Hidden thrombocytopenia due to blast fragments in acute monocytic leukemia

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Errors in platelet counts result most often in falsely low counts as a consequence of partial clotting of the specimen, ethylene diamine tetracetic acid (EDTA) induced agglutination[1] or platelet satellitism to polynuclear neutrophils.[2] Spuriously elevated platelet counts are less common and may result from the presence of platelet-sized particles such as microcytes, schizocytes, cellular debris, cryoglobulins or lipidic particles (chylomicrons or nutritional emulsion).[3] Here, we report a hidden thrombocytopenia due to the interference of blast fragments in a case of acute monocytic leukemia. We would like to show how to detect this anomaly and to correct the platelet count.

A 62-year old woman was hospitalized because of asthenia, weight loss and hyperthermia. The clinical examination showed gingivitis and hepatomegaly. An automated complete blood count was performed on the automated analyzer Technicon H*2 (Bayer, Tarrytown, NY, USA). Relevant hematologic findings were a normocytic anemia (hemoglobin: 8.3 g/dL, mean cell volume: 95.9 fL) and a marked hyperleukocytosis (White Blood Cells (WBC): 348x10^9/L). The automated platelet count could not be validated because of an abnormal triangular-shaped platelet volume distribution histogram (alarm No Fit, *NF*) (Figure 1.).

The blood film stained according to the May-Grünwald-Giemsa technique revealed 100 % blasts with a lot of blast fragments mimicking platelets (Figure 2.). The true platelet count was estimated on the blood film as the ratio of platelets to erythrocytes and was found to be 45x10^9/L. According to size characteristics, we hypothesized that the erroneous automated platelet count was due to the blast fragments. The bone marrow aspirate showed a proliferation of abnormal blast cells (100%), positive for naphthol AS-D acetate esterase (85% of the cells) and myeloperoxidase (35%). The leukemic cells were monoblasts and the immunophenotyping confirmed the myeloid lineage. The diagnosis was acute monocytic leukemia referred to as AML-M5 in the French-American-British cooperative group classification.[4]

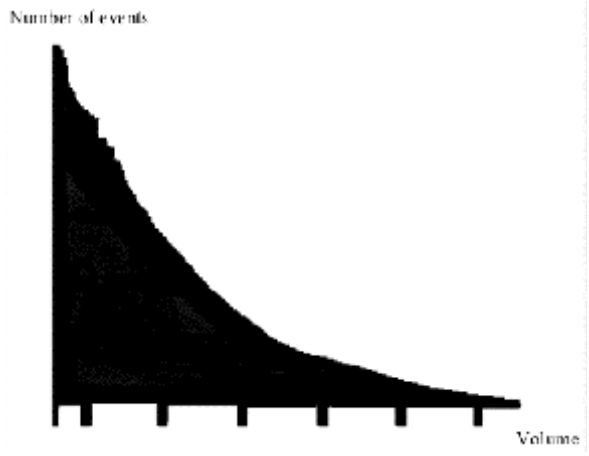

Figure 1: Abnormal histogram of platelet volume distribution, triangular figure instead of the Log-normal curve.

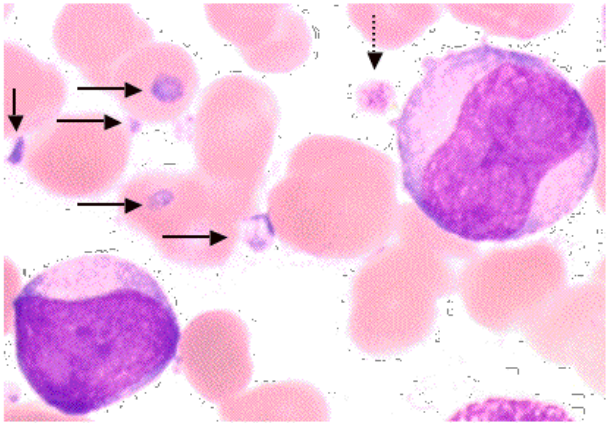

Figure 2: Blast cell fragments mimicking platelets (continuous arrows) and true platelet (dotted arrow).

The thrombocytopenia was first associated with minor bleeding complications such as hematuria and the confirmed low platelet count prompted transfusion of platelets before central line placement.

Even if leukemic cells are inherently fragile, it is probably rare that the blast fragments are numerous enough and of the appropriate size to interfere with the automated platelet count. This may explain why this interference has been seldom reported. As far as we know, 5 cases have been published, associated with 2 acute myelogenous leukemias,[5, 6] 2 hairy cell leukemias[7, 8] and 1 lymphoma.[9] It has been demonstrated that the platelet-sized cell fragments had the same cytochemical and immunological staining as the leukemia blasts.[5] When platelets are distributed evenly in a blood film, the platelet count can be validated by counting the ratio of platelets to erythrocytes and calculating the platelet count from the erythrocytes. Because the blast fragments are refringent, platelet counting by phase-contrast microscopy may also be spurious.[8] Improved platelet counting using measurements of two-angle light scatter have been proposed to discriminate erythrocyte ghosts and fragments from platelets.[10] This method should provide more accurate automated platelet-count in samples containing potential RBC interference, but remain to be validated for WBC fragments.

As previously described, the ignorance of this interference may have serious implications as a severe thrombocytopenia may be masked, left untreated and be responsible for potentially fatal hemorrhage[5, 6]. In conclusion we would like to stress that platelet count should be cautiously validated in the presence of a high WBC count, using the analyzer alarms and examination of the stained blood film.

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