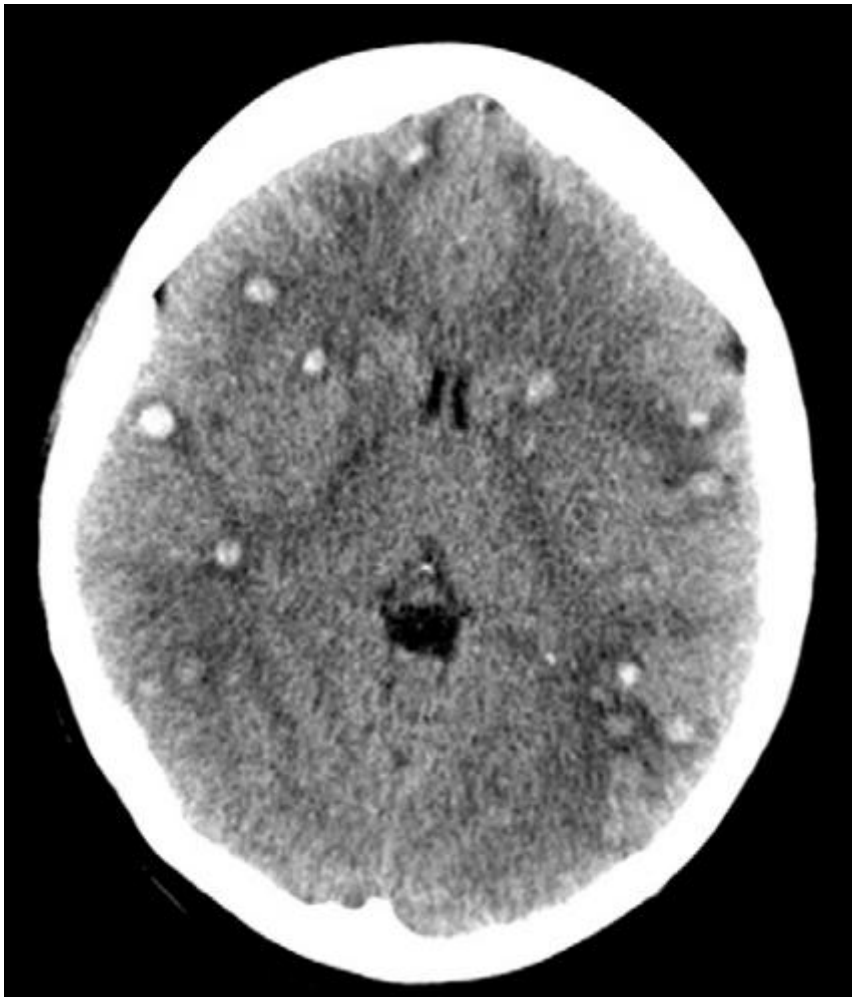
Hyperleukocytosis

Leukostasis



Hyperleukocytosis

Leukostasis



Rollig. Blood 2015,125,3246.

Hyperleukocytosis/ Leukostasis

Diagnostic/ treatment dilemmas

Differential diagnosis

a. Fluid overload/ Pneumonia
b. Electrolyte disturbances
c. Coagulopathies

Associated conditions

a. Tumour lysis syndrome
b. Disseminated Intravascular Coagulation

Hyperleukocytosis

Management

a. Hydration

b. Cytoreduction by

   (1) Chemotherapy – sometimes, hydroxyurea is not enough

   (2) ± Leukapheresis

c. Correct associated conditions, esp DIC

   (1) Plt > 20 x 10^9/L, Fibrinogen > 1.5 g/L

Hyperleukocytosis - MCQ

The following statements are true except:

1. Leukostasis mainly affects the CNS and pulmonary vasculature
2. Leukostasis rarely develops in patients with chronic leukemias with a WBC < 50 x 10^9/L
3. The mainstay of managing leukostasis is hydration and leukapheresis
4. Leukostasis is quite commonly associated with tumour lysis syndrome
5. DIC can worsen the complications associated with leukostasis

Conclusions

1. Tumour lysis syndrome
    a. Risk factors
    b. Laboratory/ clinical TLS
    c. Emergency management
2. Hyperleukocytosis
    a. Types of condition associated with leukostasis
    b. Clinical manifestations of leukostasis
    c. Emergency management

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Thank you

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