



Acute Promyelocytic Leukaemia: A Diagnostic Emergency

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Session Aims

1

Case

Example patient to discuss diagnosis

3

Management

How we manage APML, and what happens if we don't!

2

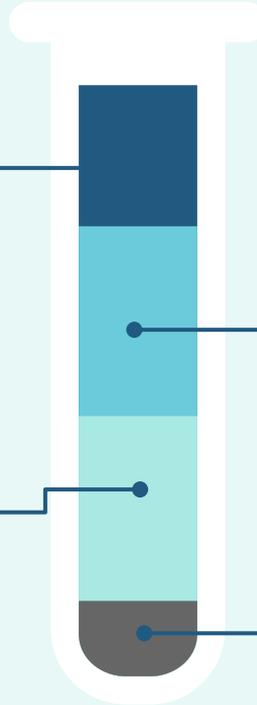
Pathophysiology

Why does APML happen?

4

Tips and Tricks

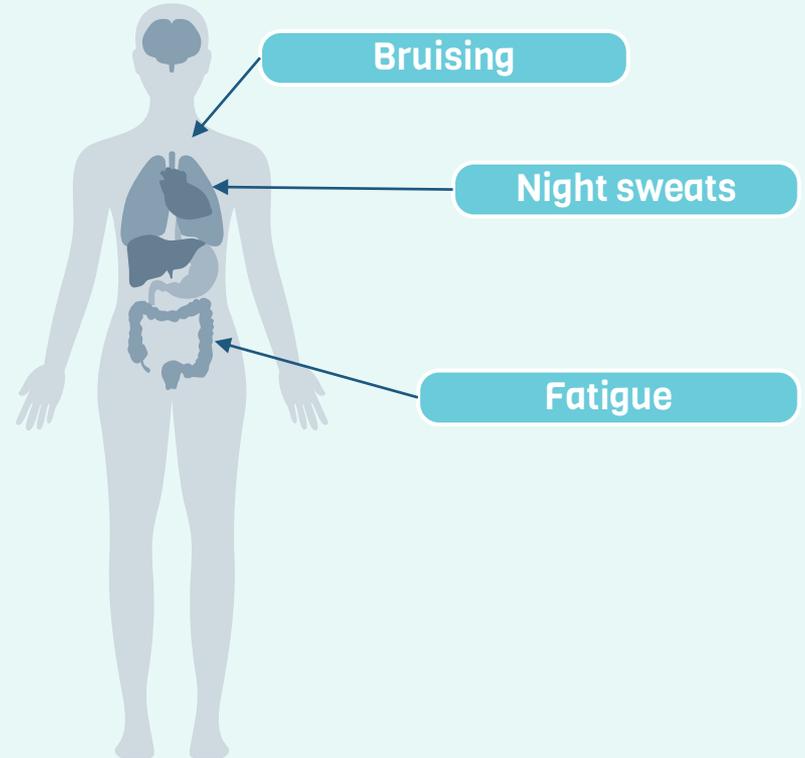
Things to think about so we don't miss a case!



Case: Presentation

59 year old Female

- Past medical history: None.
- She has 2 children and runs an online vintage clothing shop.
- She is extremely fatigued with unusual bruising and poor wound healing.
- The GP requests a generic panel of testing including an FBC.



Case: FBC Results

What's
abnormal
about this
FBC?

```
bruising ++. NONE \NONE \
Specimen No : H0836651R Haematology Date received: 28/01/2021 R
<PgUp/PgDn> for more
28/01/2021 08:45 Blood
Request Reason : bruising ++. NONE
```

HB	115	g/L	(120 to 150)	Auth
WBC	7.4	10 ⁹ /L	(4.0 to 11.0)	Auth
PLT	4	10 ⁹ /L	(150 to 410)	Auth
RBC	3.67	10 ¹² /L	(3.80 to 4.80)	Auth
HCT	0.333	L/L	(0.360 to 0.460)	Auth
MCV	90.6	fL	(83 to 101)	Auth
MCH	31.3	pg	(27.0 to 32.0)	Auth
MCHC	346	g/L	(315 to 345)	Auth
RDW	15.3		(11.6 to 14.0)	Auth
MPV	10.0	fL	(7.5 to 11.2)	Auth
Neutrophils	^0.6	10 ⁹ /L	(2.0 to 7.0)	Auth
Neutrophils.....	0.5	10 ⁹ /L	(2.0 to 7.0)	Auth
Lymphocytes	^3.0	10 ⁹ /L	(1.0 to 3.0)	Auth
Lymphocytes.....	2.8	10 ⁹ /L	(1.0 to 3.0)	Auth
Monocytes	^3.8	10 ⁹ /L	(0.2 to 1.0)	Auth
Monocytes.....	0.2	10 ⁹ /L	(0.2 to 1.0)	Auth
Eosinophils	^0.0	10 ⁹ /L	(0.00 to 0.5)	Auth
Eosinophils.....	0.0	10 ⁹ /L	(0.00 to 0.5)	Auth
BAS	^0.0	10 ⁹ /L	(0.0 to 0.1)	Auth
Basophils.....	0.1	10 ⁹ /L	(0.0 to 0.1)	Auth

Would you
make a
blood film
on this
sample?

Case: Blood Film

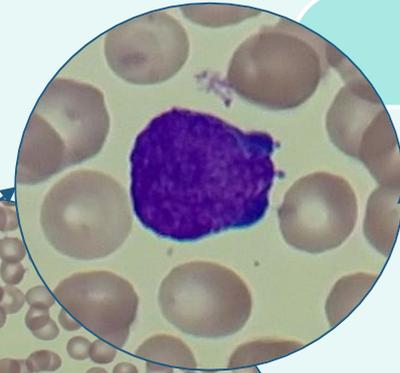
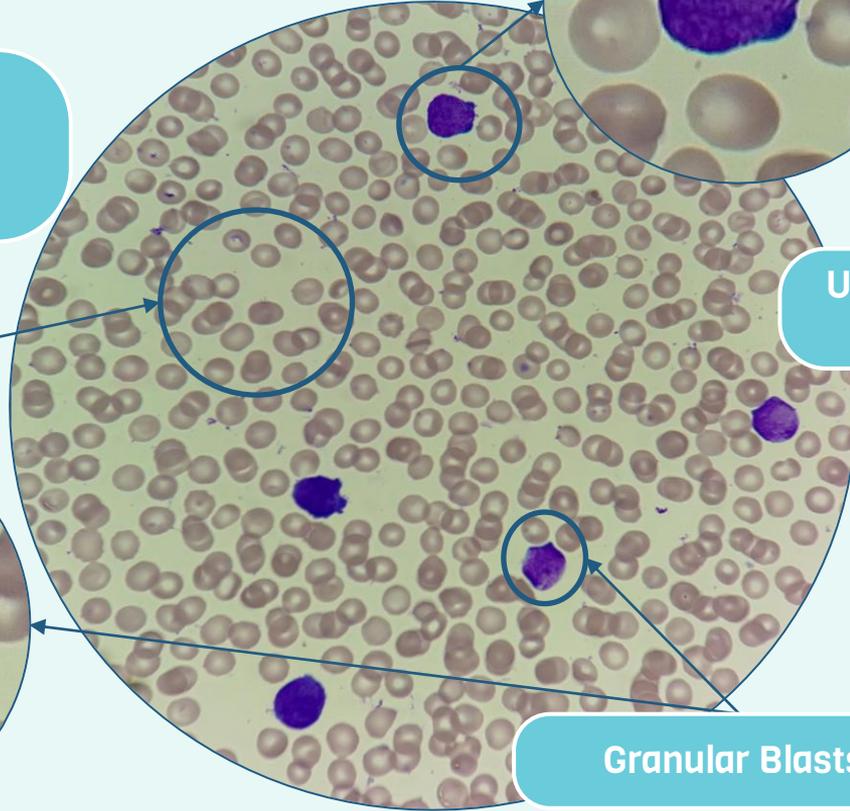
What do these features suggest?

Thrombocytopenia

Case

Undifferentiated Blasts.

Granular Blasts.

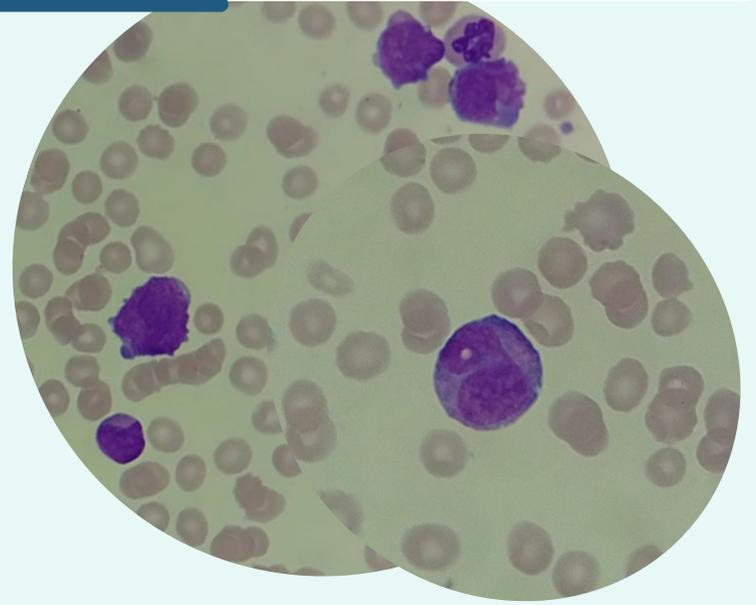


Case: Preliminary Diagnosis

- This patient likely has AML.
- Granular blasts makes Myeloid likely.
- Leukaemia causes ↓ in other cells.
 - The bone marrow is making cancer cells.
 - This contributes to symptoms
 - E.g. Fatigue, bruising, poor wound healing etc.



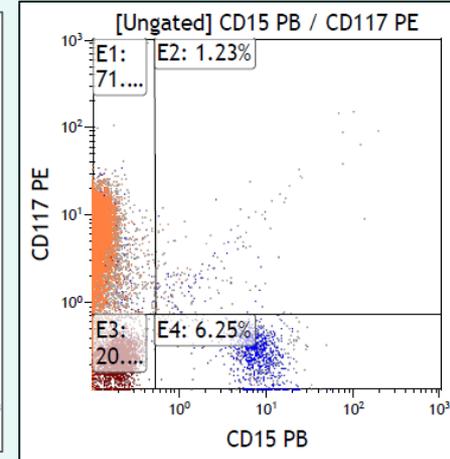
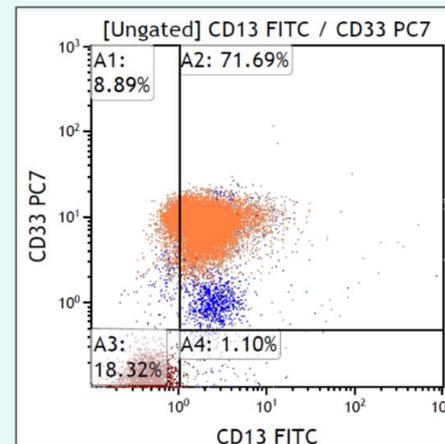
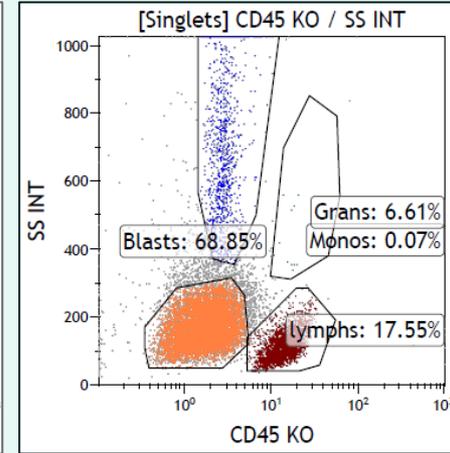
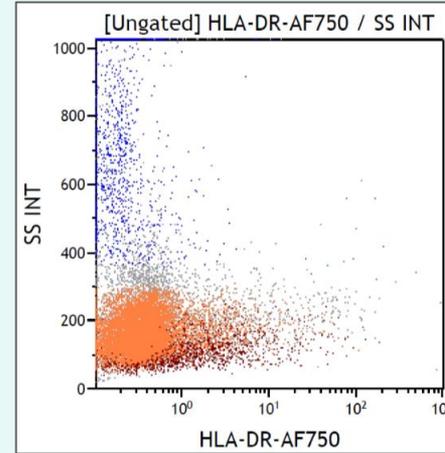
This AML in particular needs to be actioned urgently- why?



Case: Immunophenotyping.

Case

APML Marker	Patient Result
High Side Scatter	High
CD45+ (moderate)	+ (dim)
CD34-	-
CD117+ (moderate)	+ (moderate)
HLA-DR-	-
CD64+ (dim)	+
CD11b-	-
CD33+ (bright)	+
CD13-	+



Case: Genetics

Case

Referral Reason:

...ent PML-

Is this
diagnostic of
APML?

F

RESULTS:

Analysis

RT-PCR

Karyotype:

46,XX,t(15;17)(q24;q21)[20]

Key APLM Facts

Incidence

- 5-8% of AML
- 0.08 per 100,000 per year.



Age of Onset

- Median age of onset is 40 years old.
- Uncommon in the elderly.

Variants

- Comes in granular and hypo granular variants.
- Granular is classical.



WHO

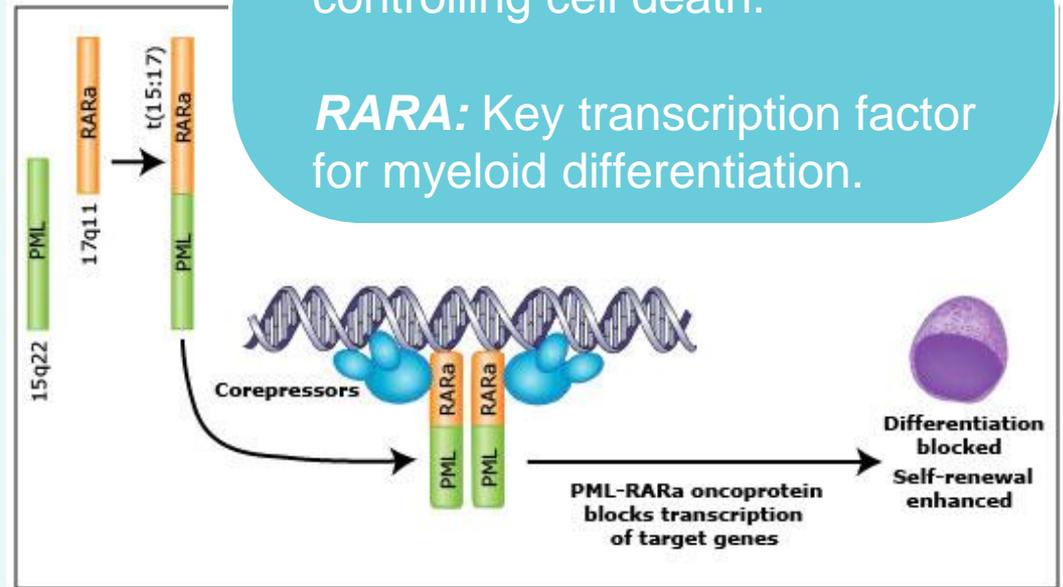
- APLM defined by the Presence of the t(15;17) mutation by the WHO.
- No mutation? Not APLM!

Pathophysiology of APML.

- T(15;17) results in the fusion product *PML-RARA*.
- *PML-RARA* prevents cell death and differentiation of myeloid blasts.
- These blasts release prothrombotic and inflammatory cytokines, results in key APML symptoms.

PML: Self-renewal and controlling cell death.

RARA: Key transcription factor for myeloid differentiation.



Treatment

Management

WBCC $>10 \times 10^9/L$

High Risk

ATRA

APML has a 90% remission rate with prompt treatment!

All trans retinoic acid (ATRA) is a form of Vitamin A.

Cytoreduction

APML Diagnosed

ATRA is nontoxic – so it's better to give it and be wrong than not!

ATRA

Pre-ATRA, patient's had a survival of 3-16 weeks.

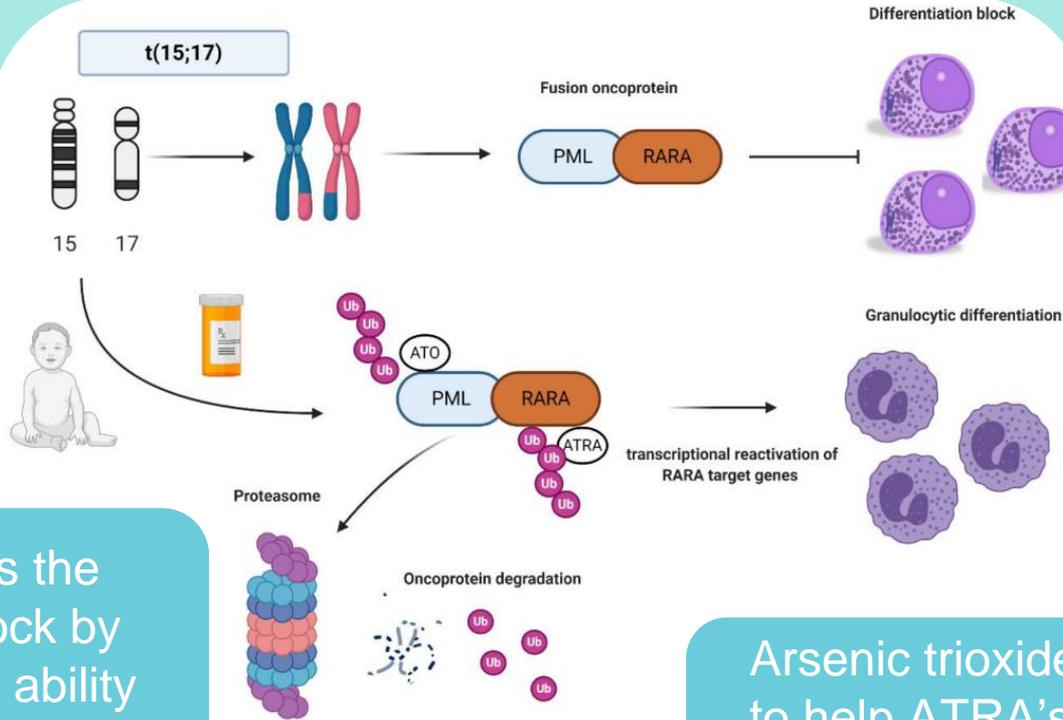
Low Risk

Arsenic Trioxide

WBCC $<10 \times 10^9/L$

Treatment

Management

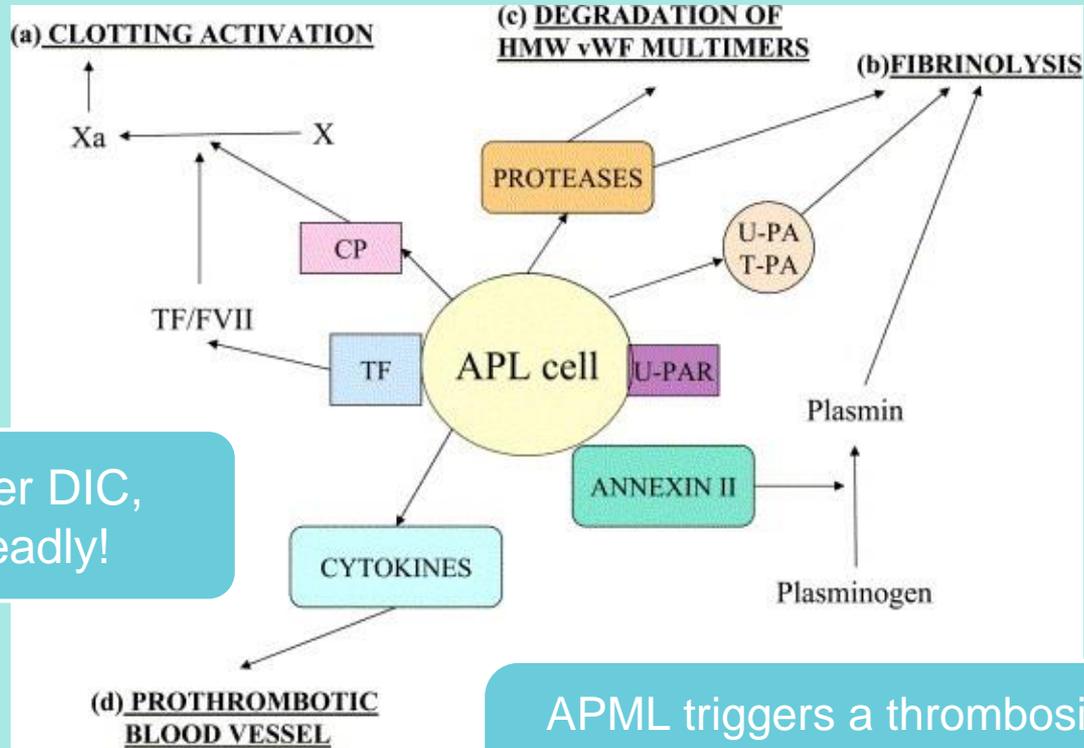


ATRA overcomes the differentiation block by restoring RARAs ability to drive transcription.

Arsenic trioxide has been found to help ATRA's effect by promoting degradation of the aberrant protein.

Risks of Missing an APML

Management



APML can trigger DIC, which can be deadly!

APML triggers a thrombosis/thrombolysis cascade which is poorly controlled, and leads to platelet consumption.

Lab Role in Management

Management



Blood Sciences



Haematology and Coagulation

Hb
WBCC
Blast count
Neutrophils

Fibrinogen
DD
INR/APTR

Blood Transfusion

PRBC

Cryo

Biochemistry

Potassium

LDH

FBC Results and APML

Tips and Tricks

```
10/02/2019 22:56 Blood
Request Reason : ?SEPSIS. NO

HB          73      g/L      ( 120 to 150 ) Auth
WBC         35.6    10*9/L   ( 4.0 to 11.0 ) Auth
PLT         18      10*9/L   ( 150 to 410 ) Auth
RBC         2.81    10*12/L  ( 3.80 to 4.80 ) Auth
HCT         0.223   L/L      ( 0.360 to 0.460 ) Auth
MCV         79.5     f
MCH         26.0     f
MCHC        327     c
```

```
14/12/2020 10:13 Blood
Request Reason : loc.

Comments :
Some of the FBC ranges were reviewed
01/06/2018 to align with current cli

RDW         26.4
MPV         9.1     f

HB          75      g/L      ( 120 to 150 ) Auth
WBC         0.4     10*9/L   ( 4.0 to 11.0 ) Auth
PLT         116     10*9/L   ( 150 to 410 ) Auth
RBC         2.17    10*12/L  ( 3.80 to 4.80 ) Auth
HCT         0.217   L/L      ( 0.360 to 0.460 ) Auth
MCV         100.0    fL       ( 83 to 101 ) Auth
MCH         34.6     pg       ( 27.0 to 32.0 ) Auth
MCHC        345     g/L      ( 315 to 345 ) Auth
RDW         19.4     ( 11.6 to 14.0 ) Auth
MPV         6.5     fL       ( 7.5 to 11.2 ) Auth
Neutrophils 0.2     10*9/L   ( 2.0 to 7.0 ) Auth
Lymphocytes 0.2     10*9/L   ( 1.0 to 3.0 ) Auth
Monocytes   0.0     10*9/L   ( 0.2 to 1.0 ) Auth
```

FBC Results and APML

Tips and Tricks

27/12/2018 u/k Blood

Request Reason : haematuria/bruising/rectal bleeding >cause. NO

HB	131	g/L	(130 to 170)	Auth
WBC	3.6	10 ⁹ /L	(4.0 to 11.0)	Auth
PLT	6	10 ⁹ /L	(150 to 410)	Auth
RBC	4.03	10 ¹² /L	(4.50 to 5.50)	Auth

HCT 0.388 08/07/2022 14:20 Blood

MCV 96.1 Request Reason : STG OV CA

MCH 32.4

MCHC 338

Comments :

Some of the FBC ranges were reviewed

01/06/2018 to align with current cl

RDW 14.1

MPV 11.7

HB	117	g/L	(120 to 150)	Auth
WBC	0.8	10 ⁹ /L	(4.0 to 11.0)	Auth
PLT	68	10 ⁹ /L	(150 to 410)	Auth
RBC	3.51	10 ¹² /L	(3.80 to 4.80)	Auth
HCT	0.342	L/L	(0.360 to 0.460)	Auth
MCV	97.4	fL	(83 to 101)	Auth
MCH	33.3	pg	(27.0 to 32.0)	Auth
MCHC	342	g/L	(315 to 345)	Auth
RDW	16.7		(11.6 to 14.0)	Auth
MPV	7.5	fL	(7.5 to 11.2)	Auth
Neutrophils	0.1	10 ⁹ /L	(2.0 to 7.0)	Auth
Lymphocytes	0.7	10 ⁹ /L	(1.0 to 3.0)	Auth
Monocytes	0.0	10 ⁹ /L	(0.2 to 1.0)	Auth

FBC Results and APML

Tips and Tricks

03/03/2021 13:40 Blood

Request Reason : Panctopenia, bloods requested by haematologist.

HB	110	g/L	(130 to 170)	Auth
WBC	2.9	$10^9/L$	(4.0 to 11.0)	Auth
PLT	104	$10^9/L$	(150 to 410)	Auth
RBC	4.13	$10^{12}/L$	(4.50 to 5.50)	Auth
HCT	0.320	L/L	(0.400 to 0.500)	Auth
MCV	77.4	fL	(83 to 101)	Auth
MCH	26.6	pg	(27.0 to 32.0)	Auth
MCHC	343	g/L	(315 to 345)	Auth
RDW	17.6		(11.6 to 14.0)	Auth
MPV	7.1	fL	(7.5 to 11.2)	Auth
Neutrophils	1.4	$10^9/L$	(2.0 to 7.0)	Auth
Lymphocytes	1.2	$10^9/L$	(1.0 to 3.0)	Auth
Monocytes	0.2	$10^9/L$	(0.2 to 1.0)	Auth

Granular vs Hypo-granular.

Features

Granular (Classical)

Hypogranular (Variant)

Leucocytosis?

No.

Yes.

Nucleus Shape?

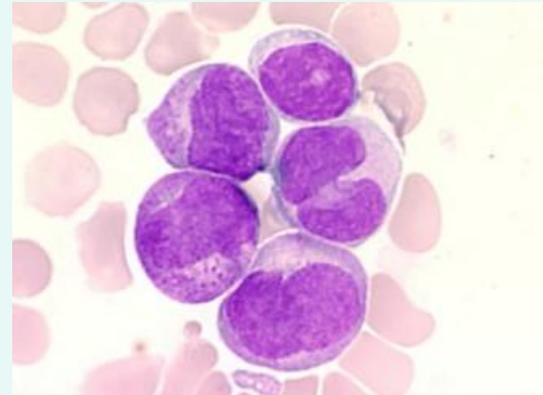
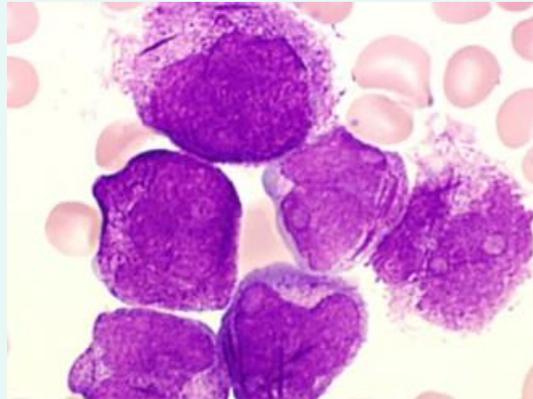
Round to oval with some bi-lobed

Majority/All bi-lobed

Granules?

Densely packed with Auer rods.

Few/No granules



APML Check List

Tips and Tricks

FBC Features

Leucopenia

Leucocytosis

Thrombocytopenia

Blast flags

Blood Film

Cytopenic patients need careful review

Check film edges

Are they dysplastic?

Blast Features

Granularity?

Lobes?

Auer Rods?

Maturation signs?

What's the history?

Bleeding?

Bruising?

<50 years old?

Any known comorbidities?

What should I do?

Phone to the requester.

Put the film on HQ

Contact a Haematologist.

Authorise.

All of these steps are essential!



Thanks!

Do you have any questions?

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