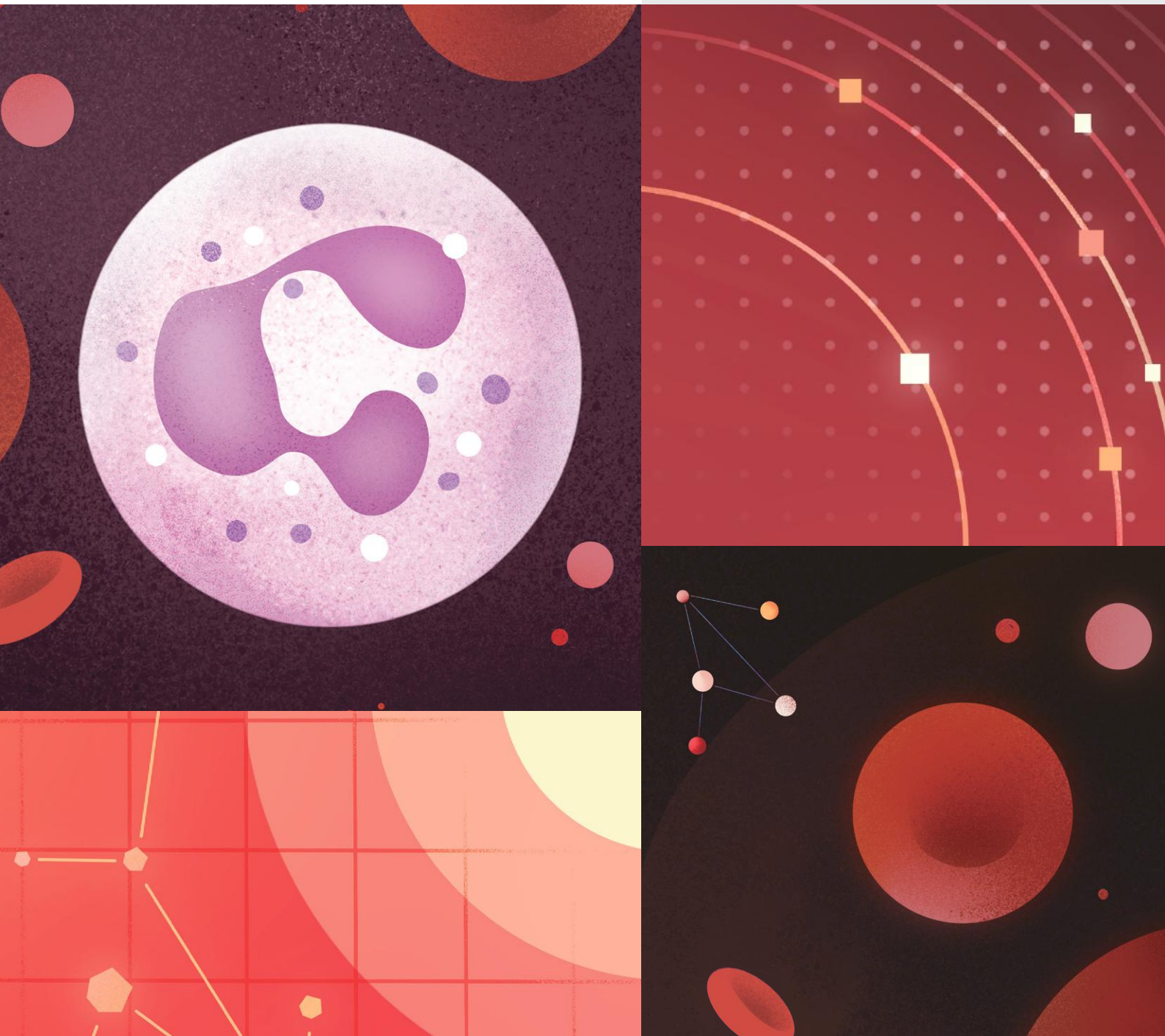
mindray

HemaCase

Clinical Case Booklet

By using Mindray Fully Automated Cellular Analysis Lines

Volume 1



Preface

We are delighted to present you with this clinical case booklet on hematology. At Mindray, our mission has always been to bring cutting-edge technology within reach, ensuring that high-quality healthcare is available to all. As part of this commitment, we have dedicated ourselves to enhancing the accuracy and efficiency of hematology tests in clinical laboratories.

Through the pages of this booklet, we aim to provide you with real clinical cases that vividly illustrate the seamless integration of information from blood analyzers, morphological analysis, and clinical diagnostic data. With the assistance of our state-of-the-art Automated Digital Cell Morphology Analyzer MC-80, these cases showcase how early disease identification and diagnosis can be achieved.

Our ultimate aspiration is for these cases to empower laboratory personnel, like yourself, to gain invaluable insights in their daily work. By immersing yourself in these scenarios, we hope you will not only expand your knowledge but also elevate the quality of patient care you provide.

Contents

List of Abbreviations

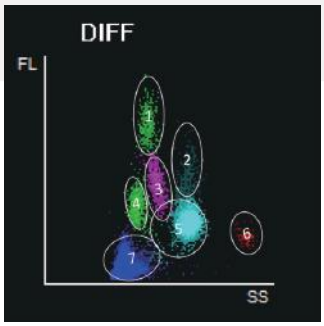
WBC → White blood cell	Eos → Eosinophil	RET# → Reticulocyte count
Neu → Neutrophil	Eos# → Eosinophil count	RET% → Reticulocyte percentage
Neu# → Neutrophil count	Eos% → Eosinophil percentage	RHE → Reticulocyte hemoglobin expression
Neu% → Neutrophil percentage	Bas → Basophil	IRF → Immature reticulocyte fraction
Lym → Lymphocyte	Bas# → Basophil count	PLT → Platelet
Lym# → Lymphocyte count	Bas% → Basophil percentage	PLT-I → Platelet counting with impedance method
Lym% → Lymphocyte percentage	RBC → Red blood cell	PLT-O → Platelet counting with optical method
Mon → Monocyte	HGB → Hemoglobin	IPF → Immature platelet fraction
Mon# → Monocyte count	MCV → Mean corpuscular volume	
Mon% → Monocyte percentage	NRBC → Nucleated RBCs	

Scattergrams of 5-part differential hematology analyzer

SF Cube™

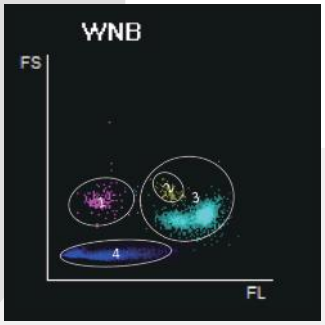
DIFF Scattergram

❶ Abnormal lymphocytes
❷ Immature granulocytes
❸ Monocytes
❹ Lymphocytes



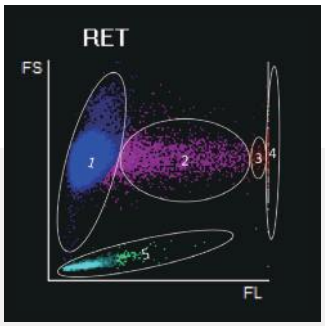
❺ Neutrophils and basophils
❻ Eosinophils
❼ Ghost

WNB Scattergram



❶ Nucleated RBCs
❷ Basophils
❸ White blood cells
❹ Ghost

RET Scattergram



❶ Mature red blood cells
❷ Low-fluorescence reticulocytes
❸ Medium-fluorescence reticulocytes
❹ High-fluorescence reticulocytes
❺ Optical platelets

All morphological images in this case study book, unless otherwise noted, are stained with Wright-Giemsa solution

Case 01

Acute myeloblastic leukemia without maturation (M1)

01

Clinical information

One year ago, the patient presented with a history of recurrent dry coughing for over six months, with worsening symptoms in the last month. A chest CT scan revealed a nodule in the right middle lung, and further testing below confirmed a diagnosis of AML-M1.

Item	Parameter	Result
CBC	WBC	195.4*10^9/L
	HGB	92g/L
	PLT	11*10^9/L
Bone marrow morphology	Bone marrow morphology	Highly active bone marrow with 95% of myeloblasts, indicating acute myeloid leukemia of the AML-M1 subtype.
Immunophenotyping	Immunophenotyping	Immunophenotyping suggested AML
Chromosome	Chromosome	46，XX[20]
Bone marrow NGS	FLT3-ITD mutation	AR=0.271
	CEBPA p.Thr310dup	45.6%
	CEBPA p.Gln83fs	47.1%
	WT1 p.Gly356Ter	44.7%

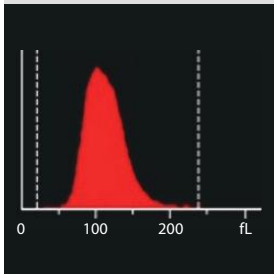
After more than 4 months of chemotherapy, the patient improved and was discharged. However, the patient relapsed 2 months later and underwent 6 months of continued chemotherapy. Bone mzarrow morphology suggested that the disease was not resolved, so the patient was readmitted for treatment on Jun. 2.

CBC results

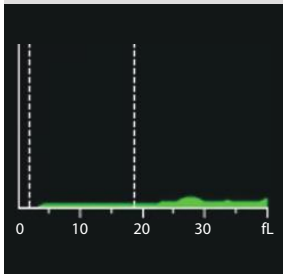
CBC results on Jun. 1

Parameter	Alarm	Result	Unit
WBC	& L	0.85	10^9/L
Neu#	& R L	0.26	10^9/L
Lym#	& R L	0.57	10^9/L
Mon#	R L	0.02	10^9/L
Eos#	L	0.00	10^9/L
Bas#		0.00	10^9/L
IMG#	R	0.00	10^9/L
Neu%	& R L	30.6	%
Lym%	& R H	66.0	%
Mon%	R L	2.5	%
Eos%		0.6	%
Bas%		0.3	%
IMG%	R	0.5	%
RBC	L	2.01	10^12/L
HGB	L	75	g/L
HCT	L	22.8	%
MCV	H	113.3	fL
MCH	H	37.0	pg
MCHC		327	g/L
RDW-CV	H	22.3	%
RDW-SD	H	90.3	fL
PLT	R L	4	10^9/L
MPV		****	fL
PDW		****	
PCT		****	%
P-LCC		****	10^9/L
P-LCR		****	%
NRBC#		0.130	10^9/L
NRBC%		15.28	/100WBC

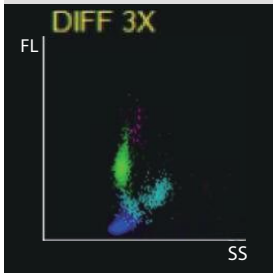
RBC



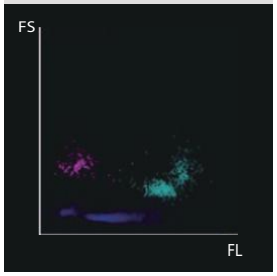
PLT



DIFF



WNB



Alarm

- Pancytopenia
- Blasts?
- Abn Lymph/blast?

……

- WBC decreased with inverted Neu% and Lym%; decreased RBC and HGB; extremely low PLT count.
- NRBCs were visible in the WNB channel; due to the decreased WBC, the DIFF 3X channel was used to increase the particle count by 3 times, thereby improving the repeatability of classification results and the ability to detect abnormal cells. The scattergram showed that Mon particles extended upward into the abnormal lymphocytes/blasts region. The instrument also gave an alarm.

Peripheral blood morphology examination

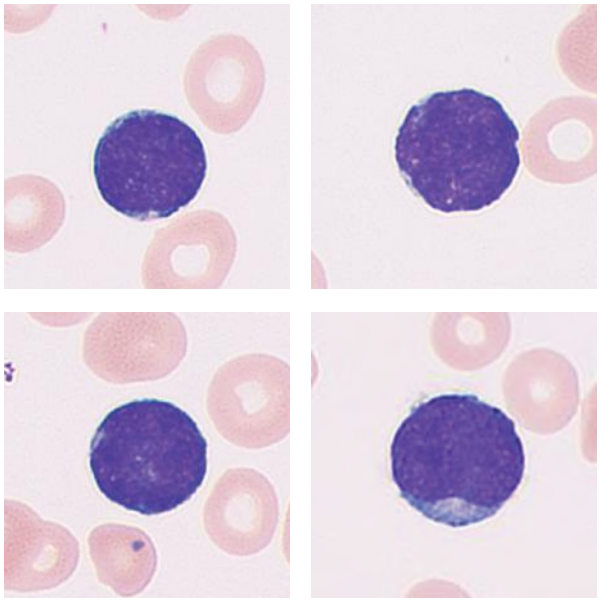
Pre-classification by the reader on Jun. 1

	White blood cells		
	White blood cells	100	100%
L	Segmented neutrophils	18	18.0
	Band neutrophils	4	4.0
H	Lymphocytes	70	70.0
	Eosinophils	1	1.0
!	Blasts	7	7.0
	Non-white blood cells	45	%
!	Nucleated RBCs	12	12.0
	Large platelets	1	
	Smudge cells	9	9.0

	Platelet		
	PLT estimate	Estimated result	Estimation method
	Platelet concentration	6*10^9/L	Automated
	Platelet concentration	9*10^9/L	Manual

	Red blood cells		
	Size	Degree	%
!	Anisocytosis	3+	
	Macrocytes	0	6.7
	Microcytes	0	5.3
	Color	Degree	%
!	Hypochromic cells	2+	15.0
	Polychromasia	0	0.8
	Shape	Degree	%
!	Poikilocytosis	3+	
!	Schistocytes	1+	0.6
	Echinocytes	0	0.0
	Elliptocytes	0	0.9
!	Ovalocytes	3+	21.9
	Stomatocytes	0	1.6
	Target cells	0	0.2
	Teardrop cells	0	2.2

Blasts



Results from manual re-classification

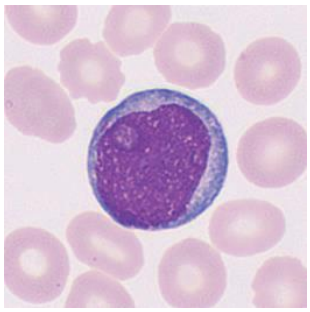
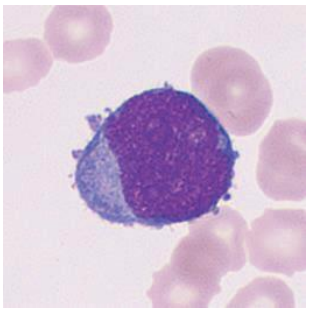
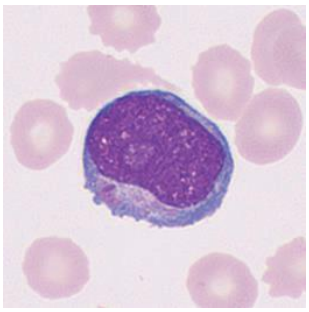
Segmented neutrophils accounted for 16%, band neutrophils accounted for 3%, metamyelocytes accounted for 3%, lymphocytes accounted for 70%, and myeloblasts accounted for 7%. The blasts had small round cell bodies and large, round or oval nuclei with fine chromatins. Some blasts had visible nucleoli and scant cytoplasm that appeared pale blue. The PLT estimate was consistent with the CBC result.

Case analysis

- At the initial diagnosis, the patient had a bone marrow blast percentage of 95% and was diagnosed with Acute myeloblastic leukemia (AML-M1). There were no chromosomal abnormalities, but CEBPA mutation was present. Generally, AML patients with biallelic CEBPA mutation have a good prognosis, but in this case, the patient also had an FLT3-ITD (FMS-like tyrosine kinase 3-internal tandem duplication) mutation, which is a strong indicator of poor prognosis as it leads to increased tyrosine kinase activity and the activation of various tumors, especially AML. Therefore, the patient relapsed after only two months following improvement with treatment, and subsequent treatment results were not ideal.
- The DIFF scattergram of the CBC showed that the upper part of the Lym cluster was pointed and slightly extended to the upper right; although the Mon particles were scarce, they were significantly elevated, some of which entered the abnormal lymphocytes/myeloblast region, and was shifted to the right overall, indicating the possible presence of abnormal cells. This corresponds to the results of the peripheral blood smear reading. Blasts were observed in 7% of peripheral blood cells. Compared with typical myeloblasts (as shown in the figure below), blasts have scant cytoplasm and less fine and loose chromatins, which to some extent affected the binding of nucleic acid fluorescent dyes, resulting in relatively weak FL signals of the corresponding particles in the DIFF scattergram.

Case analysis

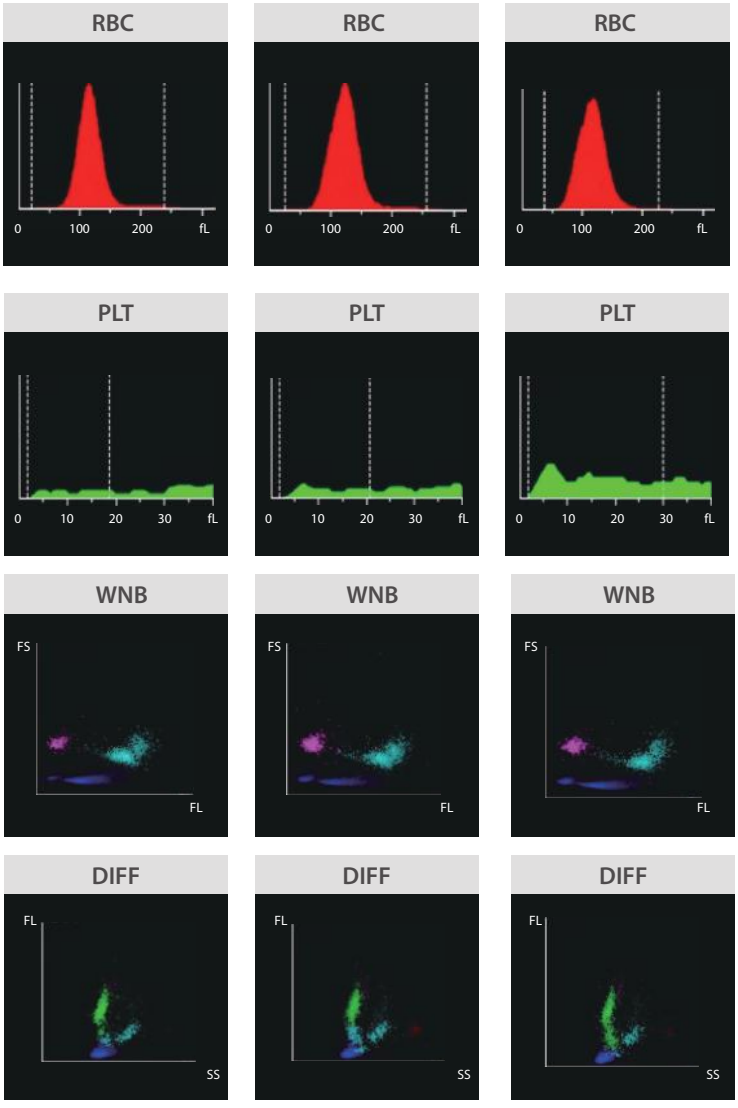
Reference figures of blasts

After the patient was admitted to the hospital, the chemotherapy regimen was changed. We tracked the CBC and peripheral blood morphology results as follows:

The CBC results from Jul. 6, Jul. 13, and Aug. 3 are shown from right to left

Parameter	Alarm	Result	Delta#	07-13	07-6	Unit
WBC	& L	2.35	0.040	2.31	1.96	10^9/L
Neu#	& R L	0.62	-0.200	0.82	0.55	10^9/L
Lym#	& R	1.70	0.310	1.39	1.35	10^9/L
Mon#	R L	0.02	-0.010	0.03	0.03	10^9/L
Eos#	R L	0.01	-0.060	0.07	0.03	10^9/L
Bas#	R	0.00	0.000	0.00	0.00	10^9/L
IMG#	R	0.08	-0.050	0.13	0.08	10^9/L
Neu%	& R L	26.2	-9.40	35.6	28.2	%
Lym%	& R H	72.2	12.40	59.8	68.8	%
Mon%	R L	1.0	-0.40	1.4	1.3	%
Eos%	R	0.5	-2.50	3.0	1.6	%
Bas%	R	0.1	-0.10	0.2	0.1	%
IMG%	R	3.2	-2.50	5.7	4.2	%
RBC	L	2.83	0.350	2.48	2.05	10^12/L
HGB	L	96	7.0	89	76	g/L
HCT	L	30.9	2.40	28.5	24.1	%
MCV	H	109.4	-5.50	114.9	117.4	fL
MCH	H	34.1	-1.70	35.8	36.9	pg
MCHC	L	312	1.0	311	315	g/L
RDW-CV		14.9	-2.70	17.6	19.1	%
RDW-SD	H	63.5	-15.00	78.5	81.2	fL
PLT	& L	13	4.0	9	18	10^9/L
MPV	R	10.6	-1.00	11.6	15.2	fL
PDW	R	16.3	0.10	16.2	17.8	
PCT	R L	0.008	-0.0010	0.009	0.027	%
P-LCC	R L	6	2.0	4	11	10^9/L
P-LCR	R	44.8	-2.00	46.8	61.3	%
IPF	H	26.9	-1.10	28.0		%
RET#		0.1974	-0.1371	0.3345		10^12/L
RET%	H	6.98	-6.500	13.48		%
IRF		24.4	-15.70	59.9		%
LFR	L	75.6	15.70	59.9		%
MFR		19.8	-9.70	29.5		%
HFR		4.6	-6.00	10.6		%
RHE		34.6	0.00	34.6		pg



- The results from the three tests were similar. Compared with the results before admission, there was an increase in WBC and HGB. The DIFF scattergram showed that Lym particles further shifted towards the upper right corner, with an increase in the density of particles in the upper region, suggesting that abnormal cells still existed and their percentage might be increasing.

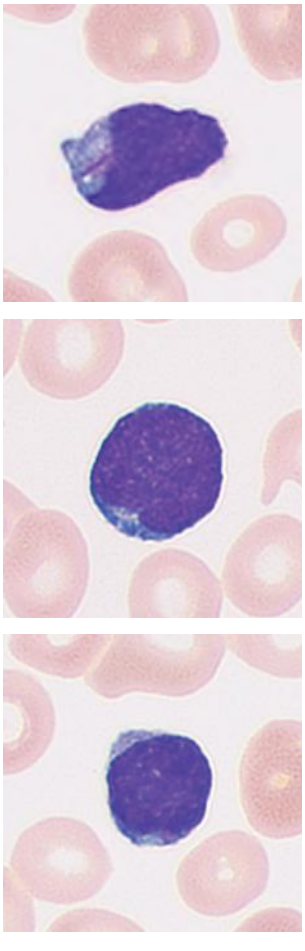
Peripheral blood morphology results from Jul. 6 to Aug. 3

Analysis time 09:07, Jul. 6, 2022

White blood cells

	White blood cells	302	100%
L	Segmented neutrophils	48	15.9
	Band neutrophils	20	6.6
	Lymphocytes	97	32.1
L	Monocytes	3	1.0
	Eosinophils	4	1.3
	Metamyelocytes	1	0.3
!	Myelocytes	17	5.6
!	Blasts	112	37.2
	Non-white blood cells	**116**	**%**
!	Nucleated RBCs	93	30.8
	Giant platelets	1	
	Large platelets	3	
	Smudge cells	14	4.6

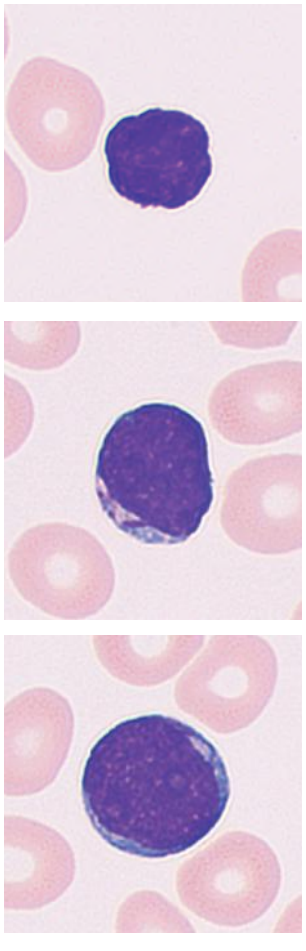
Blasts



Analysis time 08:14, Jul. 13, 2022

White blood cells

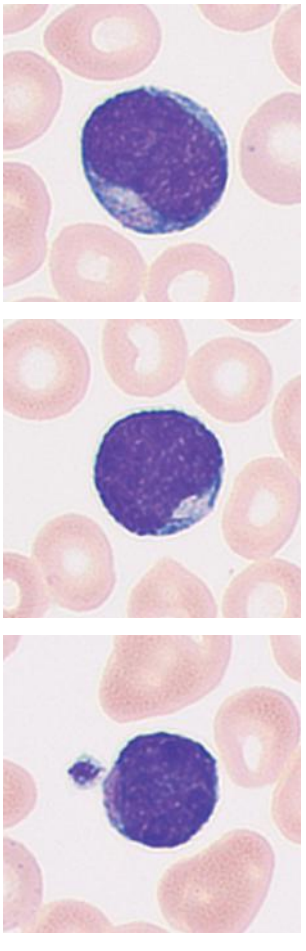
	White blood cells	301	100%
L	Segmented neutrophils	58	19.3
	Band neutrophils	20	6.6
	Lymphocytes	90	29.9
L	Monocytes	3	1.0
	Eosinophils	11	3.7
	Metamyelocytes	3	1.0
!	Myelocyte	15	5.0
	Promyelocytes	1	0.3
!	Blasts	99	32.9
	Reactive lymphocytes	1	0.3
	Non-white blood cells	**116**	**%**
!	Nucleated RBCs	66	21.9
	Large platelets	2	
	Smudge cells	14	4.7



Analysis time 08:51, Aug. 8, 2022

White blood cells

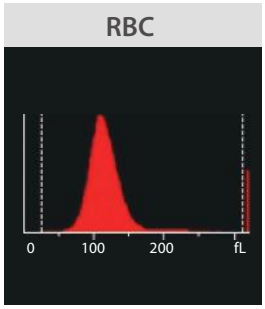
	White blood cells	300	100%
L	Segmented neutrophils	50	16.7
	Band neutrophils	15	5.0
H	Lymphocytes	133	44.4
L	Monocytes	4	1.3
!	Myelocytes	10	3.3
!	Promyelocytes	4	1.3
!	Blasts	83	27.7
	Reactive lymphocytes	1	0.3
	Non-white blood cells	**65**	**%**
!	Nucleated RBCs	33	11.0
	Giant platelets	1	
	Large platelets	10	
	Smudge cells	11	3.7

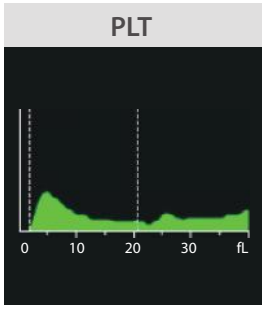


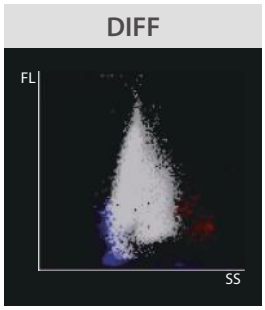
- Three peripheral blood morphology results were consistent with the CBC results. Myeloblasts and immature granulocytes at all stages of development were visible. Due to reasons including drug-induced cell differentiation, myeloblast morphology was atypical, with small cell bodies and less fine and loose chromatins, but nucleoli and Auer bodies were still visible.
- Despite almost 3 months of treatment, the patient's condition further deteriorated.

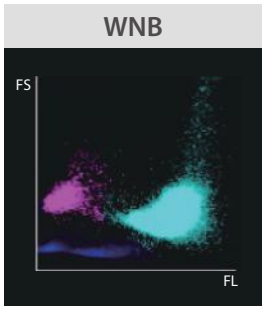
CBC results on Aug. 24

Parameter	Alarm	Result	Delta#	08-03	07-13	Unit
WBC	& H	201.32	198.970	2.35	2.31	10^9/L
Neu#		****		0.62	0.82	10^9/L
Lym#		****		1.70	1.39	10^9/L
Mon#		****		0.02	0.03	10^9/L
Eos#	R	0.30	0.290	0.01	0.07	10^9/L
Bas#	R	0.02	0.020	0.00	0.00	10^9/L
IMG#		****		0.08	0.13	10^9/L
Neu%		****		26.2	35.6	%
Lym%		****		72.2	59.8	%
Mon%		****		1.0	1.4	%
Eos%	R L	0.1	-0.40	0.5	3.0	%
Bas%	R	0.0	-0.10	0.1	0.2	%
IMG%		****		3.2	5.7	%
RBC	L	2.66	-0.170	2.83	2.48	10^12/L
HGB	L	85	-11.0	96	89	g/L
HCT	L	28.6	-2.30	30.9	28.5	%
MCV	H	107.4	-2.00	109.4	114.9	fL
MCH		31.8	-2.30	34.1	35.8	pg
MCHC	L	296	-16.0	312	311	g/L
RDW-CV	H	16.4	1.50	14.9	17.6	%
RDW-SD	H	68.4	4.90	63.5	78.5	fL
PLT	L	20	7.0	13	9	10^9/L
MPV		9.0	-1.60	10.6	11.6	fL
PDW	H	17.1	0.80	16.3	16.2	
PCT	L	0.018	0.0100	0.0008	0.0009	%
P-LCC	L	6	0.0	6	4	10^9/L
P-LCR		27.3	-17.50	44.8	46.8	
NRBC#		3.208	2.9740	0.234	0.632	10^9/L
NRBC%		1.59	-8.380	9.97	27.32	/100WBC









Alarm

- Abn. WBC scattergram
- Blasts?
- Abn Lymph/blast?
- Immature Gran?

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- WBC increased with classification results of poor reliability that were blocked; RBC and HGB decreased; extremely low PLT count.
- In the WNB channel, a large number of NRBCs were observed, and some WBC particles extended upwards, indicating the presence of a large amount of abnormal cells. In the DIFF scattergram, the particles in the Lym and Neu regions extended together towards the high-fluorescence area and eventually merged, causing particle clusters to be indistinguishable and presenting a droplet-like appearance, indicating the presence of a large number of immature granulocytes and blasts.

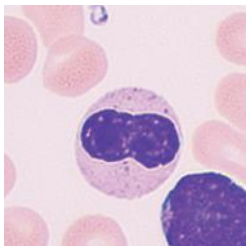
Peripheral blood morphology results on Aug. 24

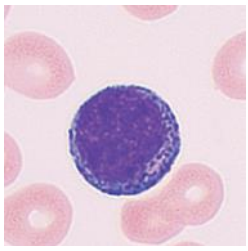
Analysis time 08:57, Aug. 24, 2022

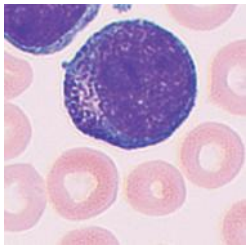
White blood cells

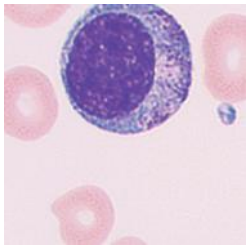
	White blood cells	325	100%
L	Segmented neutrophils	2	0.6
	Band neutrophils	2	0.6
L	Lymphocytes	11	3.4
L	Monocytes	2	0.6
L	Eosinophils	1	0.3
	Metamyelocytes	4	1.2
!	Myelocytes	39	12.0
!	Promyelocytes	49	15.1
!	Blasts	215	66.2
	Non-white blood cells	**92**	**%**
!	Nucleated RBCs	8	2.5
	Smudge cells	79	24.3

Immature granulocytes:

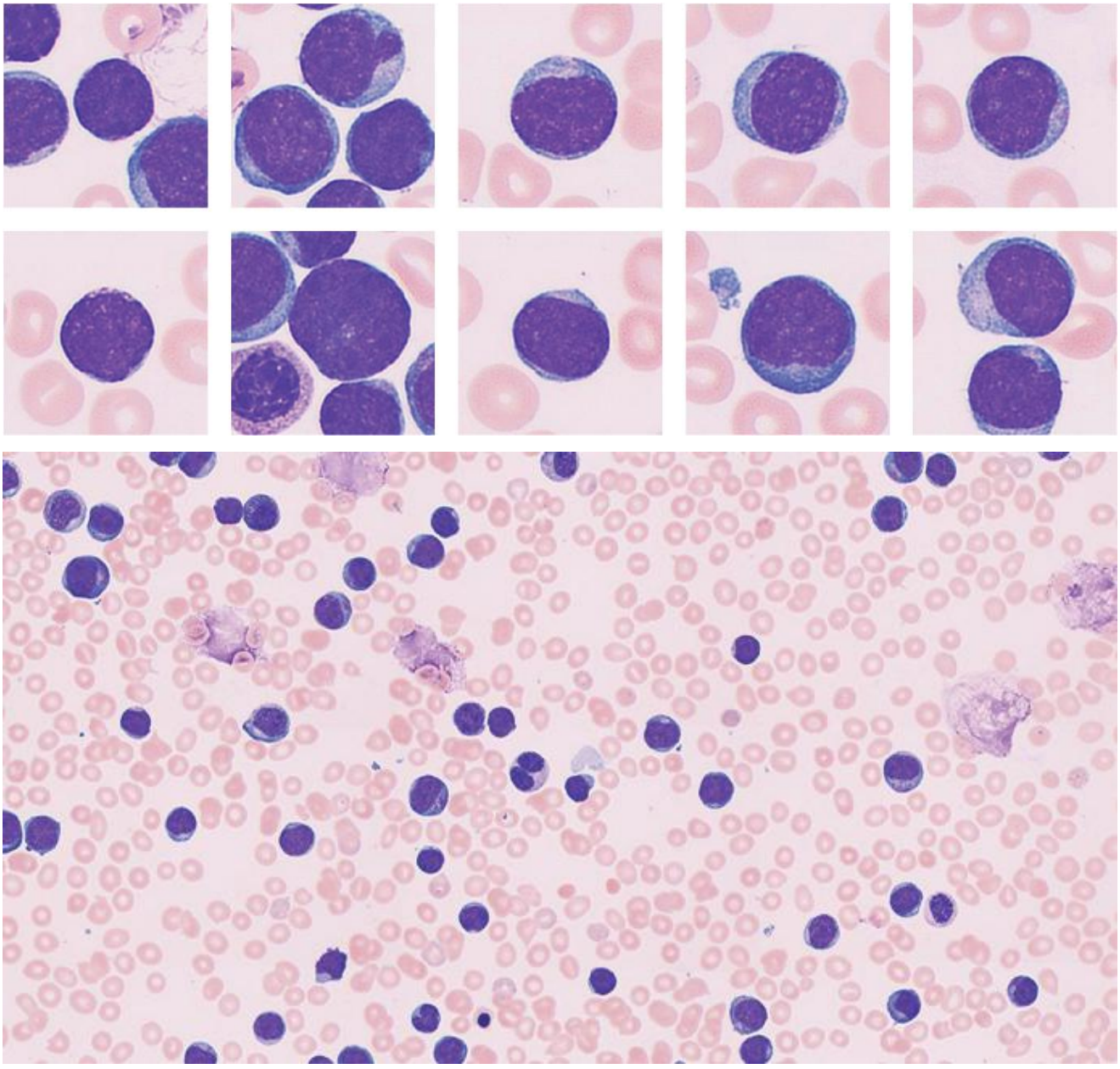








Blasts



- Pseudo Pelger–Huët anomaly was observed in some neutrophilic metamyelocytes and band neutrophils. The blasts accounted for 66.2%, varied in sizes, and were generally larger compared with previous results, with 2–3 nucleoli visible in some blasts.

Discussion

- Although scattergrams cannot directly reflect the morphology of cells, the changes in their optical signal values can faithfully reflect changes in cell morphology. For example, in this case, although blasts appeared frequently, the monoclonal proliferation was inhibited by the drug and the transcriptional and translational activities of nucleic acids were weakened. Meanwhile, the cell volume was reduced and chromatin was aggregated. As a result, the binding of fluorescent dye was not as pronounced as in typical blasts during the CBC, and Lym and Mon particle cluster distribution were slightly suppressed in the fluorescence direction on the DIFF scattergram. Nevertheless, the Lym particle cluster was more skewed to the right than that under normal circumstances, indicating the presence of abnormal cells. In the last examination, a large number of myeloblasts and immature granulocytes proliferated and were released, rendering the DIFF scattergram more distinct features.

Case 02
Acute promelocytic leukemia (APL)

02

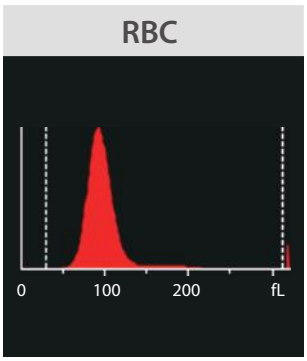
Clinical information

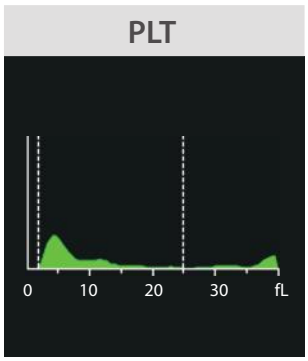
The patient was a 52-year-old female, previously healthy, who presented to the hospital on Nov. 1 with left ear bleeding without any obvious cause (which later stopped spontaneously). One week prior to the visit, the patient had experienced fatigue without obvious cause. The skin showed no petechiae or ecchymoses, and there was no hepatosplenomegaly or superficial lymphadenopathy.

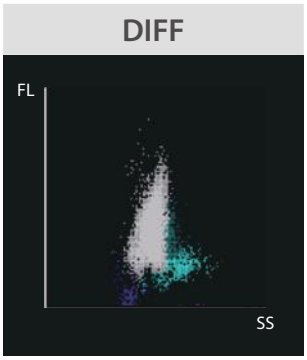
CBC results

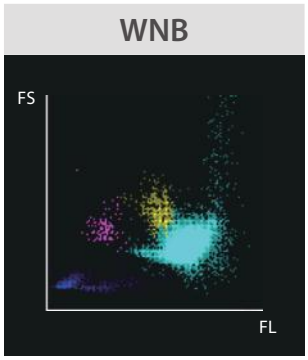
CBC results on Nov. 1

Parameter	Alarm			Result	Unit
WBC	&		H	93.05	10^9/L
Neu#	&	R	L	1.15	10^9/L
Lym#				****	10^9/L
Mon#				****	10^9/L
Eos#			L	0.00	10^9/L
Bas#			H	0.90	10^9/L
IMG#		R		0.80	10^9/L
Neu%	&	R	L	1.2	%
Lym%				****	%
Mon%				****	%
Eos%			L	0.0	%
Bas%				1.0	%
IMG%		R		0.9	%
RBC			L	2.84	10^12/L
HGB			L	89	g/L
HCT			L	26.6	%
MCV				93.6	fL
MCH				31.2	pg
MCHC				333	g/L
RDW-CV				15.1	%
RDW-SD				52.0	fL
PLT			L	17	10^9/L
MPV				8.9	fL
PDW			H	18.0	
PCT			L	0.015	%
P-LCC			L	4	10^9/L
P-LCR				22.3	%
NRBC#				0.195	10^9/L
NRBC%				0.21	/100WBC









Alarm

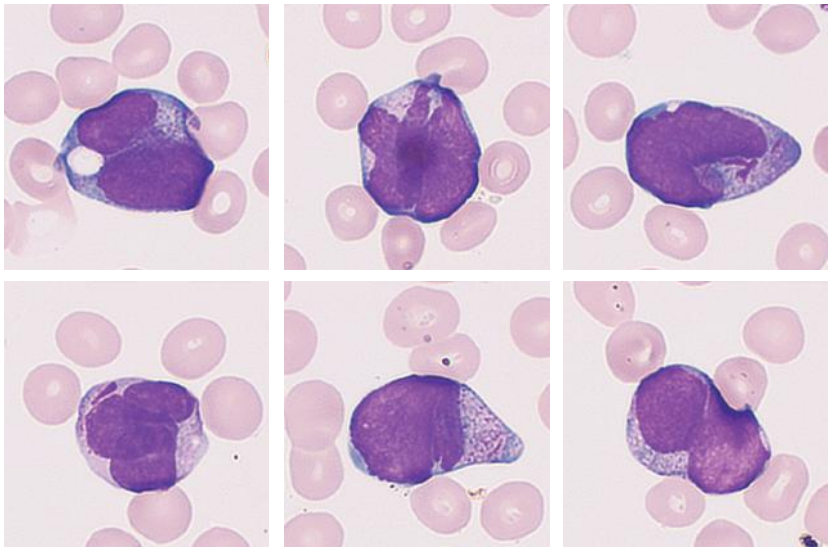
- Abn. WBC scattergram
- Blasts?
- Abn Lymph/blast?
- Immature Gran?
- Basophilia
- Leukocytosis
- Anemia
- Thrombocytopenia

- WBC increased with poor classification reliability; RBC and HGB decreased; extremely low PLT count.
- The WNB channel showed the presence of NRBCs, and some particles extended upward. The DIFF channel showed particles in the Neu region extending upward to the left and merging with particles in the Mon region to advance towards the high-fluorescence region, leading to some particles entering the abnormal lymphocytes/blasts region. The instrument also gave an alarm.

Peripheral blood morphology examination

	White blood cells		
	White blood cells	**500**	**100%**
L	Segmented neutrophils	6	1.2
	Band neutrophils	1	0.2
L	Lymphocytes	5	1.0
L	Eosinophils	2	0.4
	Metamyelocytes	1	0.2
	Promyelocytes	4	0.8
!	Blasts	473	94.6
	Reactive lymphocytes	8	1.6
	Non-white blood cells	**70**	**%**
!	Nucleated RBCs	4	0.8
	Smudge cells	60	12.0
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	29*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
!	Anisocytosis	3+	
	Macrocytes	0	1.2
!	Microcytes	3+	40.4
	Color	**Degree**	**%**
	Hypochromic cells	0	3.1
	Polychromasia	0	0.6
	Shape	**Degree**	**%**
!	Poikilocytosis	1+	
!	Schistocytes	1+	1.7
	Echinocytes	0	0.2
	Elliptocytes	0	0.4
	Ovalocytes	0	8.7
	Stomatocytes	0	0.0
	Target cells	0	0.0
	Teardrop cells	0	1.5

Abnormal promyelocytes



Results from manual re-classification

Segmented neutrophils accounted for 1.2%, band neutrophils accounted for 0.2%, metamyelocytes accounted for 0.2%, promyelocytes accounted for 0.6%, lymphocytes accounted for 1%, and abnormal promyelocytes accounted for 94.8%. Abnormal promyelocytes exhibited irregular cell bodies and nuclei with twisting and folding patterns. Chromatins were fine and nucleoli were visible. The internal and external plasma was visible in few cells, with indistinct granules while Auer's bodies were visible in the cytoplasm of some abnormal cells.

Other examinations

Item	Parameter	Result	Reference range	Item	Result
Coagulation	PT	16.3	9.4-12.5	Bone marrow	APL cells accounted for 86%, with POX-5, +37, +++28, ++++30/100, suggesting APL. Please take into account clinical findings and other genetic tests.
	APTT	23.8	25.4-38.4		
	TT	18.6	11.0-17.8	Flow cytometry	The immature myeloid cells accounted for 94.55% of the nucleated cells in the bone marrow, with large side-scatter angles; strongly positive for CD9; positive for CD117, CD45, CD34, CD64, CD13, CD33, CD123, and cMPO; weakly positive for CD7 and CD71; negative for CD22, CD10, CD19, CD38, CD14, CD15, CD11b, CD25, CD11c, DR, GlyA, cCD79a, cCD3, and other antigens
	FIB	118	200-400		
	DD	2574	<250		
	FDP	45.90	<5.00		
Chemistry	K	2.94	3.50-5.30mmol/L		
	LDH	691	120-250U/L	Chromosome	46, XX, t(15; 17)(q24; q21)
	CRP	6.2	<3.0mg/L	Gene	PML-RARA 74.49%, FLT-ITD (high) 44.23%

Case analysis

The main clinical manifestations of the patient were asthenia and bleeding; CBC showed anemia with markedly elevated WBCs and markedly reduced platelets. The coagulation results were abnormal, with markedly increased D-dimer, suggesting a tendency for DIC. Lactate dehydrogenase (LDH) was markedly elevated, while typical abnormal promyelocytes were observed in both peripheral blood and bone marrow. The diagnosis of acute promyelocytic leukemia (high-risk type) was further confirmed with the results of flow cytometry and karyotype analysis.

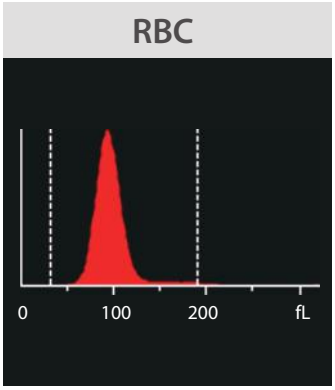
Starting on Nov. 1, platelets and fresh frozen plasma (Fib supplementation) were given for supportive treatment to correct DIC tendency.

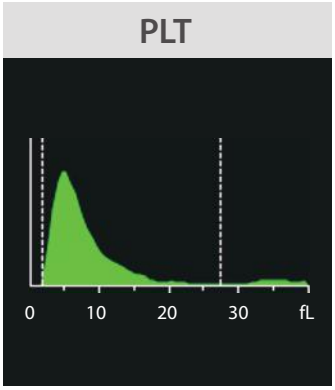
Hydroxyurea, cytarabine, and mitoxantrone were temporarily given from Nov. 1 to Nov. 4 for WBC reduction therapy;

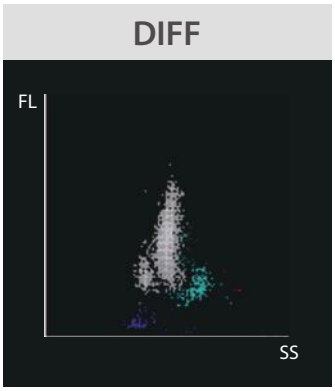
Arsenic + ATRA induction therapy was started on Nov. 3;

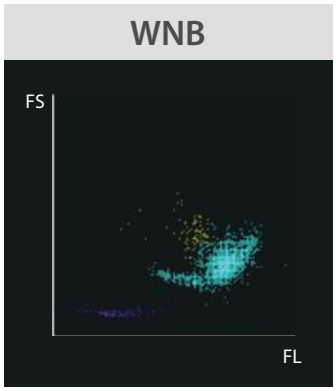
CBC results on Nov. 5

Parameter	Alarm	Result	Unit
WBC		4.48	10^9/L
Neu#	R L	0.77	10^9/L
Lym#		****	10^9/L
Mon#		****	10^9/L
Eos#	L	0.00	10^9/L
Bas#	H	0.12	10^9/L
IMG#	R	0.04	10^9/L
Neu%	R L	17.2	%
Lym%		****	%
Mon%		****	%
Eos%	L	0.1	%
Bas%	H	2.8	%
IMG%	R	1.0	%
RBC	L	2.36	10^12/L
HGB	L	74	g/L
HCT	L	22.1	%
MCV		93.8	fL
MCH		31.6	pg
MCHC		337	g/L
RDW-CV		14.5	%
RDW-SD		50.2	fL
PLT	L	49	10^9/L
MPV		8.3	fL
PDW		16.6	
PCT	L	0. 041	%
P-LCC	L	8	10^9/L
P-LCR		15.5	%
NRBC#		0.000	10^9/L
NRBC%		0.00	/100WBC







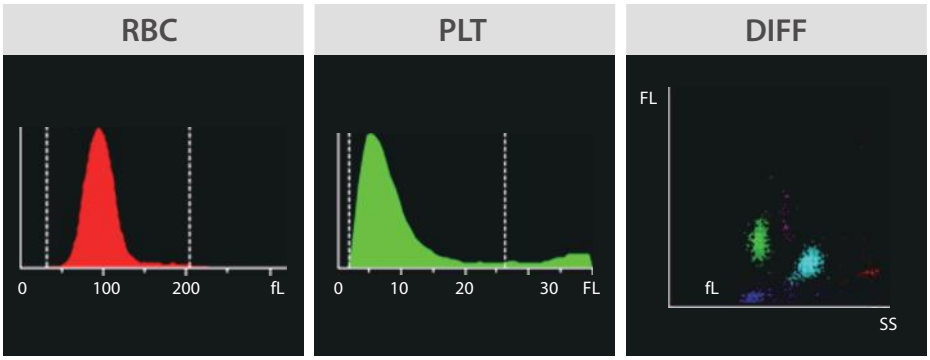


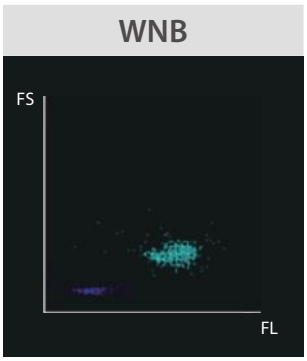
Alarm

- Abn. WBC scattergram
- Blasts?
- Abn Lymph/blast?
- Atypical Lymph?
- Neutropenia
- Anemia
- Thrombocytopenia

CBC results on Feb. 10

Parameter	Alarm	Result	Unit
WBC	L	1.11	10^9/L
Neu#	L	0.70	10^9/L
Lym#	L	0.38	10^9/L
Mon#	L	0.01	10^9/L
Eos#		0.02	10^9/L
Bas#		0.00	10^9/L
IMG#		0.00	10^9/L
Neu%		62.2	%
Lym%		34.4	%
Mon%	L	1.0	%
Eos%		2.2	%
Bas%		0.2	%
IMG%		0.1	%
RBC	L	2.87	10^12/L
HGB	L	91	g/L
HCT	L	27.2	%
MCV		94.8	fL
MCH		31.6	pg
MCHC		333	g/L
RDW-CV	H	18.5	%
RDW-SD	H	64.7	fL
PLT		123	10^9/L
MPV		8.3	fL
PDW		16.0	
PCT	L	0.103	%
P-LCC	L	19	10^9/L
P-LCR		15.0	%
NRBC#		0.000	10^9/L
NRBC%		0.00	/100WBC





Alarm

- Lymphopenia
- Neutropenia
- Leukocytopenia
- Anisocytosis

- After treatment, some improvement in anemia and thrombocytopenia was achieved, and the WBC concentration also decreased significantly. The scattergram showed that the decreased WBCs were mainly particles in the region of monocytes and abnormal cells. Because abnormal cells have fewer granules and a higher content of intracellular nucleic acid material, they typically fall in the Mon region of the DIFF scattergram, leading to a false increase in Mon. Therefore, in practice, it is advisable to set corresponding retesting rules for Mon elevation and to perform morphology screening of abnormal cells for samples that trigger the rules.

Discussion

Acute promyelocytic leukemia (APL) is an acute myeloid leukemia featured by malignant proliferation of abnormal promyelocytes and cytogenetic abnormalities t(15;17)(q22;q12) and PML-RARα. Its morphological characteristics are equivalent to those of acute promyelocytic leukemia (M3 subtype) in the FAB classification scheme. AML-M3 emphasizes abnormal promyelocyte morphology, with morphological features including internal and external plasma, "buttock" and "butterfly" cells, as well as faggot cells.

In addition to the common clinical features of AML, APL has the following characteristics:

- Granules in the cytoplasm of abnormal promyelocytes contain a large amount of procoagulant enzymes, often causing patients to develop DIC. Skin and mucous membrane bleeding is the most obvious sign, followed by gastrointestinal tract, urinary tract, respiratory tract, and vaginal bleeding, while intracranial bleeding, as the most severe case, is one of the causes of death. In this case, the patient experienced bleeding in the ear canal that stopped spontaneously, but DIC occurred soon after hospitalization. Fortunately, the diagnosis and hospitalization were timely.
- All-trans retinoic acid (ATRA) can induce the differentiation of APL cells into mature cells, while arsenic trioxide (ATO) can induce their apoptosis, resulting in a high remission rate. Therefore, early diagnosis and treatment of APL are key to improving the remission rate.

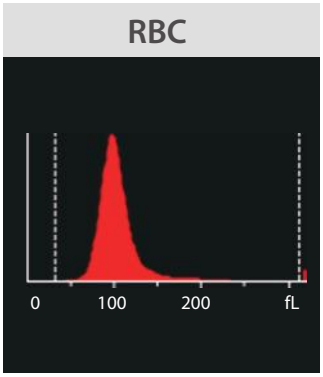
Case 03
Acute myeloblastic leukemia with maturation (M2)

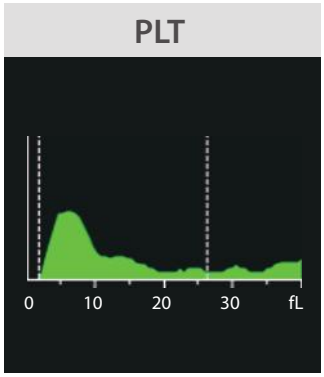
Clinical information

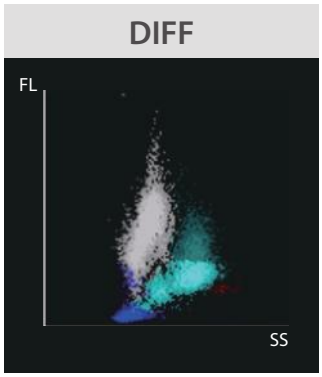
The patient, a 60-year-old female, was admitted to the hospital on Aug. 16, 2021 with dizziness and anemia.

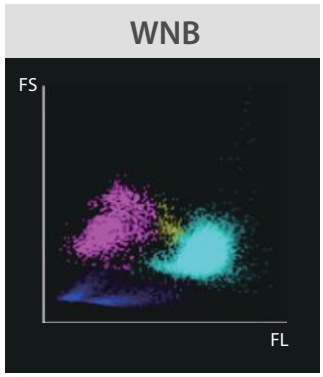
CBC results

Parameter	Alarm	Result	Unit
WBC	& H	34.99	10^9/L
Neu#	& R H	13.25	10^9/L
Lym#		****	10^9/L
Mon#		****	10^9/L
Eos#	R	0.04	10^9/L
Bas#	R H	0.27	10^9/L
IMG#	R	3.56	10^9/L
Neu%	& R L	37.8	%
Lym%		****	%
Mon%		****	%
Eos%	R L	0.2	%
Bas%	R	0.8	%
IMG%	R	10.2	%
RBC	L	2.70	10^12/L
HGB	L	89	g/L
HCT	L	27.2	%
MCV	H	100.8	fL
MCH		33.1	pg
MCHC		328	g/L
RDW-CV		14.1	%
RDW-SD		51.5	fL
PLT	L	31	10^9/L
MPV		10.5	fL
PDW	H	17.1	
PCT	L	0.033	%
P-LCC	L	10	10^9/L
P-LCR		31.3	%
NRBC#		2.762	10^9/L
NRBC%		7.89	/100WBC









Alarm

- Abn. WBC scattergram
- Blasts?
- Abn Lymph/blast?
- Immature Gran

- WBC increased with poor classification reliability; moderate anemia; PLT decreased.
- In the WNB channel, the NRBC region was significantly dense, and the WBC, NRBC, and Bas particle clusters were clearly distinguished, ensuring the accuracy of WBC. In the DIFF scattergram, the particles in the Mon region were dense and could not be effectively distinguished from Lym, with a large number of particles extending up to the abnormal cell region, suggesting the presence of abnormal cells. In addition, the left margin of the mixed Lym and Mon particle cluster was concave to the right, suggesting that the abnormal cells were possibly of myeloid lineage. The Neu particle cluster extended toward the high-fluorescence region, suggesting a left shift of the nucleus.

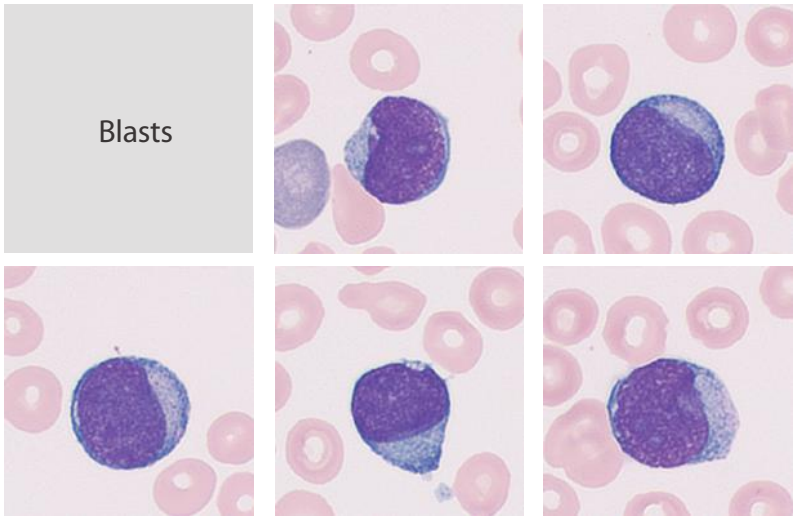
Peripheral blood morphology examination

	White blood cells		
	White blood cells	**200**	**100%**
L	Segmented neutrophils	25	12.5
	Band neutrophils	3	1.5
L	Lymphocytes	7	3.5
	Monocytes	6	3.0
H	Basophils	13	6.5
!	Metamyelocytes	15	7.5
!	Myelocytes	5	2.5
	Promyelocytes	1	0.5
!	Blasts	125	62.5
	Non-white blood cells	**70**	**%**
!	Nucleated RBCs	15	7.5
	Large platelets	1	
	Smudge cells	41	20.5

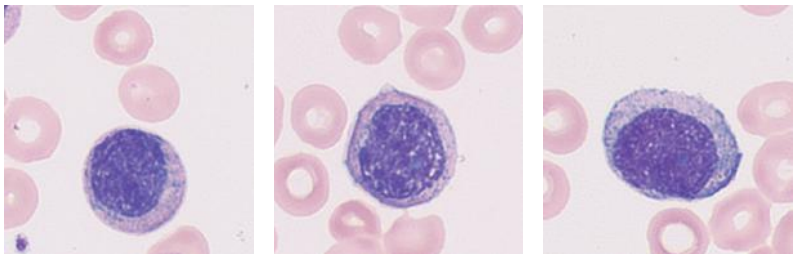
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	12*10^9/L	Automated
	Platelet concentration	18*10^9/L	Manual

	Red blood cells		
	Size	**Degree**	**%**
!	Anisocytosis	2+	
	Macrocytes	0	2.0
!	Microcytes	2+	11.9
	Color	**Degree**	**%**
!	Hypochromic cells	2+	14.9
	Polychromasia	0	1.0
	Shape	**Degree**	**%**
	Poikilocytosis	0	
	Schistocytes	0	1.0
	Echinocytes	0	0.2
	Elliptocytes	0	0.0
	Ovalocytes	0	4.4
	Stomatocytes	0	0.4
	Target cells	0	0.2
	Teardrop cells	0	2.5

Blasts



Myelocytes



Results from manual re-classification

The immature granulocytes accounted for 10.5%, which were mainly metamyelocytes; blasts accounted for 62.5%; NRBCs accounted for 7.5%, with occasional large platelets; no platelet aggregation was observed. The PLT estimate was generally consistent with the CBC result. Blasts showed oval cell bodies, eccentric nucleus, fine sandy chromatins, 2–3 nucleoli, and blue transparent cytoplasm. Abnormal myelocytes were also visible with pink cytoplasm, but the nucleoli were still visible in the nucleus, showing old nuclei and young cytoplasm.

Bone marrow cytology examination

- Blasts accounted for 84.5% and histochemical staining showed POX+.
- Acute myeloid leukemia with a predilection for M2, further subtyping is recommended through integration of flow cytometry and relevant molecular biology testing.

Case analysis

Characteristics of M2 (acute myeloid leukemia with partial differentiation):

- Hemogram: Significant anemia, moderate leukocytosis similar to M1, mainly myeloblasts and promyelocytes, and moderate to severe thrombocytopenia.
- Myelogram: A diagnosis of this subtype can be made with 30%–89% blasts in bone marrow (NEC) with morphological abnormalities; monocytes < 20%, promyelocytes and cells in earlier stages > 10%.
- Cell histochemical staining: POX and SBB staining were positive; PAS staining: most blasts were negative, most promyelocytes were weakly positive with fine granular positivity; neutrophilic alkaline phosphatase (NAP): activity was obviously decreased, even disappearing. When accompanied by infection, NAP score might increase transiently.

Based on the myelogram characteristics and histochemical staining, the diagnosis of acute myeloid leukemia M2 subtype was favored. Further subtyping requires the results of flow cytometry and relevant genetic testing.

Case 04

Acute myelomonocytic leukemia (AMML)

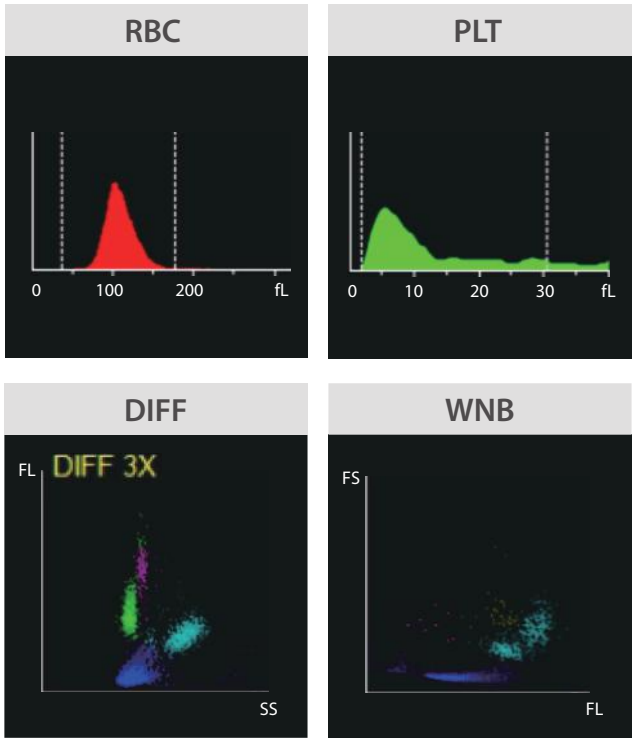
04

Clinical information

The patient was a 49-year-old female who presented with asthenia more than 10 days ago with no obvious cause. She had a medical history of "malignant breast tumor" for 7 years and had undergone surgical treatment, with 1 month of post-operative radiotherapy and 8 cycles of chemotherapy.

CBC results

Parameter	Alarm	Result	Unit
WBC	& L	0.95	10^9/L
Neu#	& R L	0.39	10^9/L
Lym#	& R L	0.46	10^9/L
Mon#	R L	0.06	10^9/L
Eos#	L	0.00	10^9/L
Bas#		0.04	10^9/L
IMG#	R	0.01	10^9/L
Neu%	& R L	40.6	%
Lym%	& R H	47.9	%
Mon%	R	6.8	%
Eos%	L	0.1	%
Bas%	H	4.6	%
IMG%	R	1.2	%
RBC	L	1.43	10^12/L
HGB	L	50	g/L
HCT	L	15.6	%
MCV	H	109.1	fL
MCH	H	35.3	pg
MCHC		323	g/L
RDW-CV		15.8	%
RDW-SD	H	62.6	fL
PLT	L	30	10^9/L
MPV		11.8	fL
PDW	H	18.2	
PCT	L	0.035	%
P-LCC	L	10	10^9/L
P-LCR		33.0	%
NRBC#		0.012	10^9/L
NRBC%		1.24	/100WBC



Alarm

- Pancytopenia
- Blasts?
- Abn Lymph/blast?
- NRBC Present
- Lymphopenia
- Neutropenia
- Leukocytopenia
- Anemia
- Thrombocytopenia

- Decreased trilineage, severe anemia, increased Bas%.
- The particle clusters in the Diff scatter plot were clearly defined, and the Mon particle clusters were distributed in the high-fluorescence region, which were suspected to be blasts.

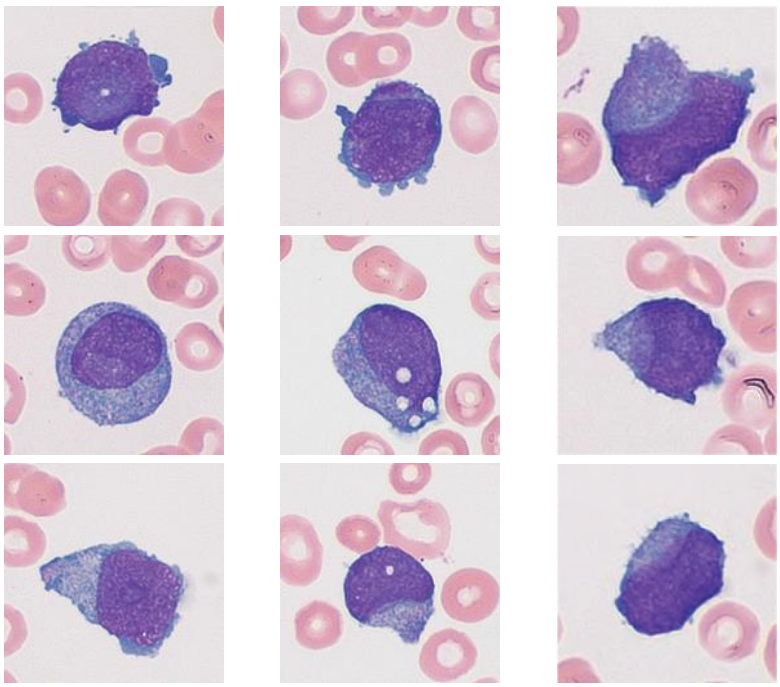
Peripheral blood morphology examination

	White blood cells		
	White blood cells	**200**	**100%**
L	Segmented neutrophils	64	32
	Band neutrophils	6	3.0
	Lymphocytes	53	26.5
L	Monocytes	1	0.5
H	Basophils	4	2.0
!	Metamyelocytes	4	2.0
!	Myelocytes	2	1.0
!	Blasts	66	33.0
	Non-white blood cells	**59**	**%**
!	Nucleated RBCs	2	1.0
	Giant platelets	1	
	Large platelets	7	
	Smudge cells	10	5.0

	Platelets		
	PLT estimate	**Estimated resu**	**Estimation method**
	Platelet concentration	40*10^9/L	Automated
	Platelet concentration	62*10^9/L	Manual

	Red blood cells		
	Size	**Degree**	**%**
!	Anisocytosis	2+	
	Macrocytes	0	1.9
!	Microcytes	2+	13.2
	Color	**Degree**	**%**
!	Hypochromic cells	3+	53.9
	Polychromasia	0	0.5
	Shape	**Degree**	**%**
	Poikilocytosis	0	
	Schistocytes	0	0.8
	Echinocytes	0	0.3
	Elliptocytes	0	0.3
	Ovalocytes	0	14.7
	Stomatocytes	0	0.0
	Target cells	0	0.0
	Teardrop cells	0	1.9

Blasts



Results from manual re-classification

Immature granulocytes accounted for 3% and blasts accounted for 33%; the cell bodies were large and irregular in shape; the cytoplasm was dark blue, and cytoplasm of some cells contained dust-like granules; the chromatins were coarse and granular; 1-2 large and pronounced nucleoli were visible; cup-like blasts were occasionally observed. Pancytopenia, blasts in peripheral blood > 20%, suggesting AML.

Other examinations

Item	Result
Bone marrow	Abnormal granulocytic hyperplasia; granulocytes at all stages of maturation were visible, with myeloblasts accounting for 27%, mainly intermediate and late-stage granulocytes. Monoblasts and promonocytes accounted for 39% and mature monocytes accounted for 6%. MPO (+); NAP (35%, 54 points). Extracellular iron (+), erythroblasts with intracellular iron were rare. Suggested diagnosis: AML-M4b.
Flow cytometry	A group of abnormal myeloid blasts were observed, accounting for 26.04% of the v cells, which was consistent with the AML phenotype
Chromosome	46,XX,t(6:9)(p23;q34.1)
Gene	DEK-CAN positive. FLT3-ITD allelic ratio: 0%. NPM1(-). FLT3-TKD negative

Case analysis

- Acute granulocytic leukemia (M4) is classified into four subtypes (per the classification criteria in China), of which M4b is characterized by the hyperplasia of monoblasts and promonocytes, with myeloblasts and promyelocytes accounting for > 20%.
- The MICM diagnosis of this case was AML with t(6;9) (p23;q34). DEK-NUP214 (also known as CAN) is a unique and relatively rare type of AML, accounting for 0.7% to 1.8% of AML. The translocation t(6;9) (p23;q34) results in the fusion of DEK on chromosome 6 and NUP214 on chromosome 9, forming a nucleoporin fusion protein that acts as an aberrant transcription factor and alters nuclear transport by binding soluble transport factors. The median onset ages in children and adults are 13 and 35 years, respectively. Patients often present with anemia and thrombocytopenia or show full blood count decreased. The prognosis is poor. Morphologically, mature type AML and acute myelomonocytic leukemia are the most common. Auer bodies can be observed in one-third of cases. MPO is positive, while NSE can be either positive or negative. About 44%–62% of patients show increased basophils in the bone marrow and peripheral blood (> 2%) (4.6% in peripheral blood for this case), which is rare in other types of AML. Most patients show granulocytic and erythroid dysplasia, and ring sideroblasts are observed in some patients, but megakaryocytic dysplasia is rare.

Case 05
Thrombotic thrombocytopenic purpura (TTP)

05

Clinical information

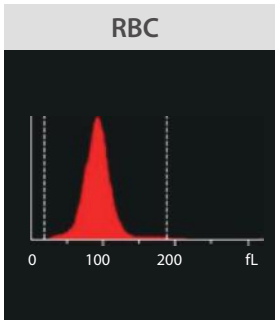
The patient was a 64-year-old male who experienced recurrent chest tightness and dizziness for 20 days, and fever for 5 days. He visited a local hospital and was discharged after the symptoms improved. However, he continued to experience recurrent chest tightness and dizziness after discharge, so he returned to the hospital for further examination 10 days later, and the relevant test results are as follows:

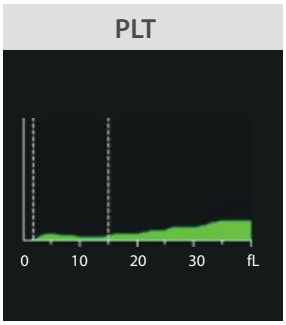
Item	Parameter	Result	Item	Paramet	Result
Chemistry	TBIL	18.9μmol/L	CBC	HGB	73g/L
	DBIL	7.7μmol/L		PLT	26*10^9/L
	IBIL	11.2μmol/L	Bone marrow	Bone marrow	Markedly active bone marrow hyperplasia, increased erythroid proportion, decreased myeloid proportion, and poor megakaryocyte platelet production
	Creatinine	115μmol/L			
	LDH	892U/L			

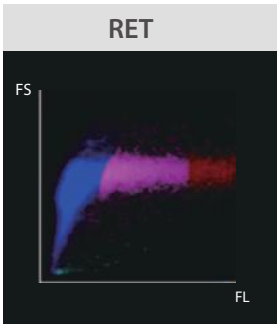
Idiopathic thrombocytopenic purpura was suggested and EVANS syndrome was to be excluded. The patient had poor treatment response and experienced recurrent fever. Ten days later, he presented to the emergency department of our hospital with symptoms of delayed response and decreased calculation ability during the emergency treatment.

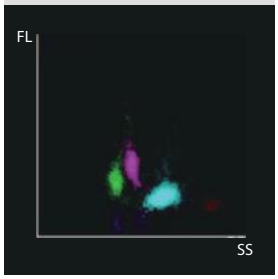
CBC results

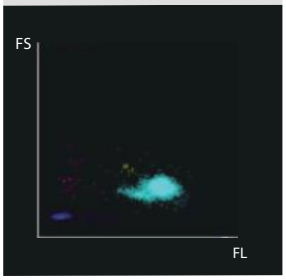
Parameter	Alarm	Result	Unit
WBC	&	8.37	10^9/L
Neu#	& R	6.68	10^9/L
Lym#	&	0.87	10^9/L
Mon#		0.75	10^9/L
Eos#	R	0.05	10^9/L
Bas#	R	0.02	10^9/L
IMG#		0.11	10^9/L
Neu%	& R H	79.7	%
Lym%	& L	10.4	%
Mon%		9.0	%
Eos%	R	0.6	%
Bas%	R	0.3	%
IMG%		1.3	%
RBC	L	2.37	10^12/L
HGB	L	80	g/L
HCT	L	23.5	%
MCV		98.9	fL
MCH		33.8	pg
MCHC		341	g/L
RDW-CV	H	17.2	%
RDW-SD	H	58.2	fL
PLT	& L	5	10^9/L
MPV	R	7.9	fL
PDW	R	15.5	
PCT	R L	0.008	%
P-LCC	R L	1	10^9/L
P-LCR	R	21.9	%
IPF		5.0	%
RET#	R H	0.3752	10^12/L
RET%	R H	15.82	%
IRF	R	22.8	%
LFR	R L	77.2	%
MFR	R	15.5	%
HFR	R H	7.3	%
RHE	R	30.4	pg
NRBC#		0.034	10^9/L
NRBC%		0.41	/100WBC











Alarm

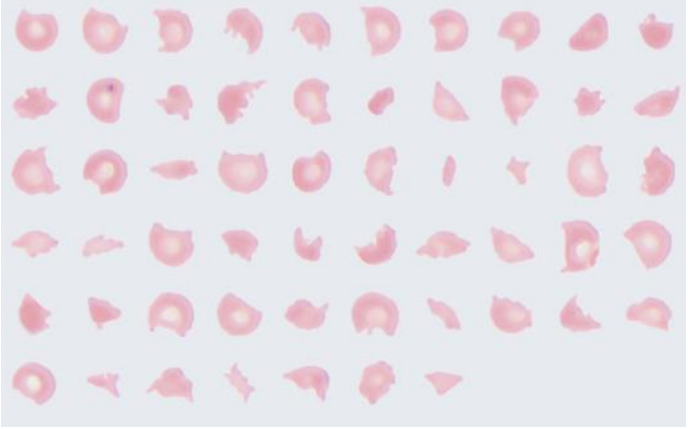
- Immature Gran?
- Fragments?
- RET Scattergram Abn.
- Anemia
- Reticulocytosis
- PLT Histogram Abn
- Thrombocytopenia

- WBCs were generally normal; moderate anemia and extremely low PLT.
- In the RET scattergram, the RBC cluster extended towards the direction of low forward scattered light, even falling below the PLT particles, suggesting the presence of RBC fragments.

Peripheral blood morphology examination

	Red blood cells		
	Size	**Degree**	**%**
!	Anisocytosis	3+	
	Macrocytes	0	0.3
	Microcytes	0	0.6
	Color	**Degree**	**%**
!	Hypochromic cells	3+	25.8
	Polychromasia	0	3.2
	Shape	**Degree**	**%**
!	Poikilocytosis	3+	
!	Schistocytes	3+	9.0
	Echinocytes	0	0.5
	Elliptocytes	0	0.2
	Ovalocytes	0	2.7
	Stomatocytes	0	0.5
	Target cells	0	0.2
	Teardrop cells	0	2.1

Schistocytes



Results from manual re-classification

Schistocytes accounted for 9% and were found as helmet-shaped, triangular, pointed-shaped, etc.

Other examinations

Item	Parameter	Result
Chemistry	TBIL	45.5μmol/L
	DBIL	8.8μmol/L
	IBIL	36.7μmol/L
	Creatinine	106μmol/L
	LDH	1070U/L
ADAMTS13	Activity	<6%
	Titer	<0.6BU

Case analysis

- Due to the failure to diagnose Thrombotic thrombocytopenic purpura (TTP) and initiate corresponding treatment in a timely manner, the patient's condition gradually worsened. The disease progressed from anemia and thrombocytopenia to fever and neurological symptoms, with a gradual decrease in PLT and gradual increases in IBIL and LDH. Finally, idiopathic thrombocytopenic purpura and EVANS syndrome were excluded by the discovery of intravascular hemolysis and schistocytes in peripheral blood morphology examination.
- Patients with Thrombotic thrombocytopenic purpura (TTP) suffer from significant thrombocytopenia and anemia due to loose platelets or fibrin depositing in the numerous small blood vessels, causing damage to passing platelets and RBCs. The decrease in ADAMTS13 activity leads to the accumulation of larger vWF aggregates on endothelial cells, forming many platelet-vWF thrombi that consume platelets, resulting in thrombocytopenia.

Case 06
Chronic myelomonocytic leukemia (CMML)

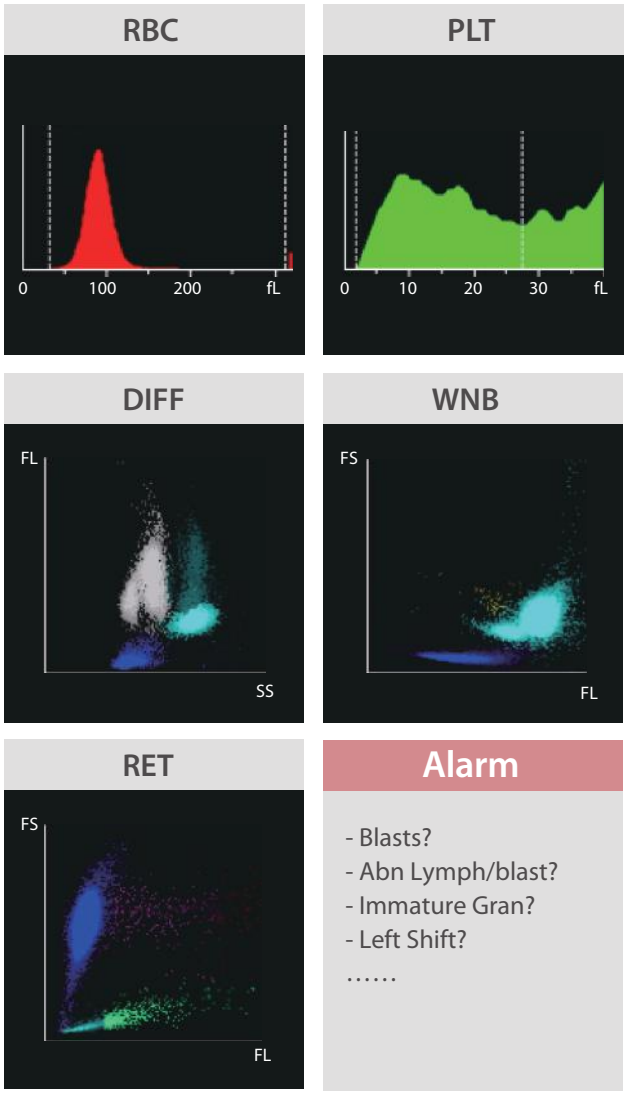
06

Clinical information

The patient was a 56-year-old male who was admitted for treatment on Aug. 14 due to fever and hepatosplenomegaly.

CBC results

Parameter	Alarm		Result	Unit
WBC		H	57.10	10^9/L
Neu#	R	H	21.86	10^9/L
Lym#	R	H	4.91	10^9/L
Mon#	R	H	30.26	10^9/L
Eos#	R	L	0.01	10^9/L
Bas#	R		0.09	10^9/L
IMG#	R		3.54	10^9/L
Neu%	R	L	38.3	%
Lym%	R	L	8.6	%
Mon%	R	H	53.0	%
Eos%	R	L	0.0	%
Bas%	R		0.1	%
IMG%	R		6.2	%
RBC		L	1.85	10^12/L
HGB		L	54	g/L
HCT		L	16.6	%
MCV			89.5	fL
MCH			29.3	pg
MCHC			328	g/L
RDW-CV			16.0	%
RDW-SD			52.9	fL
PLT	&	L	60	10^9/L
MPV	R	H	14.6	fL
PDW	R		16.3	
PCT	R	L	0.064	%
P-LCC	R		37	10^9/L
P-LCR	R	H	61.0	%
IPF		H	37.7	%
RET#		L	0.0175	10^12/L
RET%			0.94	%
IRF		H	31.2	%
LFR		L	68.8	%
MFR		H	25.1	%
HFR		H	6.1	%
RHE			32.1	pg



Alarm

- Blasts?
- Abn Lymph/blast?
- Immature Gran?
- Left Shift?

……

- WBC increased, mainly Mon; Neu#, Lym#, and Mon# increased; severe anemia; PLT decreased; IPF and IRF increased.
- The boundaries of each particle cluster in the Diff scattergram were clear, and particles in the Mon region were significantly dense and extended in the high-fluorescence direction, suggesting the possible presence of myeloblasts and promyelocytes. The Neu particle cluster also extended upwards to a higher region, suggesting the presence of myelocytes and metamyelocytes. Increased IPF and IRF suggested strong hematopoietic function of erythrocyte and platelet.

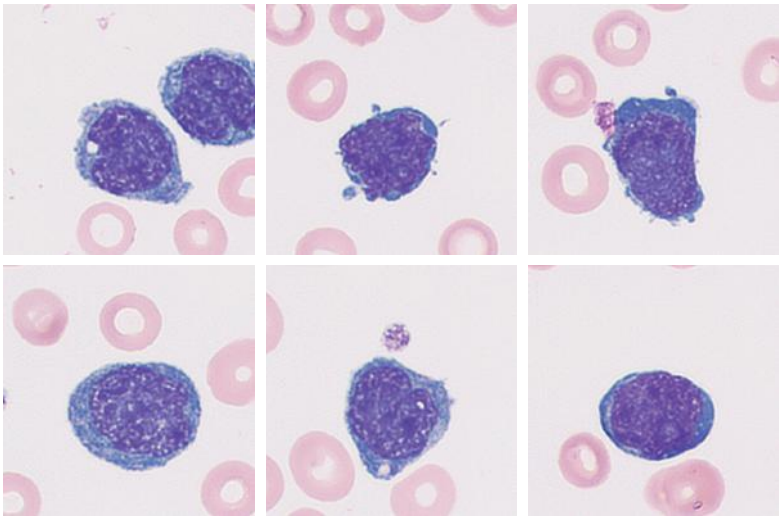
Peripheral blood morphology examination

	White blood cells		
	White blood cells	**205**	**100%**
L	Segmented neutrophils	51	24.9
	Band neutrophils	10	4.9
L	Lymphocytes	16	7.8
	Monocytes	103	50.1
	Metamyelocytes	3	1.5
!	Myelocytes	4	2.0
!	Blasts	3	1.5
!	Reactive lymphocytes	15	7.3
	Non-white blood cells	**70**	**%**
	Giant platelets	1	
	Large platelets	9	
	Smudge cells	58	28.3

	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	54*10^9/L	Automated
	Platelet concentration	66*10^9/L	Manual

	Red blood cells		
	Size	**Degree**	**%**
!	Anisocytosis	2+	
	Macrocytes	0	0.0
	Microcytes	0	0.7
	Color	**Degree**	**%**
!	Hypochromic cells	2+	10.8
	Polychromasia	0	0.1
	Shape	**Degree**	**%**
	Poikilocytosis	0	
	Schistocytes	0	0.2
	Echinocytes	0	0.3
	Elliptocytes	0	0.3
	Ovalocytes	0	4.6
	Stomatocytes	0	0.0
	Target cells	0	0.4
	Teardrop cells	0	0.2

Blasts



Results from manual re-classification

Immature granulocytes accounted for 3.5% and myeloblasts and promyelocytes accounted for 6.3%; some cells had larger cell bodies with scant cytoplasm of blue color; chromatins were fine, and nucleoli were visible; some cells had more cytoplasm with dust-like granules, chromatins were coarse, loose, and reticulate, and the nuclei were twisted and folded.

Bone marrow cytology examination

- Myelocytes and cells in earlier stages were visible, with increased proportion of neutrophilic metamyelocytes; unbalanced nucleus and cytoplasm growth as well as degranulation were observed in some cells; eosinophils were visible.
- Blasts accounted for 2.5%; monocyte percentage was high; premonocytes were visible.
- The morphology suggested chronic myelomonocytic leukemia. Further diagnosis was recommended through flow cytometry and CMML-related genetic testing.

Case analysis

- Chronic myelomonocytic leukemia (CMML) was previously considered a subtype of myelodysplastic syndrome (MDS) due to its myelodysplastic and myeloproliferative characteristics. In 2001, WHO classified CMML as a myelodysplastic/myeloproliferative neoplasm (MDS/MPN).
- According to the FAB classification criteria, CMML with WBC < 13 × 10^9/L is the myelodysplastic subtype (MD-CMML), and CMML with WBC ≥ 13 × 10^9/L is the myeloproliferative subtype (MP-CMML).
- According to the 2016 WHO classification criteria, (i) CMML-0 can be diagnosed if the blasts are < 2% in peripheral blood and/or < 5% in bone marrow; (ii) CMML-1 can be diagnosed if the blasts are 2%–4% in peripheral blood and/or 5%–9% in bone marrow; (iii) CMML-2 can be diagnosed if the blasts are 5%–19% in peripheral blood, 10%–19% in bone marrow, and/or if Auer bodies are present;
- The patient in this case had splenomegaly, markedly increased WBCs in peripheral blood, and increased monocytes. Based on the diagnosis report of bone marrow smear, chronic myelomonocytic leukemia was suspected, and flow cytometry and CMML-related genetic testing were required for further diagnosis.

Case 07
MDS with single lineage dysplasia (MDS-SLD)

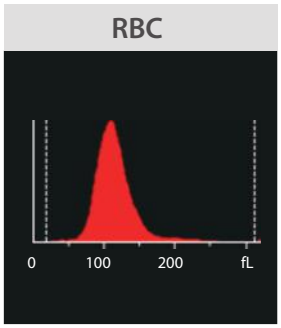
07

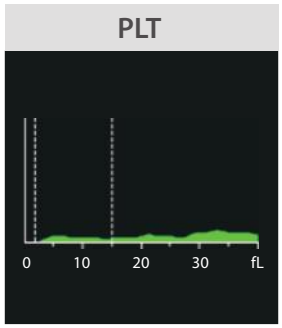
Clinical information

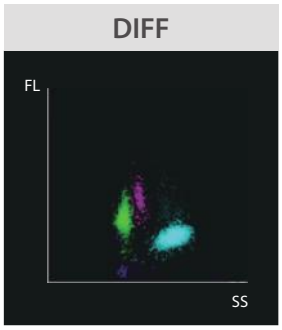
The patient was a 55-year-old female who was admitted with a history of "diagnosed with systemic lupus erythematosus for 16 years and found to have decreased platelets for more than 1 month". She had visited the hospital 1 month ago for systemic lupus erythematosus and was found to have decreased PLT and moderate anemia. RBC and platelet transfusions were given along with danazol therapy. Hemoglobin and platelet levels increased after treatment. The patient refused bone marrow aspiration and insisted on leaving the hospital. She is currently readmitted due to asthenia.

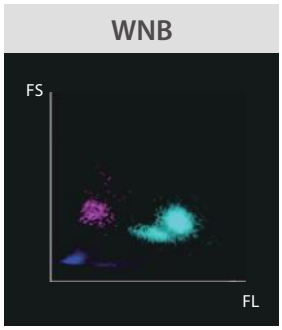
CBC results

Parameter	Alarm			Result	Unit
WBC	&			7.66	10^9/L
Neu#	&	R		5.83	10^9/L
Lym#	&			1.53	10^9/L
Mon#				0.30	10^9/L
Eos#		R	L	0.00	10^9/L
Bas#		R		0.00	10^9/L
IMG#				0.19	10^9/L
Neu%	&	R	H	76.0	%
Lym%	&			20.0	%
Mon%				3.9	%
Eos%		R	L	0.0	%
Bas%		R		0.1	%
IMG%				2.4	%
RBC			L	2.67	10^12/L
HGB			L	96	g/L
HCT			L	30.1	%
MCV			H	112.5	fL
MCH			H	36.1	pg
MCHC				321	g/L
RDW-CV			H	18.4	%
RDW-SD			H	75.2	fL
PLT		R	L	7	10^9/L
MPV		R		8.5	fL
PDW		R		15.0	
PCT		R	L	0.006	%
P-LCC		R	L	1	10^9/L
P-LCR		R		18.9	%
NRBC#				0.302	10^9/L
NRBC%				3.95	/100WBC









Alarm

- Immature Gran?
- NRBC Present
- Anisocytosis
- Macrocytosis
- PLT Histogram Abn.
- Thrombocytopenia

- WBCs were generally normal; macrocytic anemia; extremely low PLT.
- In the WNB scattergram, a large number of pink particles are visible in the NRBC region.

Parameter	1-31	2-1	2-2	2-4	3-1
WBC	3.63	5.68	6.56	6.24	7.66
PLT	7	8	44	33	7
HGB	71	62	77	77	96
RBC	1.93	1.65	2.10	2.16	2.67

Peripheral blood morphology examination

	White blood cells		
	White blood cells	**100**	**100%**
H	Segmented neutrophils	81	81.0
	Band neutrophils	3	3.0
L	Lymphocytes	14	14.0
L	Monocytes	1	1.0
	Metamyelocytes	1	1.0
	Non-white blood cells	**11**	**%**
!	Nucleated RBCs	1	1.0
	Smudge cells	8	8.0
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	13*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
!	Anisocytosis	2+	
!	Macrocytes	3+	30.9
	Microcytes	0	1.3
	Color	**Degree**	**%**
!	Hypochromic cells	2+	12.1
	Polychromasia	0	0.8
	Shape	**Degree**	**%**
!	Poikilocytosis	2+	
	Schistocytes	0	0.6
	Echinocytes	0	0.0
	Elliptocytes	0	0.4
	Ovalocytes	0	13.9
!	Stomatocytes	2+	6.4
	Target cells	0	3.2
	Teardrop cells	0	1.4

Results from manual re-classification

The WBC classification results and PLT estimate were consistent with the CBC results, with increased stomatocytes.

Bone marrow cytology examination

- Markedly active bone marrow hyperplasia, G/E = 0.89/1.
- Granulocytic hyperplasia was fair, mainly intermediate and late-stage granulocytes with visible eosinophiles.
- Active erythroid hyperplasia, mainly polychromatic normoblasts and orthochromatic normoblasts, with mild size variation of mature red blood cells.
- No megakaryocytes were observed on the slide and few platelets were found.
- The myelogram showed marked hyperplasia, with an inverted M/E ratio; no megakaryocytes and few platelets were observed.

Case analysis

The preliminary diagnosis of this case was MDS with single lineage dysplasia (MDS-SLD).

According to the WHO's revised classification of MDS (4th edition, 2016), the conventional karyotyping of MDS-SLD is as follows: any karyotype that does not meet the standard of MDS with isolated del(5q), and dysplasia is often predominant in 1 lineage, with dysplasia of 1–2 lineages in the CBC.

Additionally, the presence of increased stomatocytes in this case is often observed in hereditary stomatocytosis, disseminated intravascular coagulation, liver disease, systemic lupus erythematosus, alcohol poisoning, glutathione deficiency, hereditary spherocytosis, thalassemia minor, etc. Due to their poor deformability, stomatocytes are often retained in the splenic sinuses. In the acidic environment of the splenic sinus, the destruction of RBCs is more than three times greater in the spleen than in other sites due to the lack of glucose, reduced available ATP, and further increased cellular permeability to sodium.

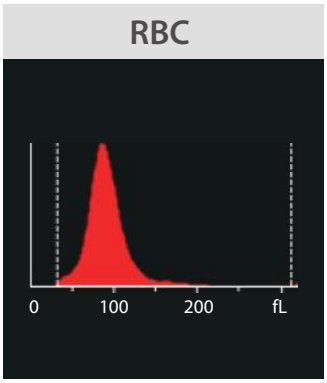
Case 08
MDS with excess blasts (MDS-EB)

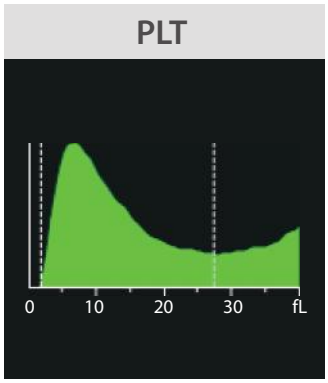
Clinical information

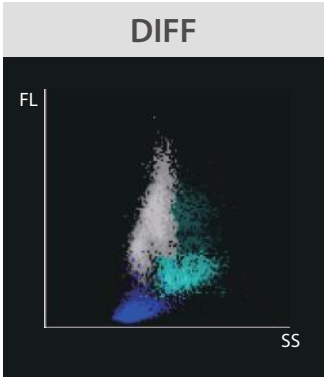
The patient, an 80-year-old female, was admitted to the hospital in early August with dizziness and anemia.

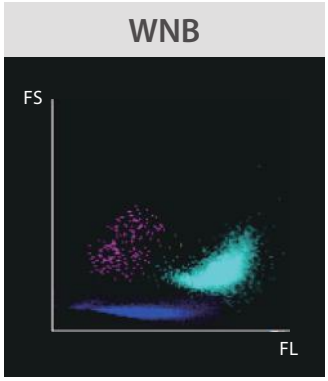
CBC results

Parameter	Alarm			Result	Unit
WBC	&		H	13.04	10^9/L
Neu#	&	R		5.05	10^9/L
Lym#		R		2.35	10^9/L
Mon#		R		5.62	10^9/L
Eos#		R	L	0.01	10^9/L
Bas#		R		0.01	10^9/L
IMG#		R		1.20	10^9/L
Neu%	&	R	L	38.7	%
Lym%		R	L	18.0	%
Mon%		R	H	43.1	%
Eos%		R	L	0.1	%
Bas%		R		0.1	%
IMG%		R		9.2	%
RBC			L	2.63	10^12/L
HGB			L	75	g/L
HCT			L	23.4	%
MCV				88.9	fL
MCH				28.4	pg
MCHC				320	g/L
RDW-CV			H	19.0	%
RDW-SD			H	61.9	fL
PLT		R		292	10^9/L
MPV		R		12.0	fL
PDW		R		16.9	
PCT		R	H	0.352	%
P-LCC		R	H	125	10^9/L
P-LCR		R		42.8	%
NRBC#				0.261	10^9/L
NRBC%				2.00	/100WBC









Alarm

- Blasts?
- Abn Lymph/blast?
- Immature Gran?
- Atypical Lymph?

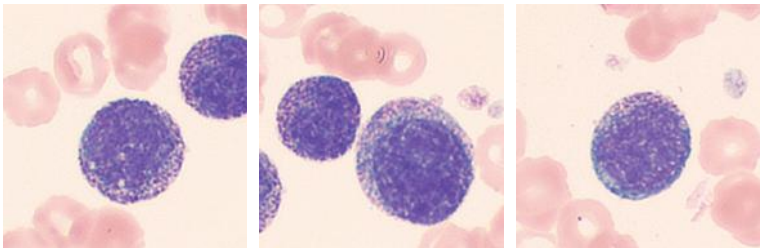
……

- WBC was not low, Mon% increased, moderate anemia, normal PLT.
- The presence of grayish-white particles in the DIFF scattergram was mainly due to the extension of the Neu cluster towards the upper left corner. Dense particles in the Mon region led to ill-defined boundaries between Lym and Mon particle clusters, suggesting the possible presence of immature granulocytes, especially promyelocytes and blasts. The PLT histogram showed raised tail. Large platelets or interference from red blood cell fragments and microcytes should be ruled out.

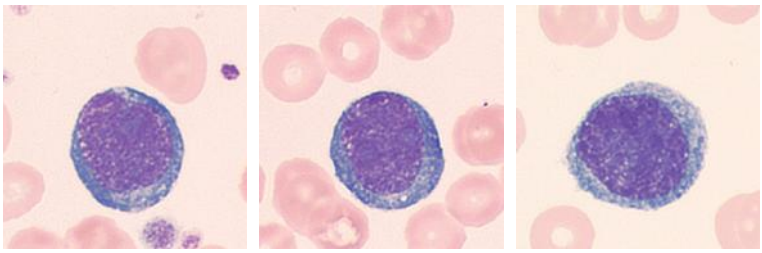
Peripheral blood morphology examination

	White blood cells		
	White blood cells	**201**	**100%**
L	Segmented neutrophils	39	19.4
	Band neutrophils	12	6.0
L	Lymphocytes	39	19.4
H	Monocytes	31	15.4
!	Metamyelocytes	12	6.0
!	Myelocytes	15	7.5
!	Promyelocytes	4	2.0
!	Blasts	40	19.8
	Reactive lymphocytes	9	4.5
	Non-white blood cells	**78**	**%**
!	Nucleated RBCs	8	4.0
	Giant platelets	9	
	Large platelets	7	
	Smudge cells	43	21.4
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	241*10^9/L	Automated
	Platelet concentration	268*10^9/L	Manual

Promyelocytes



Myeloblasts



Results from manual re-classification

Immature granulocytes accounted for 16.9%, of which promyelocytes accounted for 3.4%, with large, round or oval cell bodies; nuclei were deviated to one side; chromatins were coarser than those of blasts; nucleoli were starting to close, and were less prominent than those of blasts; cytoplasm was blue, containing varying numbers of purple-red granules with different morphology and uneven distribution. Myeloblasts and promyelocytes accounted for 18.4%, with large oval cell bodies and blue cytoplasm without granules; chromatins were fine; 2–3 nucleoli could be seen.

The PLT estimate was consistent with CBC, and giant platelets were observed.

Bone marrow cytology examination

- Active nucleated cell hyperplasia in bone marrow. Myeloids accounted for 54.5% and erythroids for 4%, with M:E ratio being 13.63:1.
- Myeloids: Promyelocytes and cells in earlier stages were observed, with a higher proportion of metamyelocytes and segmented neutrophils. Some myeloids exhibited unbalanced nucleus and cytoplasm development as well as degranulation.
- Erythroids: Mainly polychromatic normoblasts and orthochromatic normoblasts, with low proportions of cells at each developmental stage. Erythroblast morphology was generally normal. Mature RBCs varied in sizes.
- One megakaryocyte and small platelet clumps were observed on the slide.
- Blasts accounted for 17%, with medium-sized cell bodies, fine chromatins, and visible nucleoli; cytoplasm was blue and the amount was fair.
- The morphology was consistent with myelodysplastic syndrome with excess blasts (MDS-EB-2). Further diagnosis is recommended by flow cytometry analysis.

Case analysis

MDS with excess blasts (MDS-EB) can be divided into 2 subtypes:

Type	Dysplasia	Cytopenia	Ring sideroblasts	Blasts in bone marrow and peripheral blood	Conventional karyotyping
MDS-EB1	0–3 lineages	1–3 lineages	Any ratio	5%–9% in bone marrow or 2%–4% in peripheral blood, without Auer bodies	Any karyotype
MDS-EB2	0–3 lineages	1–3 lineages	Any ratio	10%–19% in bone marrow or 5%–19% in peripheral blood or with Auer bodies	Any karyotype

MDS-EB has a higher risk of AML transformation compared with other subtypes, and MDS-EB with excess blasts generally has a poorer prognosis. Treatment options include bone marrow transplantation or demethylation therapy. However, in this case, the patient was elderly, and interventions aimed at improving individual disease resistance and slowing dysplasia.

Case 09
Multiple myeloma (MM)

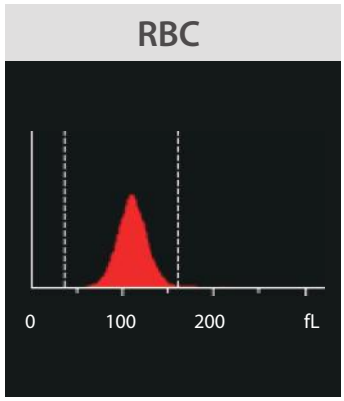
09

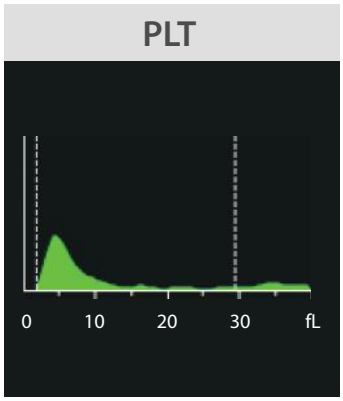
Clinical information

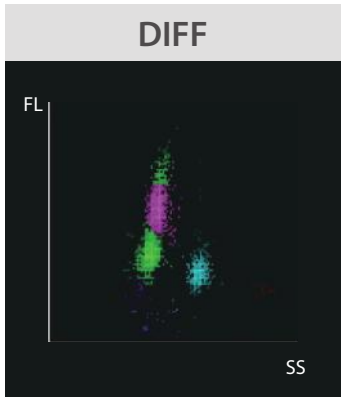
The patient was a 64-year-old male who was admitted to the emergency room due to severe anemia and lumbar vertebral fracture.

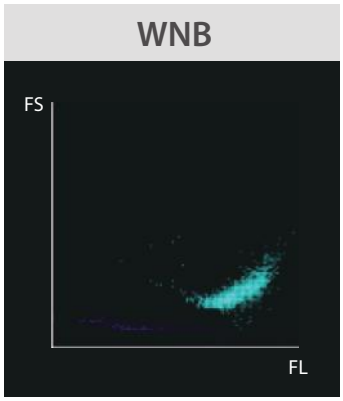
CBC results

Parameter	Alarm		Result	Unit
WBC		L	3.51	10^9/L
Neu#	R	L	0.86	10^9/L
Lym#	R		1.58	10^9/L
Mon#	R		1.06	10^9/L
Eos#		L	0.01	10^9/L
Bas#			0.00	10^9/L
IMG#	R		0.01	10^9/L
Neu%	R	L	24.4	%
Lym%	R	H	44.9	%
Mon%	R	H	30.2	%
Eos%		L	0.4	%
Bas%			0.1	%
IMG%	R		0.4	%
RBC		L	1.22	10^12/L
HGB		L	47	g/L
HCT		L	13.8	%
MCV		H	112.6	fL
MCH		H	38.4	pg
MCHC			341	g/L
RDW-CV			15.6	%
RDW-SD		H	63.7	fL
PLT		L	24	10^9/L
MPV			9.3	fL
PDW		H	18.9	
PCT		L	0.022	%
P-LCC		L	5	10^9/L
P-LCR			21.1	%
NRBC#			0.000	10^9/L
NRBC%			0.00	/100WBC









Alarm

- Pancytopenia
- Blasts?
- Abn Lymph/blast?
- Atypical Lymph?

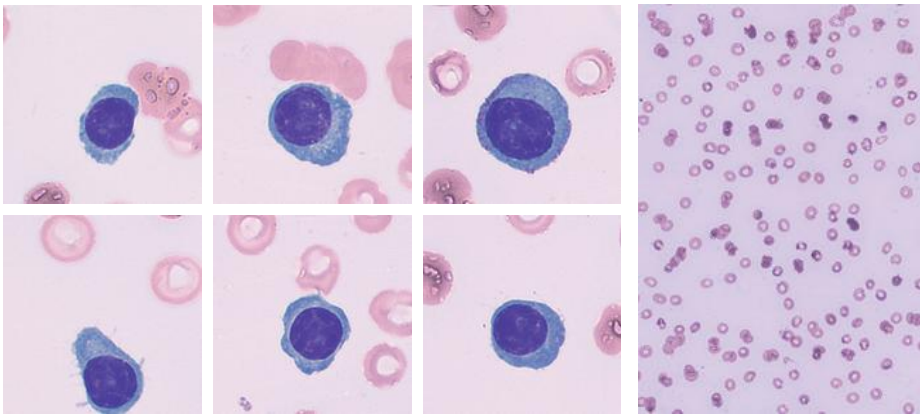
……

- Slightly decreased WBC, decreased Neu; severe anemia and MCV was not small; extremely low PLT.
- Due to the decreased RBC/PLT, the area under the histogram was significantly reduced. Abnormal distribution of Lym and Mon particle clusters was observed in the DIFF scattergram, with Lym particles extending towards the upper right and Mon particles distributed in the high-fluorescence region, shifting to the right. Above Mon, some particles were identified as abnormal lymphocytes and blasts. The scattergram of this patient was overall similar to that of lymphocytic leukemia.

Peripheral blood morphology examination

	White blood cells		
	White blood cells	**113**	**100%**
L	Segmented neutrophils	17	15.0
	Band neutrophils	5	4.4
H	Lymphocytes	46	40.7
L	Monocytes	2	1.8
	Reactive lymphocytes	1	0.9
!	Plasma cells	42	37.2
	Non-white blood cells	**29**	**%**
	Smudge cells	17	15.0
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	12*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
	Anisocytosis	0	
	Macrocytes	0	3.7
!	Microcytes	2+	11.9
	Color	**Degree**	**%**
!	Hypochromic cells	3+	44.1
	Polychromasia	0	0.9
	Shape	**Degree**	**%**
!	Poikilocytosis	2+	
!	Schistocytes	2+	1.0
	Echinocytes	0	0.8
	Elliptocytes	0	0.3
!	Ovalocytes	2+	11.8
	Stomatocytses	0	0.0
	Target cells	0	0.4
	Teardrop cells	0	0.3

Plasma cells



Results from manual re-classification

The classification results of Neutrophils and lymphocytes were consistent with the CBC results. Few Monocytes and a large number of plasma cells were observed under microscopy. The nuclei of the plasma cells were often round and eccentric, with chromatins agglutinated into large blocks and no nucleolus visible, and the cytoplasm was deep blue and appeared foamy. Rouleaux RBCs were also observed.

Other examinations

Item	Result	Reference range
Rheumatoid factor	<20	0-20(IU/ml)
Anti-streptolysin "O"	<25	0-100(IU/ml)
C-reactive protein	4.45	0-8(mg/L)
Immunoglobulin A	41	0.7-4.0(g/L)
Immunoglobulin G	4.76	7-16(g/L)
Immunoglobulin M	0.18	0.4-2.3(g/L)
κ light chain	512	6.7-22.4(mg/L)
λ light chain	13.4	8.3-27.0(mg/L)
κ light chain/λ light chain	38.209	0.31-1.56
Immunophenotype electrophoresis	IgA-Kappa lambda monoclonal band	Negative
Total protein	99.5	65-85(g/L)
Albumin	28	40-55(g/L)
Globulin	71.5	20-40(g/L)
A/G ratio	0.39	1.2-2.4
Blood urea nitrogen	17.3	2.8-7.14mmol/L
Creatinine	174.78	40-135μmol/L

Case analysis

- The patient was diagnosed with multiple myeloma IgA-Kappa type.
- Multiple myeloma (MM) is a malignant disease characterized by clonal proliferation of plasma cells. It is more common in middle-aged and elderly population. With the aging of the Chinese population, the incidence of MM is increasing. Due to the massive secretion and deposition of monoclonal antibodies on the bone marrow stroma, osteoclasts are activated, leading to bone disease and hypercalcemia. Moreover, the malignant proliferation of plasma cells inhibits normal hematopoiesis, leading to anemia. The large amount of globulin also results in renal insufficiency. Therefore, the acronym CRAB, which stands for the first letter of the four main symptoms, is used as an alternative name for MM, commonly known as "crab disease".
- Patients with MM are prone to rouleaux formation of RBCs due to the increased fibrinogen and globulin in the blood, which shield the surface potential of RBCs and weaken the mutual repulsion between RBCs. If rouleaux RBCs are observed, attention must be paid to abnormal lymphocyte screening and protein electrophoresis assay to avoid the missed diagnosis of MM.

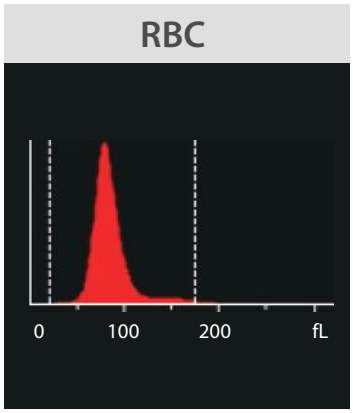
Case 10
B-cell lymphoblastic leukemia (B-ALL)

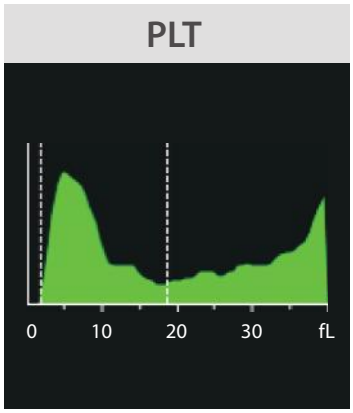
Clinical information

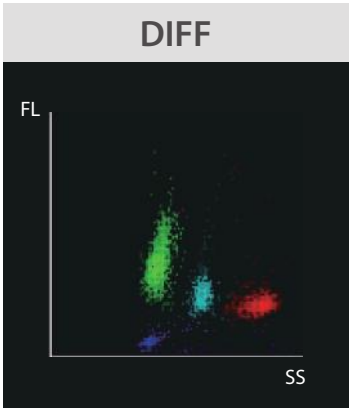
The patient was a 7-year-old male who was admitted to the hospital due to intermittent back pain for more than two months, along with chest pain and pain in both lower limbs for over a month. Abdominal ultrasound showed splenomegaly.

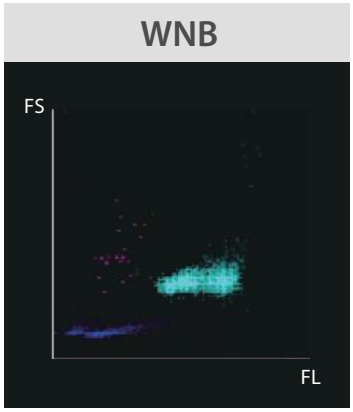
CBC results

Parameter	Alarm			Result	Unit
WBC		&		6.09	10^9/L
Neu#	&	R	L	0.88	10^9/L
Lym#	&	R		3.50	10^9/L
Mon#		R	L	0.00	10^9/L
Eos#			H	1.71	10^9/L
Bas#				0.00	10^9/L
IMG#		R		0.09	10^9/L
Neu%	&	R	L	14.5	%
Lym%	&	R		57.3	%
Mon%		R	L	0.1	%
Eos%			H	28.1	%
Bas%				0.0	%
IMG%		R		1.5	%
RBC				3.86	10^12/L
HGB			L	107	g/L
HCT			L	32.6	%
MCV				84.4	fL
MCH				27.7	pg
MCHC				328	g/L
RDW-CV				15.3	%
RDW-SD				45.5	fL
PLT			L	57	10^9/L
MPV				8.0	fL
PDW				16.0	
PCT			L	0.046	%
P-LCC			L	11	10^9/L
P-LCR				18.8	%
NRBC#				0.039	10^9/L
NRBC%				0.64	/100WBC









Alarm

- Blasts?
- Abn Lymph/blast?
- Immature Gran?

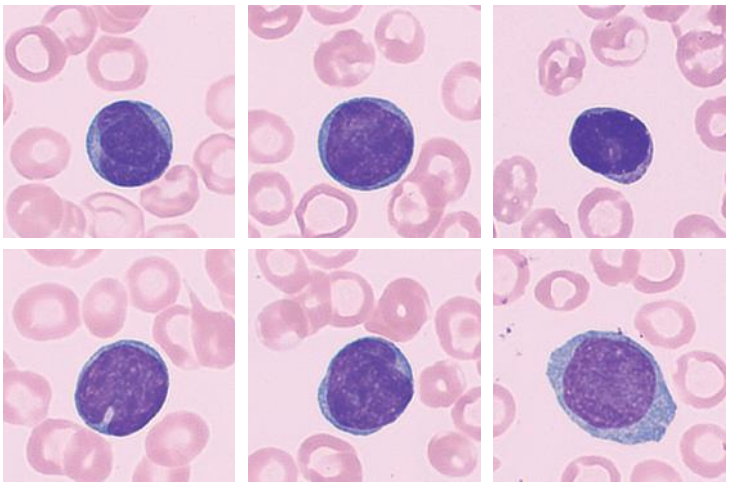
……

- WBC was not low; Neu and Mon decreased; Eos increased; moderate anemia; PLT decreased.
- In the PLT histogram, the tail of the plot was elevated and in a serration pattern; interference from large platelets, platelet aggregation, or RBC fragments should be ruled out by microscopy. In the DIFF scattergram, the Eos particles was significantly dense and Lym particle cluster extended to the high-fluorescence region. Abnormal cells were suspected.

Peripheral blood morphology examination

	White blood cells		
	White blood cells	**110**	**100%**
L	Segmented neutrophils	7	6.4
	Band neutrophils	7	6.4
	Lymphocytes	46	41.8
L	Monocytes	1	0.9
H	Eosinophils	18	16.4
	Metamyelocytes	2	1.8
!	Myelocytes	3	2.7
!	Blasts	24	21.8
!	Abnormal lymphocyte	2	1.8
	Non-white blood cells	**76**	**%**
	Smudge cells	10	9.1
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	58*10^9/L	Automated
	Platelet concentration	51*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
	Anisocytosis	0	
	Macrocytes	0	0.8
!	Microcytes	3+	21.3
	Color	**Degree**	**%**
!	Hypochromic cells	3+	82.1
	Polychromasia	0	0.3
	Shape	**Degree**	**%**
!	Poikilocytosis	3+	
!	Schistocytes	3+	2.9
	Echinocytes	0	0.3
	Elliptocytes	0	1.3
!	Ovalocytes	2+	13.7
	Stomatocytes	0	0.0
!	Target cells	2+	5.1
	Teardrop cells	0	0.7

Blasts



Results from manual re-classification

Immature granulocytes accounted for 4.5%; myeloblasts and promyelocytes accounted for 23.6%. Myeloblasts and promyelocytes had round or oval cell bodies, round or oval nuclei, and fine chromatins; cuts marks were visible; cytoplasm was scant and in blue color. The PLT estimate was consistent with the CBC result. Schistocytes were observed.

Other examinations

Item	Result
Flow cytometry	Abnormal naive B cells accounted for 97.60% of nucleated cells, expressing CD19, CD22, cCD79a, CD34, CD10, cTdT, CD58, and not expressing CD33, CD15, CD13, CD38, CD81, CD20, CD7, cMPO, cCD3, CD117, CD56, cIgM, or CD66c. Immunophenotyping suggested B cell acute lymphoblastic leukemia, with high probability of Common B-ALL
Bone marrow cytology	Lymphocytes accounted for 97.5%, of which myeloblasts and promyelocytes accounted for 97%. Cytochemical staining results: POX (-), AS-DCE (-), a-NAE (+), a-NAF (no inhibition), a-NBE (-), PAS (+). Suggested diagnosis: ALL
Fusion gene	Negative, no large deletion of IKZF1 gene was observed, and ph-like gene rearrangement was negative.
Chromosomal examination	Chromosome karyotyping showed 46, XY(3)

Case analysis

This patient was diagnosed with B-cell acute lymphoblastic leukemia (B-ALL).

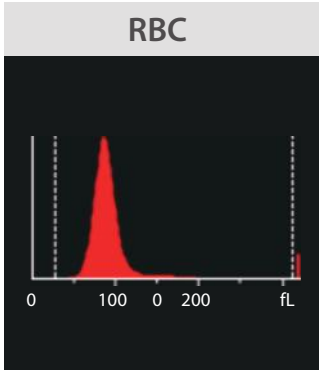
Case 11
B-cell lymphoblastic leukemia (B-ALL)

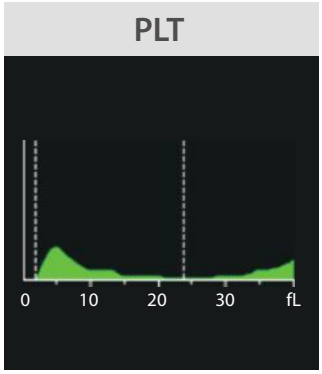
Clinical information

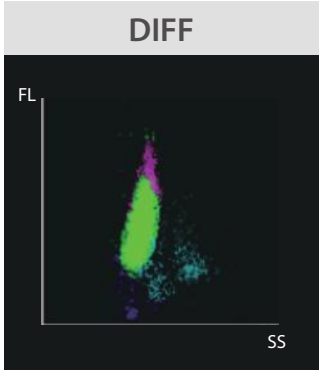
The patient was a 48-year-old female who experienced with flatulent dyspnea and low-grade fever with no obvious cause more than 10 days ago. The patient was alert and oriented with no skin or mucous membrane bleeding. No enlargement of superficial lymph nodes, liver, or spleen was observed.

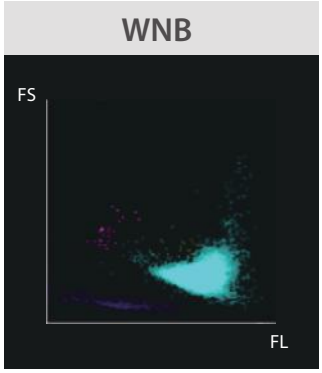
CBC results

Parameter	Alarm			Result	Unit
WBC	&		H	83.29	10^9/L
Neu#	&	R	L	0.98	10^9/L
Lym#	&	R	H	81.62	10^9/L
Mon#		R		0.66	10^9/L
Eos#		R	L	0.01	10^9/L
Bas#		R		0.02	10^9/L
IMG#		R		0.11	10^9/L
Neu%	&	R	L	1.2	%
Lym%	&	R	H	98.0	%
Mon%		R	L	0.8	%
Eos%		R	L	0.0	%
Bas%		R		0.0	%
IMG%		R		0.1	%
RBC			L	2.23	10^12/L
HGB			L	65	g/L
HCT			L	19.5	%
MCV				87.8	fL
MCH				29.1	pg
MCHC				331	g/L
RDW-CV				13.6	%
RDW-SD				43.5	fL
PLT			L	15	10^9/L
MPV				9.0	fL
PDW				17.0	
PCT			L	0.013	%
P-LCC			L	3	10^9/L
P-LCR				23.3	%
NRBC#				0.036	10^9/L
NRBC%				0.04	/100WBC









Alarm

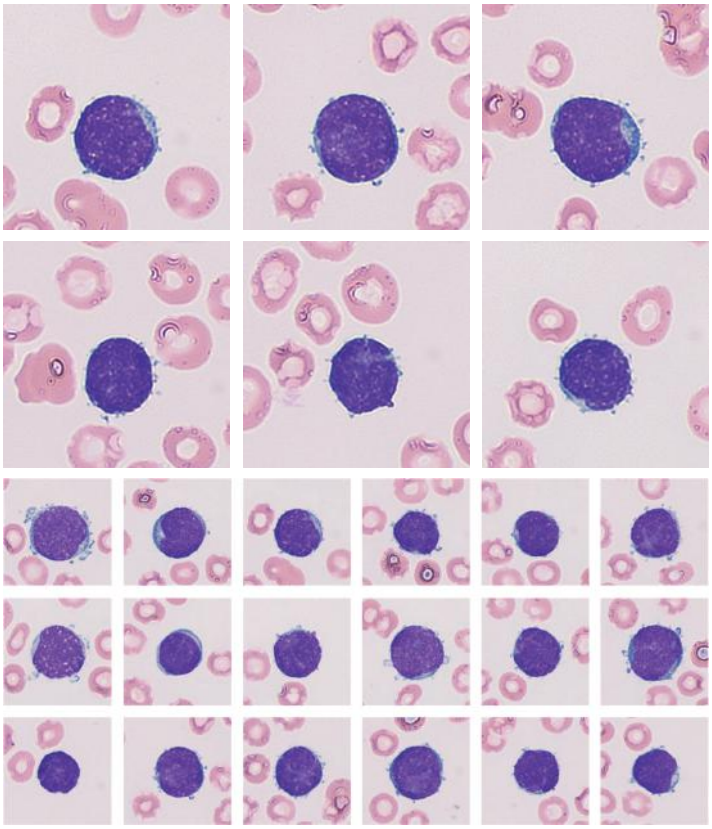
- Abn. WBC scattergram
- Abn Lymph/blast?
- Immature Gran?
- Lymphocytosis
- Neutropenia
- Leukocytosis
- Anemia
- Thrombocytopenia

- WBC increased, predominantly Lym; moderate anemia; extremely low PLT.
- In the DIFF scattergram, Lym particles extended towards the high-fluorescence region, appearing as comet-shaped clusters; neu particles were significantly decreased.

Peripheral blood morphology examination

	White blood cells		
	White blood cells	**201**	**100%**
L	Segmented neutrophils	1	0.5
	Band neutrophils	1	0.5
	Lymphocytes	49	24.4
!	Blasts	150	74.6
	Non-white blood cells	**47**	**%**
	Nucleated RBCs	1	0.5
	Smudge cells	43	21.4
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	55*10^9/L	Automated
	Platelet concentration	76*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
!	Anisocytosis	3+	
	Macrocytes	0	0.3
!	Microcytes	3+	50.2
	Color	**Degree**	**%**
!	Hypochromic cells	3+	71.3
	Polychromasia	0	0.5
	Shape	**Degree**	**%**
!	Poikilocytosis	1+	
!	Schistocytes	1+	1.9
	Echinocytes	0	1.4
	Elliptocytes	0	0.2
	Ovalocytes	0	11.9
	Stomatocytes	0	0.0
	Target cells	0	0.0
	Teardrop cells	0	0.9

Myeloblasts and promyelocytes



Results from manual re-classification

Blasts accounted for 74.6%, with variable cell sizes, scant cytoplasm, verrucous protrusions, round or oval nuclei, fine chromatins, and visible nucleoli.

Other examinations

Item	Result
Bone marrow cytology	Abnormal lymphocyte proliferation, prolymohocytes accounted for 93.5%, and mature lymphocytes accounted for 5.5%. Suggested diagnosis: ALL
Flow cytometry	Abnormal B lymphoblasts accounted for 92% of nucleated cells (Common B-ALL)
Gene	BCR-ABL (p190) positive
Chromosomal examination	46,XX,t(9;22)(q34;q11.2)

Case analysis

- The diagnosis of this case was B-ALL with t(9;22)(q34;q11.2); BCR-ABL1. This is a subtype with poor prognosis, but the prognosis of Ph+ ALL has gradually improved in recent years with the use of tyrosine kinase inhibitors.
- The DIFF scattergram of the two B-ALL cases are very similar, with Lym particles forming comet-shaped clusters extending towards the upper right, and the left edge of the clusters not showing the rightward concave observed in the AML case. Therefore, when similar scattergram are seen in practice, it is important to watch for abnormal lymphocytes.

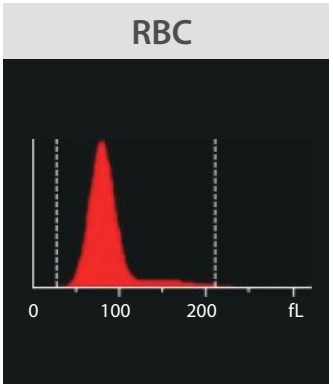
Case 12
Chronic Lymophocytic leukemia (CLL)

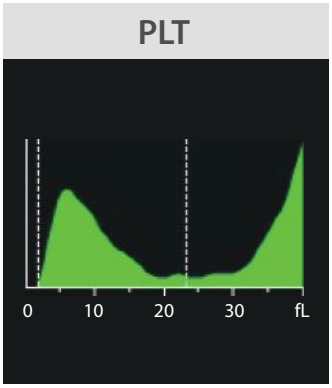
Clinical information

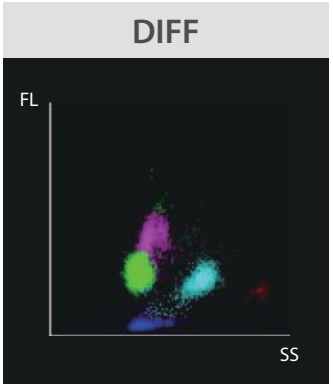
The patient was a 64-year-old female who had been diagnosed with chronic lymphocytic leukemia more than 2 years ago. Considering the patient had no indication for treatment, CBC and blood smear examination were regularly conducted at the Department of Hematology. The results showed fluctuations in WBCs ranging from 78–160 × 10^9/L and lymphocytes ranging from 75–154 × 10^9/L.

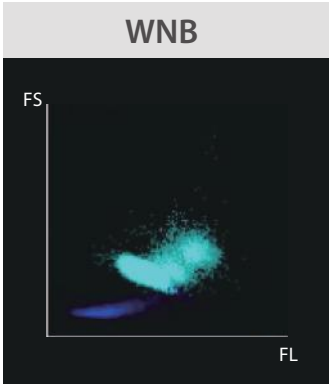
CBC results

Parameter	Alarm		Result	Unit
WBC		H	131.45	10^9/L
Neu#	R		4.18	10^9/L
Lym#	R	H	125.25	10^9/L
Mon#	R	H	1.94	10^9/L
Eos#	R		0.07	10^9/L
Bas#	R		0.01	10^9/L
IMG#	R		0.10	10^9/L
Neu%	R	L	3.2	%
Lym%	R	H	95.2	%
Mon%	R	L	1.5	%
Eos%	R	L	0.1	%
Bas%	R		0.0	%
IMG%	R		0.1	%
RBC			4.89	10^12/L
HGB			131	g/L
HCT		L	39.9	%
MCV			81.7	fL
MCH		L	26.7	pg
MCHC			327	g/L
RDW-CV		H	18.1	%
RDW-SD			53.4	fL
PLT	R		134	10^9/L
MPV	R		9.6	fL
PDW	R		15.7	
PCT	R		0.129	%
P-LCC	R		34	10^9/L
P-LCR	R		25.6	%
NRBC#			0.000	10^9/L
NRBC%			0.00	/100WBC









Alarm

- Abn. WBC scattergram
- Abn Lymph/blast?
- Immature Gran?
- Monocytosis

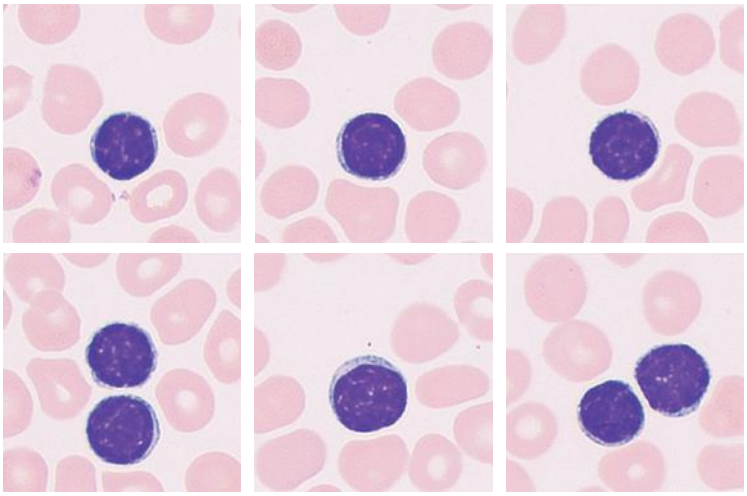
……

- WBC increased, predominantly Lymphocytes, and Monocytes also increased; RBC and PLT were roughly normal.
- In the DIFF scattergram, the Lym region was significantly dense and some particles extended towards the high-fluorescence region. These particles were classified as Mon by the software. Blood smear re-check was required to confirm whether they were abnormal cells.

Peripheral blood morphology examination

	White blood cells		
	White blood cells	**300**	**100%**
L	Segmented neutrophils	6	2.0
	Band neutrophils	1	0.3
H	Lymphocytes	287	95.7
L	Monocytes	2	0.7
!	Blasts	4	1.3
	Non-white blood cells	**93**	**%**
	Large platelets	7	
	Smudge cells	83	27.7
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	158*10^9/L	Automated
	Platelet concentration	183*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
	Anisocytosis	0	
	Macrocytes	0	0.5
!	Microcytes	2+	11.6
	Color	**Degree**	**%**
!	Hypochromic cells	3+	20.1
	Polychromasia	0	0.1
	Shape	**Degree**	**%**
!	Poikilocytosis	1+	
!	Schistocytes	1+	0.9
	Echinocytes	0	2.1
	Elliptocytes	0	4.0
	Ovalocytes	0	15.6
	Stomatocytes	0	0.0
	Target cells	0	0.0
	Teardrop cells	0	0.4

Lymphocytes



Results from manual re-classification

Mature lymphocytes accounted for 97%, with small round cell bodies and scant cytoplasm; the nuclei were round with agglutinated chromatins.

Case analysis

- Chronic lymphocytic leukemia (CLL) is a mature B lymphocyte clonal proliferative tumor. Patients have monoclonal B lymphocytes ≥ 5 × 10^9/L in peripheral blood, and leukemic cell morphology shows mature-appearing small lymphocytes, with occasional naive lymphocytes and a small number of immature or atypical lymphocytes. Neutrophil percentage is decreased, and thrombocytopenia and/or anemia may occur as the disease progresses. Smudge cells are easily seen in peripheral blood.
- The course of the disease is slow, and treatment is usually not necessary. Follow-up should be conducted every 2–6 months. However, treatment can begin if any of the following conditions occur:

1. Evidence of progressive bone marrow failure: manifested as progressive reduction in hemoglobin and/or platelets, with hemoglobin less than 100 g/L and platelets less than 100 × 10^9/L.
2. Massive splenomegaly (e.g., > 6 cm below left costal margin) or progressive or symptomatic splenomegaly.
3. Massive lymphodenopathy (e.g., longest diameter > 10 cm) or progressive or symptomatic lymphodenopathy.
4. Naive lymphocytes ≥ 30 × 10^9/L, with progressive lymphocytosis, e.g., an increase of 50% within 2 months, or lymphocyte doubling time (LDT) < 6 months. When the naive lymphocytes are < 30 × 10^9/L, LDT cannot be used as the only treatment indication, and other conditions that can cause lymphocytosis, such as infection or steroid use, should be ruled out.
5. Autoimmune hemolytic anemia and/or thrombocytopenia that do not respond well to corticosteroids or other standard of care.
6. Symptomatic or functionally impairing extranodal lesions (skin, kidney, lung, spine, etc.), especially when symptoms cannot be resolved with symptomatic treatment.
7. Presence of at least one of the following disease-related symptoms.

❶ Weight loss of ≥ 10% for no apparent reason in the past 6 months.

❷ Severe fatigue (e.g., ECOG performance status ≥ 2; unable to carry out daily activities).

❸ Body temperature > 38.0°C with no evidence of infection, lasting for more than 2 weeks.

❹ Night sweats with no evidence of infection, lasting for more than 1 month.

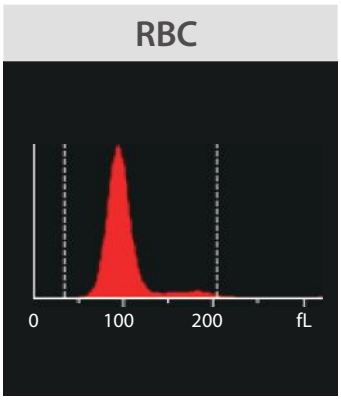
Case 13
Mantle cell lymphoma (MCL)

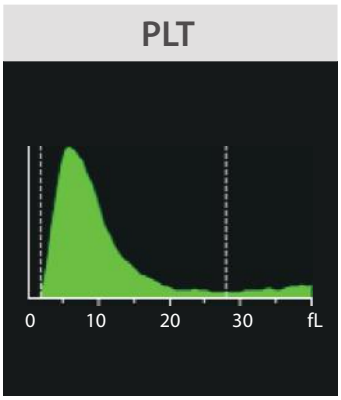
Clinical information

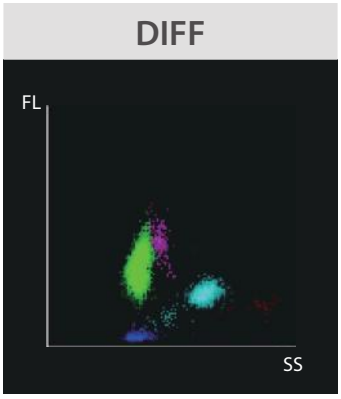
The patient was a 60-year-old male who had been experiencing left knee joint pain and limited mobility for over 2 years, which worsened over the past 3 months. There was mild deformity in the left knee joint, and the patient was admitted to the hospital for "left knee osteoarthritis".

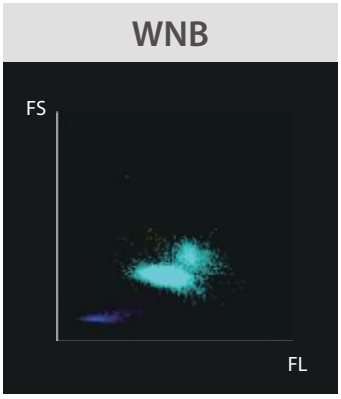
CBC results

Parameter	Alarm		Result	Unit
WBC		H	15.06	10^9/L
Neu#	R	L	1.94	10^9/L
Lym#	R	H	12.77	10^9/L
Mon#	R		0.29	10^9/L
Eos#			0.04	10^9/L
Bas#			0.02	10^9/L
IMG#	R		0.00	10^9/L
Neu%	R	L	12.9	%
Lym%	R	H	84.9	%
Mon%	R	L	1.9	%
Eos%		L	0.2	%
Bas%			0.1	%
IMG%	R		0.0	%
RBC			5.17	10^12/L
HGB			159	g/L
HCT			46.5	%
MCV			89.9	fL
MCH			30.8	pg
MCHC			342	g/L
RDW-CV			12.8	%
RDW-SD			44.6	fL
PLT			125	10^9/L
MPV			9.4	fL
PDW			15.9	
PCT			0.117	%
P-LCC		L	26	10^9/L
P-LCR			21.2	%
NRBC#			0.000	10^9/L
NRBC%			0.00	/100WBC









Alarm

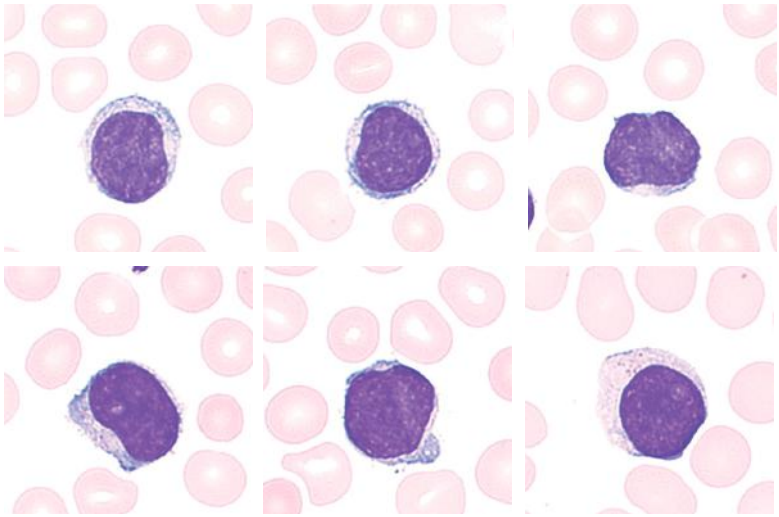
- Abn. WBC scattergram
- Abn Lymph/blast?
- Lymphocytosis

- WBC increased, predominantly Lym; Neu decreased; RBC and PLT were normal
- In the DIFF scattergram, Lym region was significantly dense, with a roughly normal overall distribution. Based on the WNB scattergram, abnormal cell alarm was given by nucleus-plasma double-check technology.

Peripheral blood morphology examination

	White blood cells		
	White blood cells	**150**	**100%**
L	Segmented neutrophils	8	5.3
	Band neutrophils	3	2.0
H	Lymphocytes	109	72.7
L	Monocytes	3	2.0
	Eosinophils	1	0.7
!	Blasts	10	6.7
	Reactive lymphocytes	2	1.3
!	Abnormal lymphocyte	14	9.3
	Non-white blood cells	**14**	**%**
	Large platelets	1	
	Smudge cells	9	6.0
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	128*10^9/L	Automated
	Platelet concentration	143*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
	Anisocytosis	0	
	Macrocytes	0	0.3
	Microcytes	0	8.3
	Color	**Degree**	**%**
	Hypochromic cells	0	0.7
	Polychromasia	0	0.1
	Shape	**Degree**	**%**
	Poikilocytosis	0	
	Schistocytes	0	0.3
	Echinocytes	0	0.2
	Elliptocytes	0	0.0
	Ovalocytes	0	4.9
	Stomatocytes	0	0.1
	Target cells	0	0.0
	Teardrop cells	0	0.3

Abnormal lymphocytes



Results from manual re-classification

Lymphocytes accounted for 82% and abnormal lymphocytes accounted for 8%, with blue and clear cytoplasm, fine chromatins, and visible nucleoli.

Other examinations

Item	Result
Bone marrow cytology	The lymphocyte percentage increased, with some irregular morphology, suggesting lymphoproliferative disorders (LPD).
Immunohistochemistry	Multiple clusters of CD3 (+), multiple foci of CD20 (+), multiple foci of CD79A (+), multiple foci of CD5 (+), CD23 (-), CD10 lymphocytes (-), few cyclinD1 (+), ki-67 (15%+) Consistent with those of small B cell lymphoma (tumor cells accounted for approximately 40%)
Flow cytometry	CD5 + CD10 + B lymphocytes accounted for 62.48%, MCL?
Chromosomal examination	46,XY,t(11;14)(q23;q32), add(14)(p11.2)[14]/46,XY[6]

Case analysis

- Mantle cell lymphoma (MCL) is a small-to-medium sized, monomorphic, mature B-cell tumor with specific immunophenotype and reproducible genetic abnormalities. CD5 and SOX11 are typically expressed, and over 95% of patients have CCND1 gene rearrangement (t(11:14)(q13;q32) abnormality), resulting in high nuclear expression of Cyclin D1 protein. MCL mainly affects elderly men and often involves extranodal sites. It has both the characteristics of rapid progression of aggressive lymphoma and incurability of indolent lymphoma. The survival time with multi-drug combination chemotherapy is about 3–5 years, and it currently belongs to incurable NHL.
- The clinical manifestations of MCL are nonspecific, so the diagnosis and prognosis evaluation at the initial visit are critical. Pathological diagnosis is the only means to confirm the diagnosis of MCL.

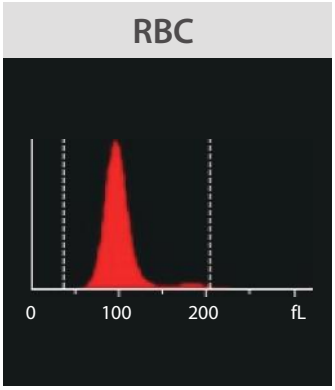
Case 14
May-Hegglin anomaly

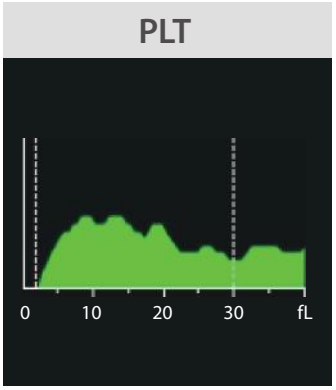
Clinical information

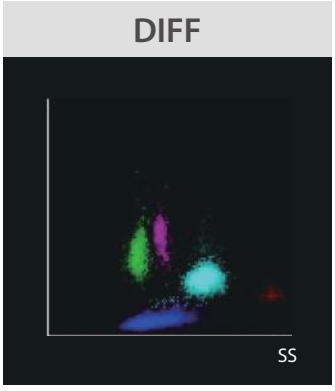
The patient was a 31-year-old female who was admitted in November due to "38 + 5 weeks of pregnancy with ultrasound indicating oligohydramnios".

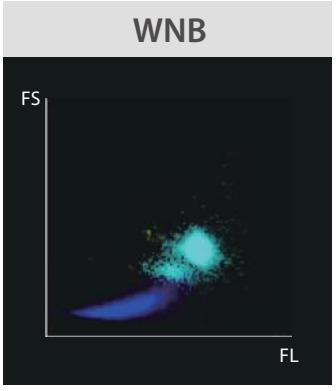
CBC results

Parameter	Alarm	BC-6800Plus_2 8:05 2022/10/26	BC-6800Plus_1 8:09 2022/10/26	Unit
WBC		9.60	9.16	10^9/L
Neu#		H 7.80		10^9/L
Lym#		1.24		10^9/L
Mon#		0.47		10^9/L
Eos#		0.07		10^9/L
Bas#		0.02		10^9/L
IMG#		0.09		10^9/L
Neu%		H 81.2		%
Lym%		L 13.0		%
Mon%		4.9		%
Eos%		0.7		%
Bas%		0.2		%
IMG%		0.9		%
RBC		3.87	3.96	10^12/L
HGB		123	122	g/L
HCT		L 35.5	36.5	%
MCV		91.9	92.1	fL
MCH		31.8	30.9	pg
MCHC		346	335	g/L
RDW-CV		12.9	13.0	%
RDW-SD		45.9	44.3	fL
PLT	R	L 31	60	10^9/L
MPV	R	H 15.5	15.9	fL
PDW	R	16.6	17.1	
PCT	R	L 0.047	0.056	%
P-LCC	R	L 20	38	10^9/L
P-LCR	R	H 64.0	62.8	%
NRBC#		0.000		10^9/L
NRBC%		0.00		/100WBC









Alarm

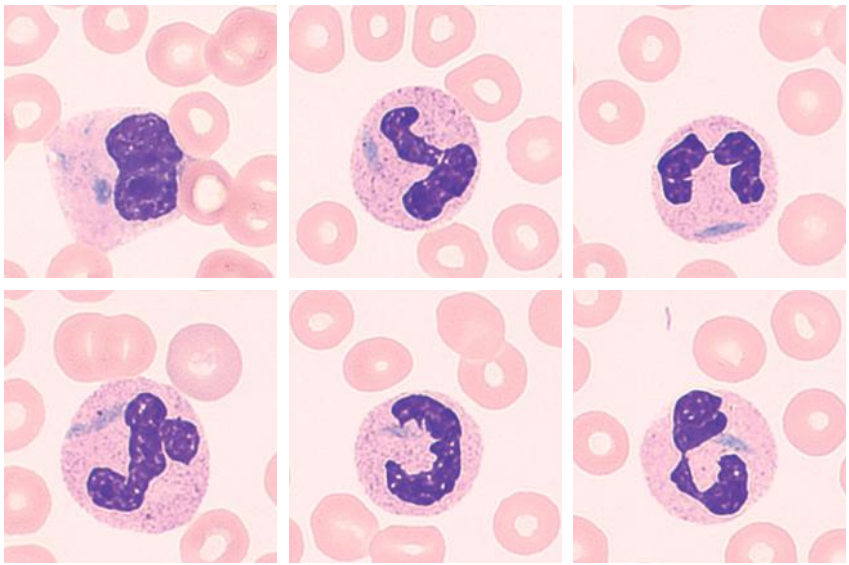
- PLT Clump?
- PLT Histogram Abn.
- Thrombocytopenia

- WBC and RBC were roughly normal; low PLT.
- Low PLT triggered a re-test rule. Upon re-test, PLT-O was found to be 60 × 10^9/L. It was speculated that PLT-I was falsely low due to interference from large platelets or platelet aggregation.

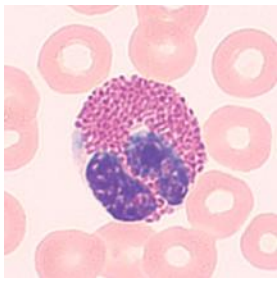
Peripheral blood morphology examination

	White blood cells		
	White blood cells	**150**	**100%**
H	Segmented neutrophils	133	88.6
	Band neutrophils	3	2.0
L	Lymphocytes	6	4.0
L	Monocytes	4	2.7
	Eosinophils	1	0.7
	Metamyelocytes	1	0.7
	Reactive lymphocytes	2	1.3
	Non-white blood cells	**97**	**%**
	Giant platelets	24	
	Large platelets	65	
	Smudge cells	7	4.7
	Platelets		
	PLT estimate	**Estimated result**	**Estimation method**
	Platelet concentration	71*10^9/L	Manual
	Red blood cells		
	Size	**Degree**	**%**
	Anisocytosis	0	
	Macrocytes	0	1.2
	Microcytes	0	5.0
	Color	**Degree**	**%**
!	Hypochromic cells	2+	14.7
	Polychromasia	0	0.2
	Shape	**Degree**	**%**
	Poikilocytosis	0	
	Schistocytes	0	0.0
	Echinocytes	0	0.0
	Elliptocytes	0	0.1
	Ovalocytes	0	2.4
	Stomatocytes	0	0.9
	Target cells	0	0.0
	Teardrop cells	0	0.8

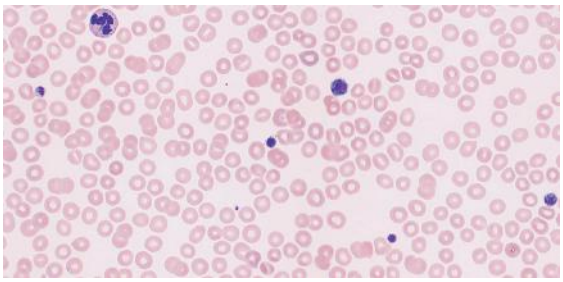
Neutrophils



Eosinophil



Giant platelets



Results from manual re-classification

The classification results were consistent with the CBC results. Blue, cloudy plaques resembling Dohle bodies, irregular in shape and large in size, were observed in the cytoplasm of neutrophils as well as eosinophils at all stages.

May-Hegglin anomaly was suspected. Additionally, giant and large platelets were observed in 59/100 WBCs, and the PLT estimate was consistent with the PLT-O result.

Case analysis

- The patient presented with thrombocytopenia, giant platelets, and neutrophil inclusions, which were consistent with the manifestations of May-Hegglin anomaly. Subsequent genetic testing confirmed the presence of a heterozygous MYH9 mutation located at 22q12.3, AD.
- May-Hegglin anomaly is a type of MYH9-related disorder, which is a rare autosomal dominant genetic disorder. Despite a decrease in platelet count, the total platelet volume in the blood is not significantly reduced due to an increase in platelet size. Platelet function remains mostly normal, and bleeding tendencies are mild. Patients are usually diagnosed in adulthood.
- Due to significant thrombocytopenia, most patients are misdiagnosed with ITP at initial diagnosis, and underwent unnecessary hormone therapy or splenectomy.

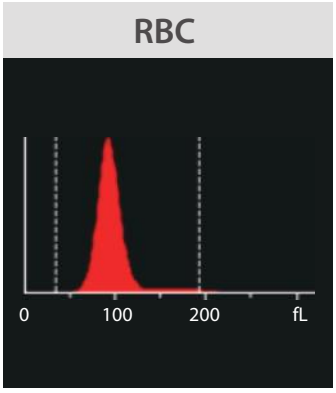
Case 15
Pelger–Huët anomaly

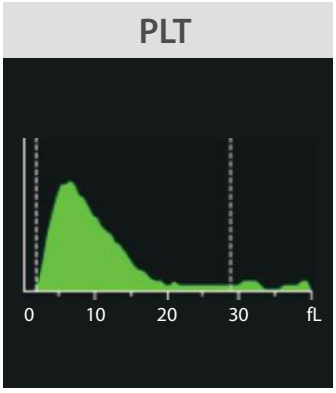
Clinical information

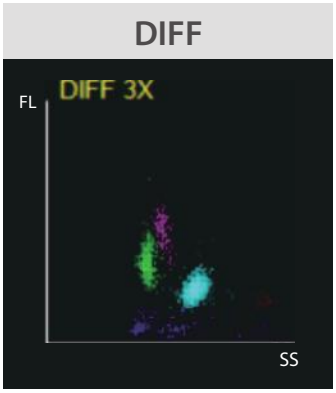
The patient was a 76-year-old female with poorly controlled type diabetes who visited the Department of Endocrinology of the hospital.

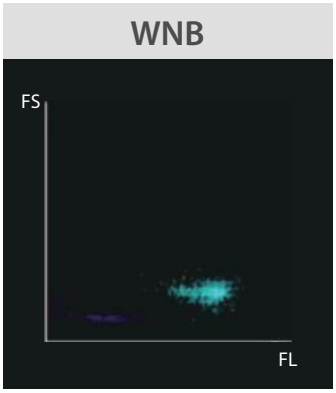
CBC results

Parameter	Alarm	Result	Unit
WBC	L	1.72	10^9/L
Neu#	L	1.28	10^9/L
Lym#	L	0.37	10^9/L
Mon#	L	0.06	10^9/L
Eos#	L	0.01	10^9/L
Bas#		0.00	10^9/L
IMG#		0.00	10^9/L
Neu%	H	74.6	%
Lym%		21.4	%
Mon%		3.6	%
Eos%	L	0.3	%
Bas%		0.1	%
IMG%		0.1	%
RBC	L	2.70	10^12/L
HGB	L	83	g/L
HCT	L	24.4	%
MCV		90.3	fL
MCH		30.7	pg
MCHC		340	g/L
RDW-CV		13.4	%
RDW-SD		46.0	fL
PLT	L	47	10^9/L
MPV		10.1	fL
PDW		16.3	
PCT	L	0.047	%
P-LCC	L	12	10^9/L
P-LCR		26.4	%
NRBC#		0.000	10^9/L
NRBC%		0.00	/100WBC









Alarm

- Pancytopenia
- Lymphopenia
- Leukocytopenia
- Anemia
- Thrombocytopenia

- Pancytopenia without abnormal cell alarm.
- No abnormality in histograms or scattergrams.

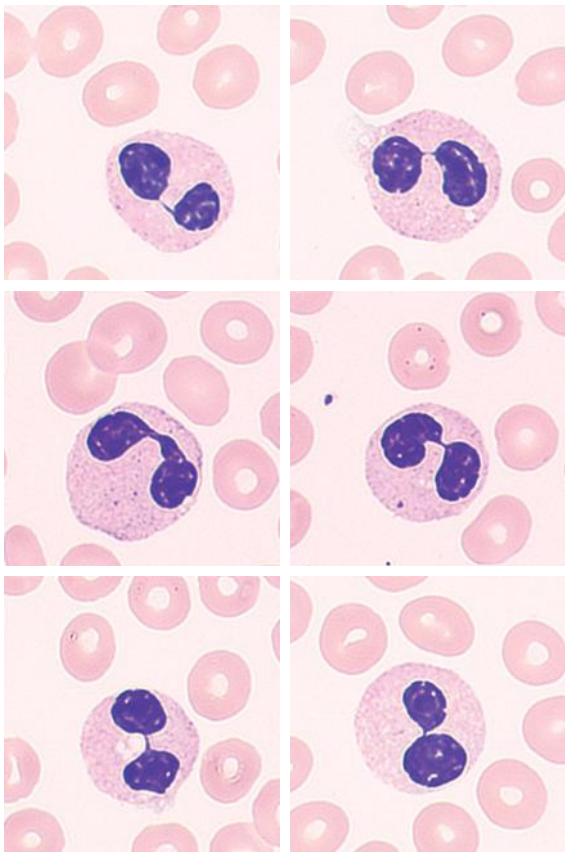
Peripheral blood morphology examination

	White blood cells		
	White blood cells	**200**	**100%**
L	Segmented neutrophils	66	33.0
!	Band neutrophils	84	42.0
	Lymphocytes	40	20.0
L	Monocytes	4	2.0
	Eosinophils	4	2.0
	Metamyelocytes	2	1.0
	Non-white blood cells	**27**	**%**
	Giant platelets	1	
	Large platelets	1	
	Smudge cells	22	11.0

Results from manual re-classification

The neutrophil nuclei appeared mostly rod-shaped or bi-lobed, with rod-shaped nuclei resembling peanuts or eyeglasses, and lobed nuclei connected by thin threads; the lobes were mostly round or elliptical; the chromatins were dense, deeply stained, and aggregated into small blocks or rod-like structures; hyperlobulated nuclei were not observed.

P-H anomaly

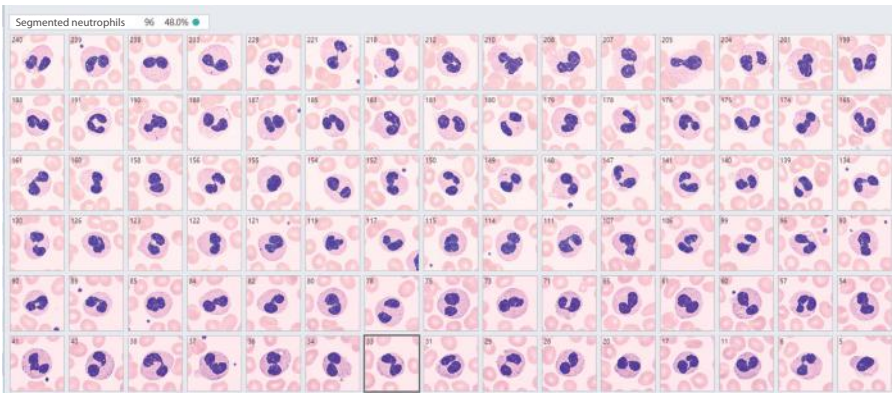


Case analysis

- Based on the special morphology of neutrophils, the possibility of hereditary Pelger-Huët anomaly was first considered for this patient. Thus, clinical consultation was made, and the patient was advised to undergo a pedigree analysis of immediate family.
- The patient has a son and a daughter who are both healthy. CBC samples were collected from the patient's son and daughter the next day for testing, and the results were normal. The blood cell morphology results are shown below:

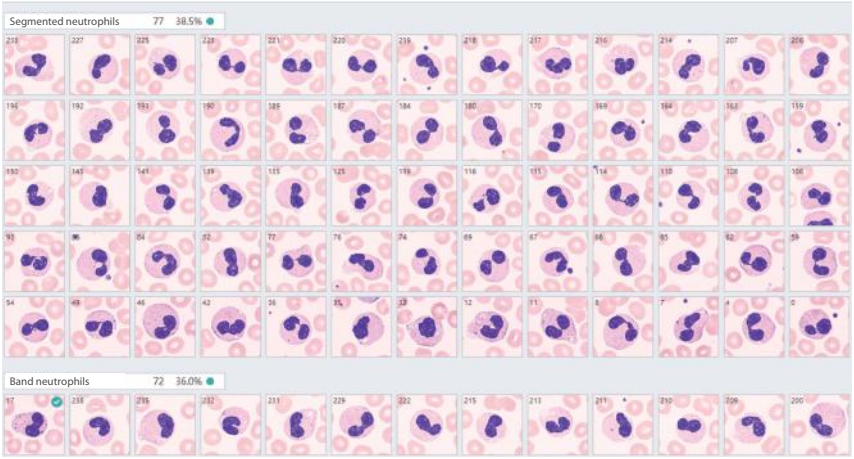
	White blood cells		
	White blood cells	**200**	**100%**
L	Segmented neutrophils	96	48.0
!	Band neutrophils	37	18.5
	Lymphocytes	59	29.5
	Monocytes	8	4.0
	Non-white blood cells	**48**	**%**
	Giant platelets	2	
	Large platelets	6	
	Platelet clumps	1	
	Smudge cells	31	15.5

Patient's son



White blood cells			
	White blood cells	**200**	**100%**
L	Segmented neutrophils	77	38.5
!	Band neutrophils	72	36.0
	Lymphocytes	41	20.5
	Monocytes	7	3.5
	Metamyelocytes	1	0.5
	Myelocytes	1	0.5
	Non-white blood cells	**39**	**%**
	Giant platelets	1	
	Large platelets	1	
	Smudge cells	20	10.0

Patient's daughter



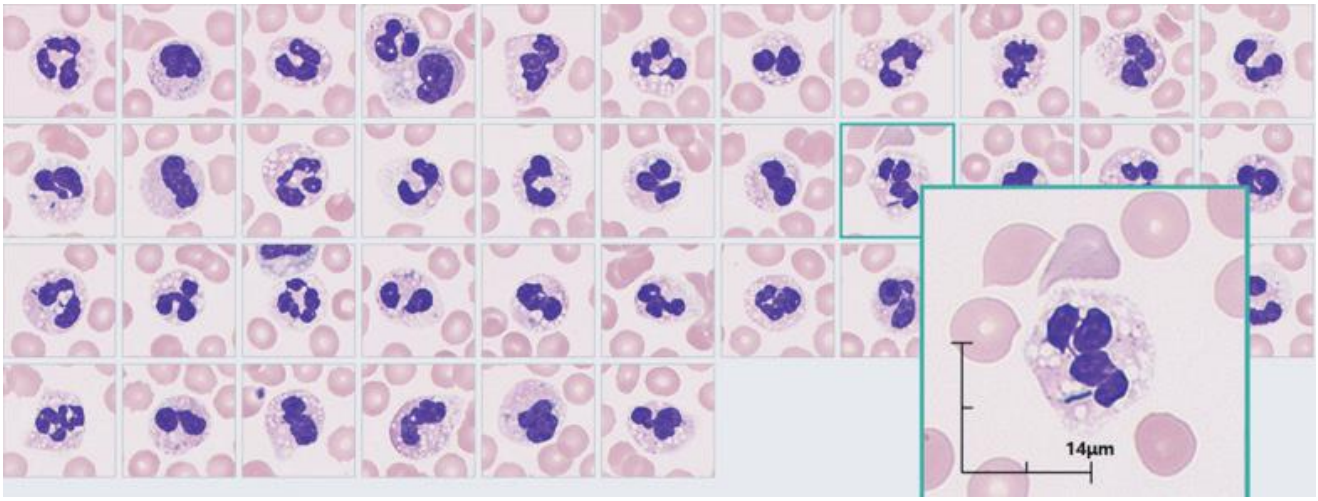
- The above results showed that the peripheral blood neutrophil morphologies of the patient's son and daughter were generally the same as that of the patient, and the neutrophil nuclei were mostly rod-shaped or bi-lobed. The MC-80 microscope was used to analyze 200 WBCs, and no cells with 3 or more lobes were observed, so the cell morphology was considered to be congenital Pelger-Huët anomaly.
- Pelger-Huët anomaly is an autosomal dominant genetic abnormality characterized by reduced lobulation of mature neutrophils. It is also known as familial neutrophil anomaly or Pelger-Huët neutrophil anomaly.
- Morphological features: Reduced lobulation of neutrophils. The nuclei were non-lobulated in an oval shape (e.g., kidney-shaped, rod-shaped) or divided into two lobes resembling peanuts, eyeglasses, or dumbbells (similar to panda eyes). The chromatins were concentrated, deeply stained, and aggregated into small blocks or thread-like structures, forming blank gaps in between.

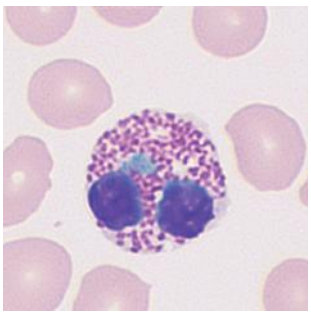
Case 16
Green neutrophilic inclusions

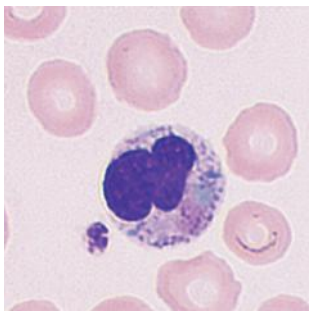
Clinical information

The patient was a 52-year-old female who experienced pyrexia, diarrhea, headache, fatigue, and nausea one week ago. The highest body temperature was 39.5 °C. She was later admitted to the intensive care unit due to confusion, transient unilateral limb convulsions, and hematemesis. Subsequently, she was diagnosed with hemophagocytic syndrome secondary to severe fever with thrombocytopenia syndrome virus (SFTSV) infection.

Peripheral blood morphology examination







Results from manual re-classification

Neutrophils exhibited vacuolar degeneration and demonstrated bacterial phagocytosis, along with the presence of blue-green round inclusions in both neutrophils and eosinophils.

Case analysis

- After the discovery of blue-green inclusions, high-sensitivity cardiac troponin I (hs-cTnI), alanine aminotransferase, WBCs, and other test indicators continued to increase or remained at high levels, and the NRBC percentage was as high as 20%. Six days later, the myocardial and pancreatic damage caused by the inflammatory cytokine storm did not show significant improvement, and the patient eventually died.
- Blue-green inclusions are bright green inclusions that appear in the cytoplasm of neutrophils or monocytes, and are usually associated with acute liver failure, lactic acidosis, and other diseases. Their appearance indicates that the patient is in critical conditions, which can alert clinicians to closely monitor the patient's emergency situation, actively treat the underlying disease, protect the liver, and promptly correct lactic acidosis. This may change the patient's outcome.

Long-standing Problems Associated With PLT Aggregation

In vitro platelet aggregation is commonly caused by EDTA-dependent pseudo thrombocytopenia (EDTA-PTCP) in clinical practice. It has been reported that the incidence of EDTA-PTCP is 0.07% ~ 0.20%, while the incidence among platelet donors is 0.2% and that among hospitalized patients is 0.1% ~ 2.0%[1]

Challenges for Clinical Departments in Handling Samples With Low PLT Counts

Complex low PLT count screening may lead to false low count reports
Clinical Disputes

Complicated time-consuming microscopic examinations add to the workload
Uncontrolled TAT

Repeated blood collections trigger patient complaints
Unsatisfactory Patient Experience

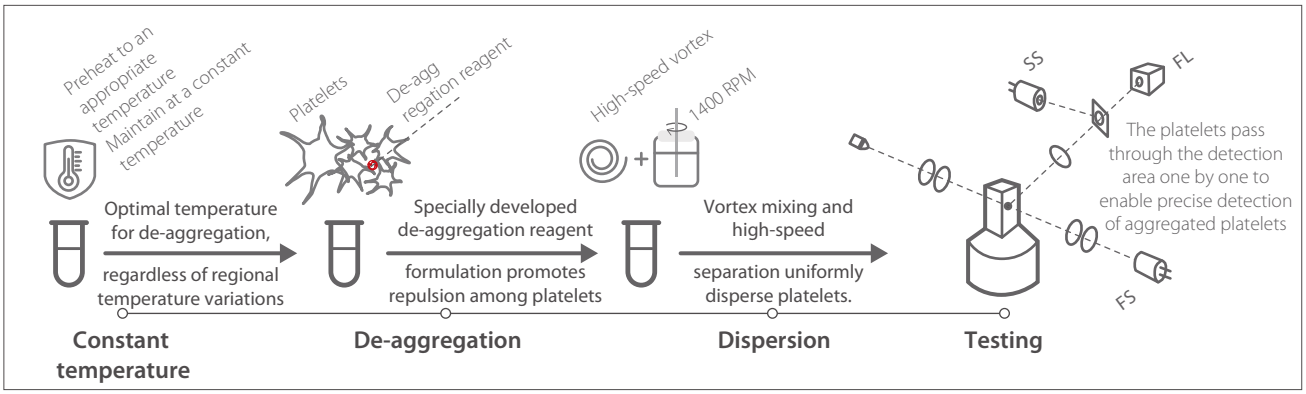
Difficulties Encountered by Traditional Instruments in Handling EDTA-PTCP Samples

- The instrument only provides alerts but cannot perform de-aggregation
- The procedure is complex and the timing of its completion beyond control.
- Deviations in sample processing require additional blood collections
- False reports may cause misdiagnosis
- Patients under intensive care may develop iatrogenic anemia[2]

Address PLT Aggregation-related Challenges Easily With PLT De-aggregation Technology

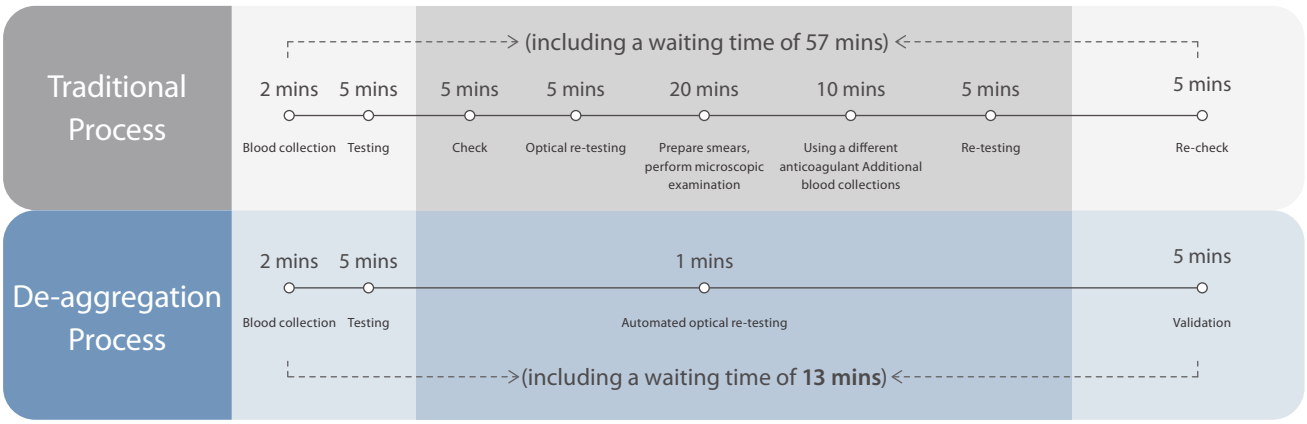
New Technology for Interference Elimination

Mindray is committed to solving the genuine concerns of customers and pursuing excellence. The groundbreaking PLT de-aggregation technology consolidates 6 years of collaboration with reputable institutions and guidance from experts, successfully addressing the PLT aggregation-related challenges in clinical laboratory settings.

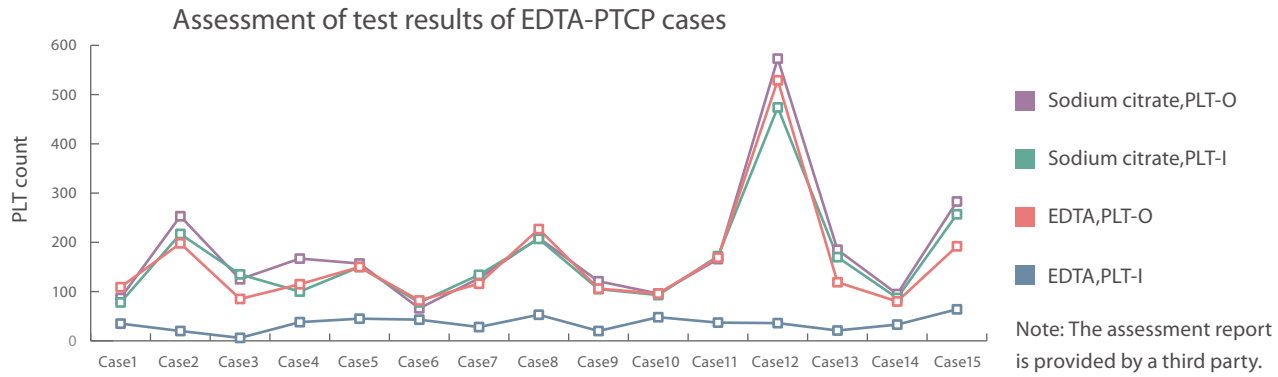


Process Comparison: De-aggregation Process is 4+ times More Efficient Than Traditional Process

Note: The testing time is estimated from the daily work of grade A tertiary hospitals



De-aggregation Technology Effectively Addresses Spurious Low PLT Count Due to EDTA-PTCP



Note: The assessment report is provided by a third party.

Advanced Hematology Analyzer & De-aggregation Technology

The instrument and technology not only can handle the samples affected by EDTA-PTCP, but also automates the entire de-aggregation process without the need for manual intervention. This uniformly controls the TAT and enhances operational efficiency and convenience in laboratories.

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