Haematological Emergencies

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Case 1

- Mr PW 67yr old man
- Presents to their local practice GP being “unwell” since waking this am
- He describes he had been “watching his temp closely over the last 3 hours given he is on chemotherapy for lymphoma” and Temps had been 37C, 37.8C, 37.4C on the last 3 readings.
- On reviewing your colleagues notes and patient correspondence in the medical record you see he has recently been diagnosed with DLBCL and is receiving R CHOP chemotherapy. The patient states he received his last dose 9 days ago.

Case 1

- On inspection he is flushed with warm peripheries.
- HR 105, BP 110/60, RR 20, Sat 98%. Temp is 38.5C.
- He has no central venous access device visible. Cardiovascular and respiratory examination are unremarkable.
- Abdomen is soft and non-tender.

Case 1

- He hands you a book of his latest blood results from clinic yesterday
- They show: Hb 105, WCC 0.5, Neut 0.05, PLT 98.
- As he sits up to put his shirt back on after being examined he collapses back on the bed.
- He is conscious, orientated and has the following obs: HR 120, BP 90/50, RR 22, Sat 98%

Case 1 - Question

- What would you do next?

a. Direct the practice nurse to call for an ambulance and continue on with the next patient?

b. Call an ambulance and whilst waiting put in a cannula and give fluids

c. Direct his wife whom is present to take him to his specialists hospital for urgent specialist care (40mins away)

d. Take blood cultures and give IV antibiotics (assuming available)

e. Both b and d

Definitions

- Neutropenia = ANC <1.00 x 10^9/L
- Severe neutropenia = ANC <0.5 x 10^9/L
- Profound neutropenia = ANC <0.1 x 10^9/L

Febrile Neutropenia

1. ANC <1.00 x 10^9/L

2. Temp ≥38.3C x 1 or > 38C sustained

Risk of infection is linked to degree, duration and cause of neutropenia

Neutropenia - Causes

1. Decreased production

- Bone marrow infiltration (ALL/ lymphoma/ non-haem malignancy etc) - pancytopenia
- Agranulocytosis/ bone marrow aplasia (Chemotherapy; drugs – clozapine, Methotrexate, azathioprine, mercaptopurine; immune- Aplastic anaemia)
- Inherited

Neutropenia –Causes:

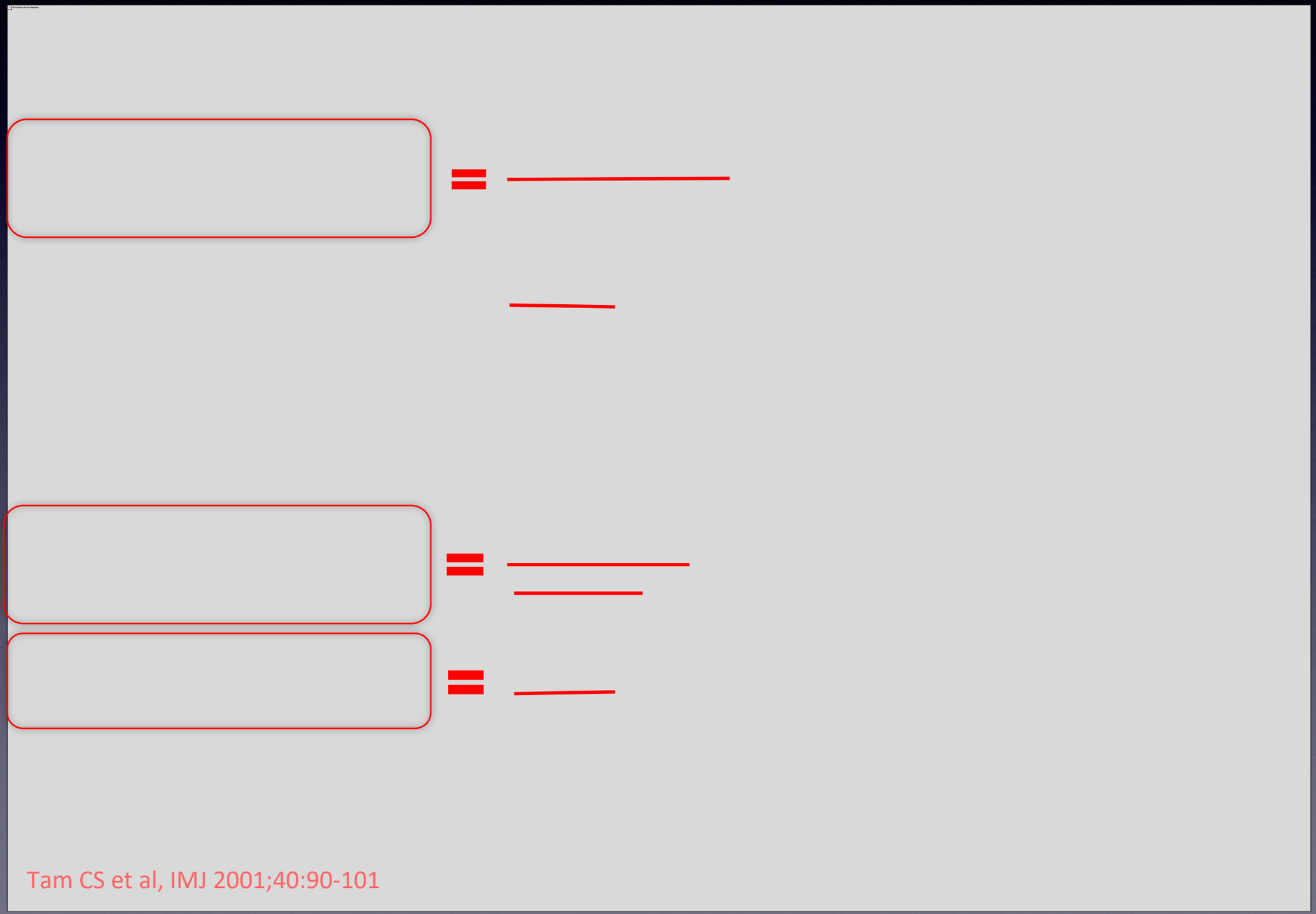
2. Peripheral destruction/sequestration

- Hypersplenism including Felty's syndrome
- Autoimmune neutropenia – including lupus etc
- Drug induced – maturation arrest (beta lactam antibiotics etc)
- Viral infections

Initial Mx FN (ED)

1. Identify FN patient at triage – ie. patient receiving chemotherapy in last 6 weeks whom presents with a fever or unwell
2. Assessed with Hx, examination & FBC, ELFT, Lactate within 15mins of triage (if stable) - ? Source ? prior MRO
3. Culture – ≥2 sets of Blood cultures, msu, sputum, NPS if indicated
4. EARLY (<60mins), appropriate antibiotics and IV fluids
5. Imaging - CXR, (+/- CT chest/abdomen)
6. Discuss with treating Haematologist/ Oncologist

ASID guidelines



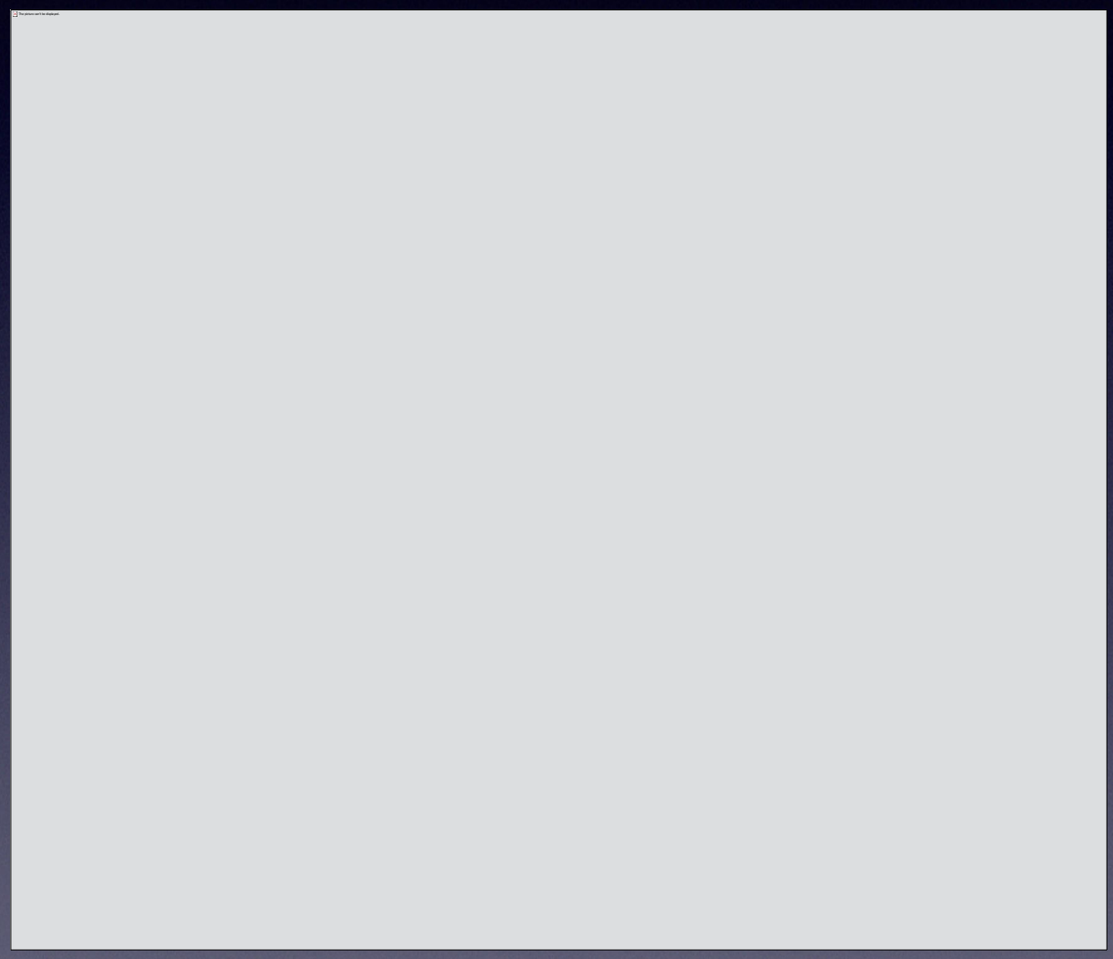
Tam CS et al, IMJ 2001;40:90-101

Time to antibiotics (TTA)

Prospective cohort study of 307 inpatients treated for FN.

TTA for first fever or any fever was associated with survival (28 day mortality) in MV analysis
RR = 1.18 (1.10-1.26).

28 day mortality increased by 18% for every hour delay in TTA.



Rosa RG, Goldani LZ, Antimicrob Agent Chemother 2014; 58:3799-3803.

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s

e. Both b and d

Case 2

- Ms TL, 19yr old woman
- Presents to her GP with a 3 week history of fevers, headaches, sore throat, arthralgias and 10 days of heavy menorrhagia. She has recently completed a course of amoxicillin for presumed strep throat.
- Previously fit and well. No travel.
- O/E: HR 100, BP 100/60, RR 18, SaO2 98%, Temp = 37C

Case 2

O/E:

- Pale, no lymphadenopathy, no tonsillar erythema or enlargement. Otoscopic examination is normal
- ecchymoses – legs, back
- Heart sounds normal, chest clear
- No hepatosplenomegaly

Case 2

- You request blood tests including:

FBC, ELFT, Coags, Iron studies

CRP, EBV, CMV, Ross River, Barmah Forest, Dengue serology

Case 2

- Urgent lab results are called through that PM:

PT 28 sec (11-16); aPTT 52 sec (23-38);

Fib 0.5ug/L (2-4); D-Dimer 27ug/ml (0-0.5)

Hb 90g/L, MCV 82fL, WCC 8.8, Neut 1.4 PLT 28

Alb 37g/L, Bili 8, GGT 150u/L, ALP 128 u/L ALT 45u/L, AST 39 u/L, LDH 250u/L

Case 2 - Question

- What is the most likely diagnosis?

a. Vitamin K deficiency due to antibiotics with poor dietary intake

b. Coagulopathy of liver disease

yes

c. DIC secondary to malignancy

d. Dengue Haemorrhagic Fever

DDx

• Vitamin K defy	prolonged PT > aPTT, normal Fib level
• Coagulopathy of liver disease	Prolonged PT > aPTT, low Fib, PLT rarely <50-80, D Dimer usually not marked elevated
• Dengue Haemorrhagic Fever	Usually prolonged aPTT, and low Fib but normal PT. usually have very low Alb

Disseminated Intravascular Coagulation (DIC)

- Acquired syndrome characterized by systemic intravascular activation of coagulation leading to microthrombi formation and a coagulopathy due to consumption.

DIC – Lab findings

Prolonged PT and aPTT

Low Fibrinogen

High D-Dimer levels

Low PLT

Possible red cell fragmentation (MAHA)

ISTH scoring system for DIC

PLT	>100 50-100 <50	0 1 2
Elevated D Dimer	No Moderate Strong	0 2 3
Prolonged PT	<3 sec 3-6 sec >6 sec	0 1 2
Fibrinogen	>1.0ug/L <1.0ug/L	0 1
		>5 = overt DIC

Sens = 93% Spec = 98%

Taylor FB Jr et al. Thromb Haemost 2001; 86:1327.

DIC - Causes

1. Malignancy – Metastatic Prostate, pancreatic, ovarian ca or APML (Acute Promyelocytic leukaemia)
2. Sepsis
3. Trauma
4. Burns
5. Pancreatitis
6. Obstetric complications – PET, IUFD, Abruptio Placentae
7. ABO incompatible transfusion reaction

DIC - Treatment

If bleeding or acute DIC

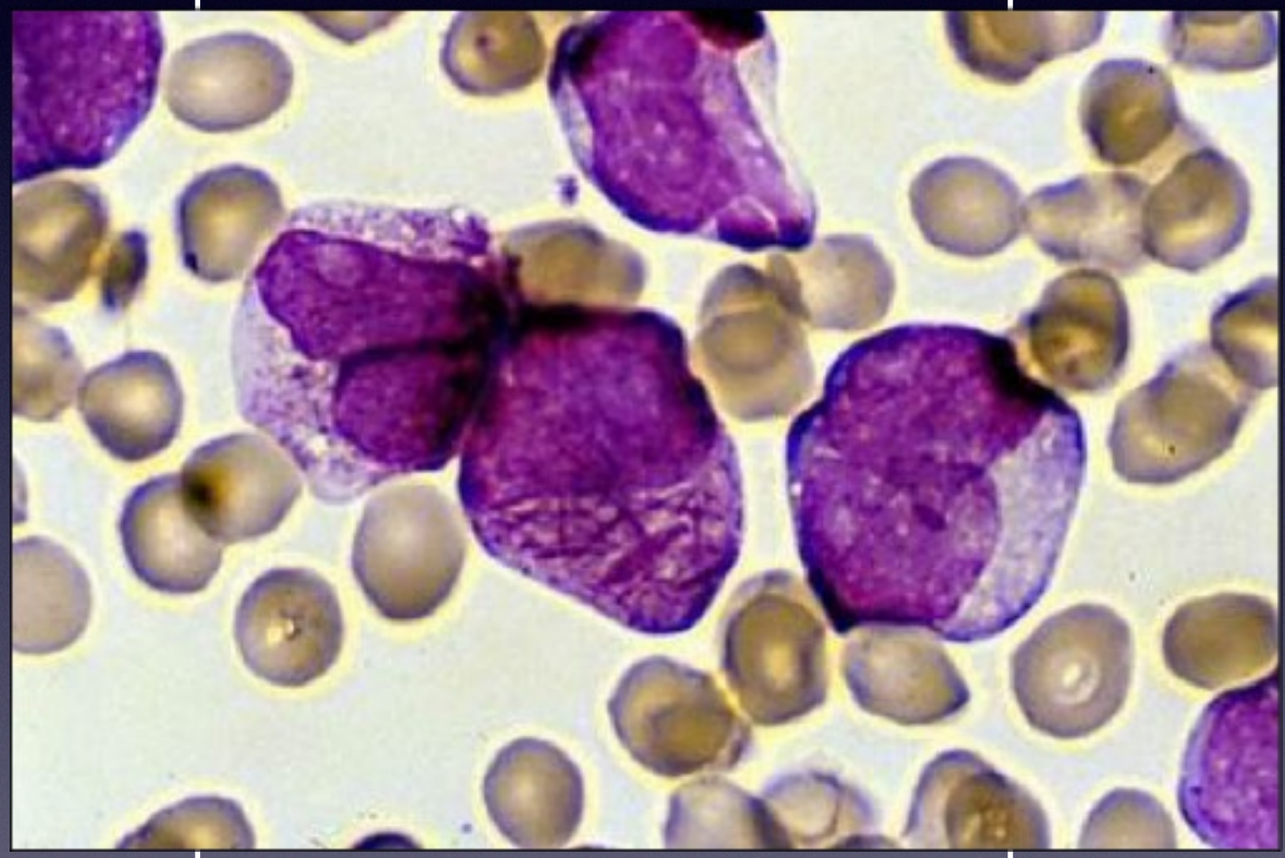
1. PLT transfusions to keep count > 50
2. Fresh Frozen Plasma (FFP) x 4 if prolonged PT/aPTT
3. Cryoprecipitate x10 if Fib <1.0ug/L
4. <u>TREAT THE CAUSE</u>

Prothrombinex and heparin have no role

Case 2

- Lab haematologist calls to inform you there are circulating abnormal promyelocytes and faggott cells

- Consistent with a diagnosis of Acute Promyelocytic Leukaemia (APML)



APML

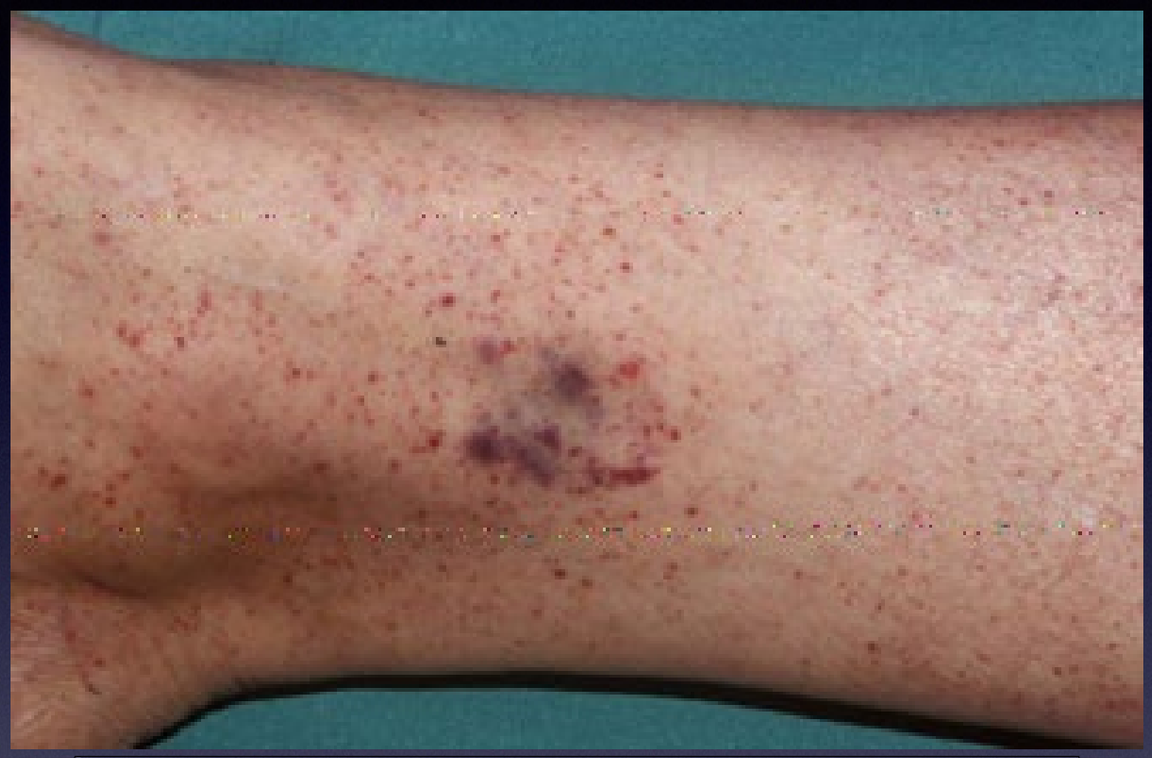
- Clear haematological emergency
- Highly curable in 90-95% of patients
- Associated with a high mortality at presentation (10%+) – due to bleeding and thrombosis
- Early: ATRA, arsenic and correction of coagulopathy are the key
- Need rapid communication and admission with a specialised haematology unit immediately

Case 3

- Mrs P.M 47yr old woman
- Presents with 4 day history of recurrent epistaxis, and a new rash on her legs.
- No past medical history.

Case 3

- O/E: Alert, orientated.
- HR 70, BP 120/65,
- RR 16, SaO2 = 98% RA
- Temp = 36 C,



Case 3 - Question

True or False:

1. The diagnosis is suggestive of meningococcal sepsis and blood cultures followed by IV ceftriaxone is recommended.
2. The picture suggests marked thrombocytopenia and a FBC should be taken and the patient reviewed the following day to confirm a diagnosis of ITP.
3. The presentation is suggestive of acquired haemophilia and blood tests for factor 8 levels are indicated.
4. The patient should proceed directly to the nearest hospital for inpatient therapy.
5. A detailed medication history may reveal a causative agent.

Case 3

True or False:

False 1. The diagnosis is suggestive of meningococcal sepsis and blood cultures followed by IV ceftriaxone is recommended.

False 2. The picture suggests marked thrombocytopenia and a FBC should be taken and the patient reviewed the following day to confirm a diagnosis of ITP.

False 3. The presentation is suggestive of acquired haemophilia and blood tests for factor 8 levels are indicated.

True 4. The patient should proceed directly to the nearest hospital for inpatient therapy.

True 5. A detailed medication history may reveal a causative agent.

Case 3

- Hb 128g/L,
- WCC 5.0; Neut 3.8
- PLT 2 x 10E9/L
- PT 16 sec; aPTT 34 sec
- Fib 2.5 ug/L
- Cr 67umol/L
- LDH 221 U/L; LFT’s normal

Case 3

- Consistent with newly diagnosed **ITP**
  - With marked thrombocytopenia
  - & non-life threatening bleeding (mucosal)

Treated with prednisolone 1mg/kg

Immune Thrombocytopaenic Purpura (ITP)

- Acquired, non-malignant bleeding disorder, where patients develop thrombocytopenia due to excessive peripheral destruction of PLT (usually in the spleen) due to most commonly the development of cross reacting auto-anti-PLT antibodies.
- Presentation depends on the degree of thrombocytopenia and the specificity of the anti-PLT ab.
- May be primary or secondary (underlying causative condition – APLS, SLE etc) and newly diagnosed (<3mths since dx), persistent (3 to 12 mths since dx) or chronic (>12mths since dx)

Diagnosing ITP

- *A diagnosis of exclusion:*

i. Isolated thrombocytopenia (no anaemia, no neutropenia)

ii. No features suggestive of a primary BM disorder (no circulating blasts, no nucleated red blood cells)

iii. Normal LDH (unless co-existing haemolysis – Evan syd)

iv. Normal coagulation prolife (Not DIC)

v. No splenomegaly/portal HTN

vi. Not drug related – Quinine, heparin etc

vii. Excluded infection causes (HIV, HCV)

ITP – Bleeding risk

- PLT count <10 (RR 46 x c/w >10)
- Age – risk of bleeding increases with age:
  - ICH risk 0.4% in children vs 1.4% in adults
  - Risk of fatal haem 0.4%/yr <40yrs vs 13%/yr age >60yr
- Duration – more common serious bleeding in chronic ITP
- Rapidity of fall (most notable with drug induced)

Note: PLT <30 indication for therapy in absence of bleeding (adult)

Treatment ITP

- In absence of active bleeding:
  - Prednisolone 1mg/kg (weaned over 3-6mths)
  - (or Dexamethasone 40mg/D by 4)
  - No PLT transfusions

Case 3

- Day 2 post admission – patient developed large volume GI bleed
- Hb dropped to 84g/L with haemodynamic instability

Case 3

- Treated with:

1. Methylprednislone 1g IV
2. Intravenous immunoglobulin (1g/kg x 2 days)
3. PLT transfusions

Treatment ITP – life threatening bleeding

- Life threatening bleeding:
  - Intracranial haemorrhage
  - Bleeding with haemodynamic instability

- Pulse methylprednisolone, IVIG and PLT transfusion
- If refractory – splenectomy/ thrombopoetin analogues (Romiplostim/Eltrombopeg)

Arnold D. Hematology 2015

Haem Emergency Summary

- Febrile neutropenia
(<1.0 + temp >38C)

- Risk relates to degree, duration and cause
- Time to antibiotics is the key to outcome
- Specific AB – PIPTAZ, Cefepime +/- Gentamicin /Vancomycin

- DIC

- high PT, aPTT and low Fib and high D-Dimer
- Causes: Malignancy, sepsis, obstetric, pancreatitis
- Treat the cause, remember APML and early ATRA, PLT and cryo

Haem Emergency Summary

- ITP

- Bleed Risk depends on degree (<10), age, duration and rapidity of fall

- Diagnosis of exclusion (isolated, normal coags, normal LDH, no drugs, no infection)

- PLT <30 needs therapy (discuss by phone)

- If bleeding need urgent inpatient care

Thank you

Tam CS, O'Reilly M, Anderson D, Lingaratnam S, Kelly A, Burbury J, Turnidge J, Slavin MA, Worth LJ, Dawson L, Thursky KA. Use of empiric antibiotic therapy in febrile neutropenia. IMJ 2011;41:90-101.

Rosa RG, Goldani LZ, Cohort study of the time to antibiotic administration on mortality in patients with febrile neutropenia. Antimicrob Agent Chemother 2014; 58:3799-3803.

Arnold D. Bleeding complications in Immune Thrombocytopenia. Hematology Am Soc Hematol Educ Program 2015:237-42.

Taylor FB Jr et al. Towards definition, clinical and laboratory criteria, and a scoring system for disseminated intravascular coagulation. Thromb Haemost. 2001; 86(5):1327-30.