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CASE REPORT ARTICLE

# Premature death due to bleeding and leukostasis in acute myeloid leukemia with unusual hyperleukocytosis

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## ABSTRACT

Hyperleukocytosis is defined as a leukocyte count greater than 100,000/mm in the peripheral blood and is more frequently observed in adults chronic lymphocytic leukemia (CLL) and pediatric acute leukemia patients. Hyperleukocytosis in acute myeloid leukemia usually has lower values than those of CLL and is characterized by the presence in the peripheral blood of large immature cells (blasts), with a tendency to stack in small vessels. Compared to lymphoid blasts, myeloid blasts are larger, less deformable,and with a higher risk of manifesting hyperviscosity syndrome and the patients may also present with tumor lysis syndrome and disseminated intravascular coagulopathy. High-dose chemotherapy is is an emergency treatment that can reduce the risk of systemic consequences, whereas the role of leukapheresis is still debated. Mortality may be 40% at 1 week and require urgent decisions for clinical management.

Here we report the case of a 69-year-old woman who came to the emergency room in June 2025 for fever and asthenia lasting for 3 days. The patient showed WBC 424x$10^3$/mmc at blood count. A few minutes after accessing the ER, the patient experienced sudden loss of consciousness and deterioration of the neurological picture with hemiparesis, was treated with clonidine for hypertensive crisis and transferred to the emergency room for intubation. The clinical signs and laboratory findings were compatible with possible M4/M5 myeloid leukemia. A cerebral CT without contrast medium documented a significant intraparenchymal hemorrhage with subdural streaks and ventricular flooding. The rapidly evolving clinical manifestations did not allow for urgent treatment, so the patient underwent hydration therapy and transfusion of a platelet concentrate. In the case described, the rapid evolution of the disease did not allow the activation neither leukapheresis, nor chemotherapy treatment and the patient died shortly after intubation.

## Introduction

### CLINICAL CASE

A 69-year-old woman with a history of hypertension, undergoing home treatment with amlodipine/olmesartan and furosemide for 2 months, was admitted to the emergency department in April 2025 for hypertensive crisis and headache. Blood count showed WBC 5.18x$10^3$/ $mm^3$, Hb 13 g/dl, PLT 163x$10^3$/$mm^3$, C reactive protein 0.05 (0-0.3), electrolytes within normal limits. She was treated with clonidine, her blood pressure returned to normal, and then discharged.

In June 2025, the patient was readmitted to the emergency department for fever and asthenia lasting 3 days. The patient presented alert and cooperative, eupneic, feverish, with edema of lower limbs, negative chest findings and evident gingival hypertrophy. COVID, Flu A, and Flu B swabs were negative. Blood count showed WBC 424x$10^3$/ $mm^3$, Hb 6.4 g/dl, platelets 20x$10^3$/ $mm^3$, K+ 2.84 mEq/L (3.5-5.1), C reactive protein 3.4 mg/dl (0-0.3), BNP 1226 pg/ml (0-125), LDH 925 IU/l (120-246). A few minutes from the doctor's visit the patient suddenly lost consciousness, she had a hypertensive crisis and her neurological condition deteriorated She was treated with clonidine and transferred to the emergency room.

The patient appeared unresponsive to verbal and active stimuli, pupils were isochoric, miotic with gaze deviated to the left , to the painful stimulus she showed a flexion response on left slide,weak response on the right slide, glasgow coma score 6 therefore she was intubated. A peripheral blood smear revealed the presence of 98,5% of large, stacked, aggregated cells with diffuse chromatin and a monocyte-like appearance. No hypergranulated blasts suggestive for promyelocytic leukemia were found (photos 1 and 2).

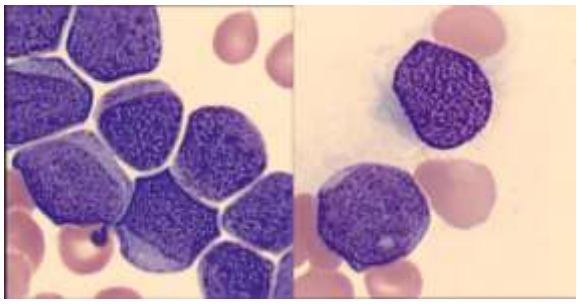

Figure 1: leukemic blasts (automatic Giemsa stain method, Dasit Sysmex technology). The large leukemic blasts represented the 98,5% of peripheral blood cells and showed a high nucleus/cytoplasm ratio and diffused chromatine. The morphological picture was compatible with M4/M5 acute myeloblastic leukemia.

The morphological findings were consistent with M4/M5 acute myeloid leukemia. A brain CT scan without contrast medium revealed significant intraparenchymal hemorrhage with subdural streaks and ventricular flooding. The hyperleukocytosis evolved in few minutes, possibly due to cerebral ischaemia, with neurological symptoms did not allow for urgent leukapheresis and neither intravenous cytarabine nor oral hydroxyurea were started, so the patient underwent only supportive therapy with bicarbonate, and physiologic solution infusion and transfusion with a pooled platelet concentrate.

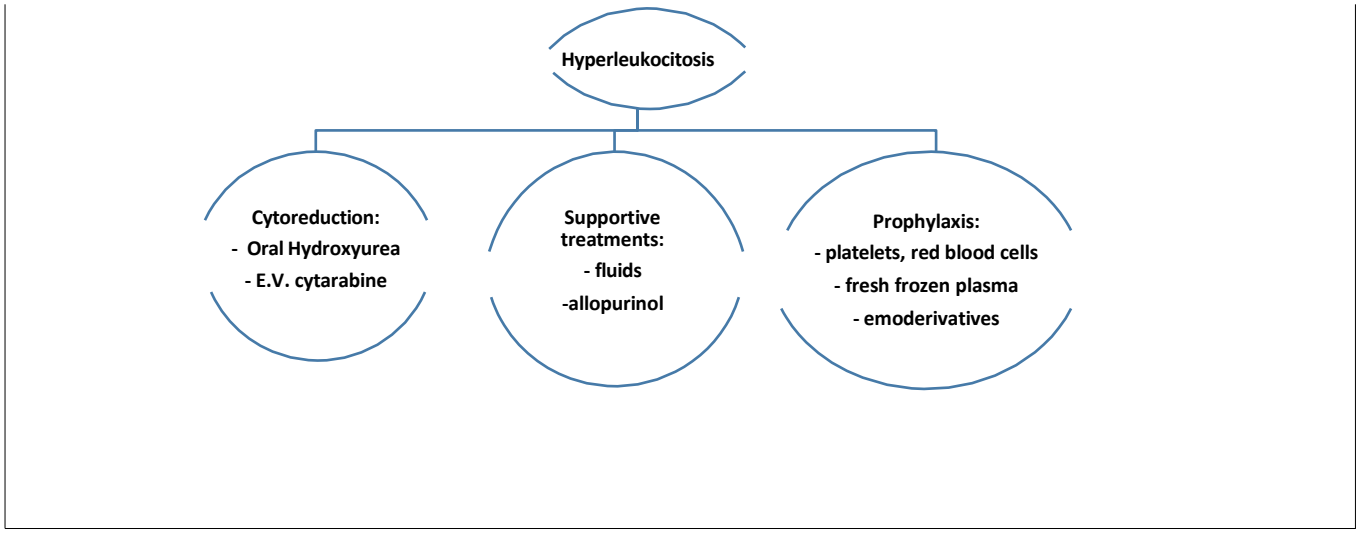


Figure 2: Clinical approach to hyperleukocitosis (modified from Bewersdorf et al, Cells, 2020).

## DISCUSSION

In cases of significant leukocytosis, the treatment of hyperviscosity syndrome and possible coagulopathy requires the rapid initiation of therapeutic leukapheresis together with cytoreductive treatment, which must also be readily available for emergency situations (Figure 2). In the case described, the rapid evolution and the sudden death of the patient did not allow to start chemotherapy and/or leukapheresis procedure.

Predominant neurological, respiratory or renal complications at onset, shown higher early mortality rates than patients without such complications. In these patients, high rate of leucoreduction seems not to be associated with improved early survival.

Furthermore, adverse events are rare during apheretic procedures and chemotherapy in haematological malignancies, and platelets concentrates transfusion in patients with thrombocytopenia and fresh frozen plasma infusion can reduce the risk of haemorrage. The usefulness of corticosteroids is controversial, in particular in myeloid leukemia, due to prevalent lympholytic action of steroids.

A dramatic clinical evolution is a frequent occurrence in adult patients with hyperleukocytosis and in the present case did not allow to consider an adeguate treatment. It is of relevance the necessity to start the treatment in the following minutes after the detection of hyperleukocytosis, particularly when the white blood cells count is unusually high, despite the possibility of adverse events due to the treatment.

## CONCLUSIONS

Significant hyperleukocytosis with >100.000/mmc white blood cells count with signs of leukostasis is a medical emergency that is most commonly observed in patients with AML and can be associated with high early mortality. Management of leukostasis includes intensive supportive care and treatment of the leukemia with chemotherapy and leukapheresis, which must also be readily available for the emergency area.

While immediate initiation of definitive induction therapy has been the gold standard treatment, it is increasingly important to safely and effectively reduce the leukemic burden while awaiting the laboratory characterization of the leukemia, thus facilitating the most effective treatment.

To our knowledge, the present case represents the highest leukocyte count described in an adult subject with acute myeloid leukemia and the dramatic clinical evolution demonstrate that >400.000/mmc white blood cells counts is a rapidly evolving condition that need prompt clinical decisions and interventions.

## Conflict of Interest:

The authors have no conflicts of interest to declare.

## Funding Statement:

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