Unexpected Increased Platelet Count in an Acute Myeloid Leukemia Patient

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CASE DESCRIPTION

A 2-year-old male patient had received a diagnosis of acute myeloid leukemia (subtype: acute myeloblastic leukemia with minimal maturation according to the French-American-British classification) (1) with a high genetic risk profile [i.e., monosomy 7, t(3;17)]. The child had initially undergone 2 courses of chemotherapy with sequential high-dose cytarabine and mitoxantrone. Because of an early relapse, allogeneic stem cell transplantation was planned, and the patient received a preparative chemotherapy regimen with fludarabine, treosulfan, thiotepa, and antithymocyte globulin. Because of an expected chemotherapy-related worsening of the pre-existing, disease-related thrombocytopenia, strict monitoring of the platelet count was started. In this context, the patient came to the attention of the laboratory due to challenges associated with measurement and interpretation of automated platelet counts.

A complete blood count prior to initiation of chemotherapy showed leukopenia [white blood cells (WBCs), 0.05×10^9/L; reference interval 6–17.5], normocytic anemia (hemoglobin, 8.38 g/dL; reference interval: 10.5–13), and moderate thrombocytopenia (platelets, 63×10^9/L; reference interval: 150–530). The hemolysis-icterus-lipemia index (reference interval: 1–8) gave a value of 4 for hemolysis and 1 each for bilirubin and lipemia; therefore, only a moderate influence due to hemolysis could be assumed. The macroscopic examination of the patient specimen also showed no abnormalities. After chemotherapy initiation, the automated hematology analyzer (Sysmex XN-20) produced very different platelet count results depending on the instrument measurement mode of operation. The platelet count increased to 361×10^9/L when measured by impedance [platelet count-impedance (PC-I)]; 536×10^9/L when measured optically (PC-O) and 156×10^9/L when measured with fluorescence (PC-F). Because of the improbable kinetics of the platelet count data, a manual count was performed on the same specimen by phase-contrast microscopy using a Burker chamber. Using this approach, the platelet count was 70×10^9/L, consistent with a moderate thrombocytopenia and in agreement with the prechemotherapy platelet count of 63×10^9/L (Table 1). Compared to the evaluation prior to chemotherapy initiation, the hemolysis index increased from 4 to 6. In addition, a remarkable dark red staining of the blood sample, indicating hemolysis, was apparent on the macroscopic examination. Concomitantly, the systematic evaluation of the May-Gruenwald-Giemsa-stained peripheral blood smear by light microscopy showed the presence of abundant white cell debris, compatible with chemotherapy-induced tumor cell lysis, which were mostly in the size range of blood platelets (Fig. 1A–E). In addition, a substantial red blood cell (RBC) anisopoikilocytosis with fragments and typical microspherocytes of similar dimensions was apparent (Fig. 1C–E).

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QUESTIONS TO CONSIDER	
1.	Which automated methods are available for platelet count, and which one shows the highest analytical inaccuracy?
2.	Which factors can influence the different platelet measuring techniques and why?
3.	Which phenomenon might cause a sudden increase of the platelet count after the start of chemotherapy?

Table 1. Platelet counts prior to and after initiation of chemotherapy.

	Platelet count ($\times 10^9$/L) [reference interval: 150–530]					HIL index (Hemolysis)[b] [range: 1–8]	LDH (U/L) [reference interval: 155–395]	Hb (g/dL) [reference interval: 10.5–13]	WBC ($\times 10^9$/L) [reference interval: 6–17.5]
	Automated								
	PC-I	PC-O	PC-F	FACS	Manual[a]				
	Prechemotherapy								
Day 0	63	—	—	—		4	1895.62	8.38	0.05
	Postchemotherapy								
Day +2	361	526	156	68	70	6	2159.57	10.47	0.02
Day +16	682	707	246	150	150	5	—	10.8	0.03
Day +19	461	580	168	80	75	4	1619.68	11.12	0.04

Abbreviations: FACS, fluorescence-activated cell sorting (i.e., reference method for platelet counting using a specific fluorochrome-conjugated monoclonal antibody anti-CD61); HIL, hemolysis-icterus-lipemia; LDH, lactate dehydrogenase; Hb, hemoglobin.
[a]Obtained by phase-contrast microscopic method using a Burker chamber.
[b]Hemolysis index obtained on the Siemens Dimension Vista.

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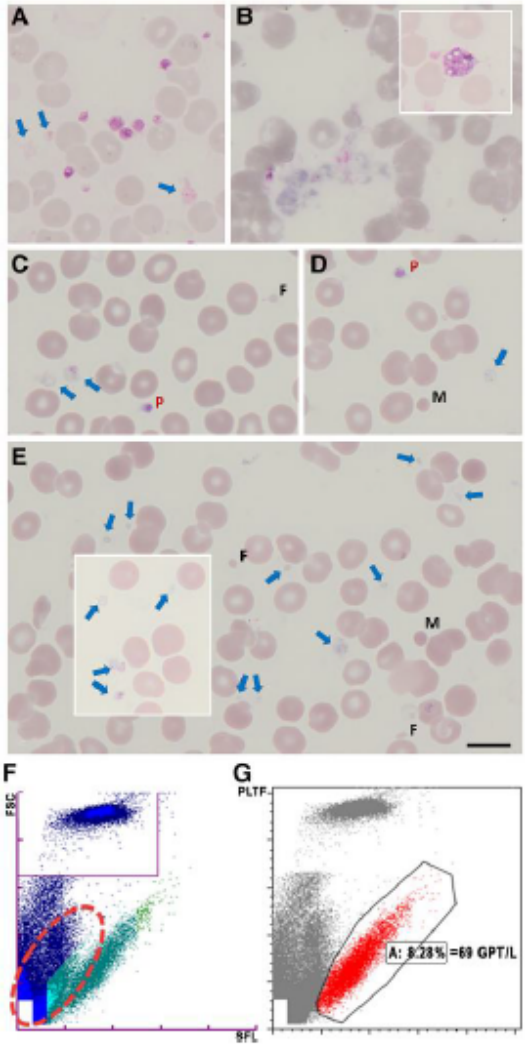

Fig. 1. Blood cell morphology on the peripheral blood smear by light microscopy and PC-F scattergram on day +2 after chemotherapy initiation. (A) Cell debris of different sizes and shapes (denoted by arrows) surrounded by normal erythrocytes and platelets. (B) Amorphous basophilic material, likely containing residual granule structures and possible remnants of disrupted cells with vacuoles (inset). (C–E and inset) Together with platelets showing normal size and granulation (P), erythrocytic fragments (F), microspherocytes (M), and cell debris (arrows) in the platelet size range are apparent. Scale bars correspond to 10 µm. (F) PC-F scattergram of the patient sample obtained on day +2 with a measured platelet count of 156×10^9/L. The dark blue cloud is the suspected cell debris population; the turquoise cloud is the suspected platelet population. (G) Manually gated PC-F scatter gram corresponding to a platelet count of 69×10^9/L. Color figure available at https://academic.oup.com/clinchem.

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Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the July 2025 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/71/7 and follow the link to the Clinical Case Study and Commentaries.

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