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Hyperleukocytosis and leukostasis as fatal consequences of childhood acute myeloid leukemia

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Introduction

Acute myeloid leukemia (AML) accounts for 15–20% of all leukemias in children [1]. AML may manifest with gingival infiltration, hyperleukocytosis, which is defined as a white blood cell count >100 × 10^9/L, and leukostasis, which is defined as a bloodflow disturbance in microcirculation associated with hyperleukocytosis [2]. This results in leukemic cells accumulating in capillaries and blocking bloodflow, leading to multi-organ failure and secondary hemorrhages. Other symptoms can involve the respiratory system (dyspnea, pulmonary edema, or acute respiratory distress syndrome), the nervous system (headache, confusion, blurred or partial vision, disturbances of consciousness up to and including coma), and acute kidney injury [3]. Priapism and ischemic necrosis of the distal extremities are encountered more rarely, but are characteristic of leukostasis. Prophylaxis of tumor lysis syndrome is necessary due to the increased disintegration of leukemic cells [4]. Its management requires strict monitoring of the patient's vital parameters and, when needed, respiratory support.

Case report

We present the case of an 11-year-old boy admitted to the Department of Pediatric Oncology, Hematology and Transplantology from a local hospital. The first symptoms of fatigue and headache had occurred a week earlier, followed by gingival infiltrations. The emergency room physician diagnosed the patient with stomatitis and prescribed clindamycin. However, the symptoms deteriorated, so he was admitted to the Urgent Care Unit and was transferred to the Department because of hyperleukocytosis of 146 × 10^9/L. The patient presented several neurological symptoms, including confusion, headache, muscle weakness, nuchal rigidity, and upper and lower Brudzinski signs. We also observed an ocular hematoma and edema of the left eye. Also, we detected tachypnea, respiratory effort, and an oxygen saturation of 86%. Laboratory findings confirmed hyperleukocytosis (178.94 × 10^9/L), anemia (7.5 g/dL), and thrombocytopenia (105 × 10^9/L). A manual smear of peripheral blood led to the suspicion of AML. Coagulopathy necessitated the administration of prothrombin complex concentrate, antithrombin concentrate, phytomenadione, and enoxaparin at the therapeutic dose. Inflammation markers increased, so we introduced empirical antibiotherapy. Diuresis failed to improve, and respiratory effort persisted. We therefore implemented optiflow nasal high-flow therapy. Less than 24 hours after admission, we transferred the child to the Department of Pediatric Anesthesiology and Intensive Care (ICU). He was circulatorily unstable, with a heart rate of 150/min and blood pressure of

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80/50 mmHg. The patient was intubated due to the need for mechanical ventilation. We performed a CT of the head and chest. Imaging showed a soft tissue mass measuring 13 mm × 10 mm × 4 mm along the anterior part of the roof of the left orbit (Figures 1A–B).

Bleeding from the nose and mouth required the use of a tamponade. Leukocytosis increased to 250 × 10^9/L. Taking into account the patient's serious clinical condition, we withheld a bone marrow biopsy and AML was diagnosed based on peripheral bloodflow cytometry. On the day after admission to the clinic (the third day of hospitalization), we implemented oncological treatment consisting of thioguanine at a dose of 40 mg/m^2/day orally and cytarabine at a dose of 20 mg/m^2/day intravenously. Over the following hours, progressive multi-organ failure occurred, and the patient required increasing doses of vasopressors. Analgosedation and continuous renal replacement therapy were introduced. On the third and fourth days of hospitalization, two leukapheresis procedures were performed, with no satisfactory result. The patient presented with cyanotic changes in the auricles, limbs, and back, subconjunctival hemorrhages, numerous skin ecchymoses, and serous blisters in the lower thighs. Anuria, general edemas, anisocoria and jaundice of the sclerae appeared. Due to the unsatisfactory effect of the implemented treatment and further multi-organ dysfunction, vasopressors were discontinued. The patient died four days after admission to the ICU.

A diagnosis of AML was confirmed according to the following studies. The GTG karyotype study showed the following complex karyotype: 46,XY,der(5)t(5;9)(q31;q21)del(9)(q21;33),der(9)t(5;9)(q31;q21)del(5)(q31;q34)[17]/46,XY[2]. Flow cytometry detected 98% of immature cells of granulocytic lineage with high side scatter and medium expression of CD45 and immunophenotypic traits of acute promyelocytic leukemia, i.e. lack of HLA-DR and differentiation markers (like CD11b) expression, high CD13 and myeloperoxidase (MPO) expression, as well as high autofluorescence. FISH testing for *PML::RARA* fusion was negative.

Discussion

Leukostasis requires immediate and aggressive treatment. Fast causal and symptomatic treatment must therefore be applied [5]. Cytoreduction can be achieved using leukapheresis, exchange transfusion and chemotherapy. Hyperleukocytosis occurs also in pediatric patients diagnosed with AML [6]. Very high leukocytosis (WBC ≥200 x 10^9/L) in myeloid leukemias correlates with a significantly lower overall survival rate [3]. The complex karyotype seen in our patient, previously undescribed in the literature, and an immunophenotype of AML M3-like blasts, demonstrate the aggressiveness of this disease and its unfavorable course.

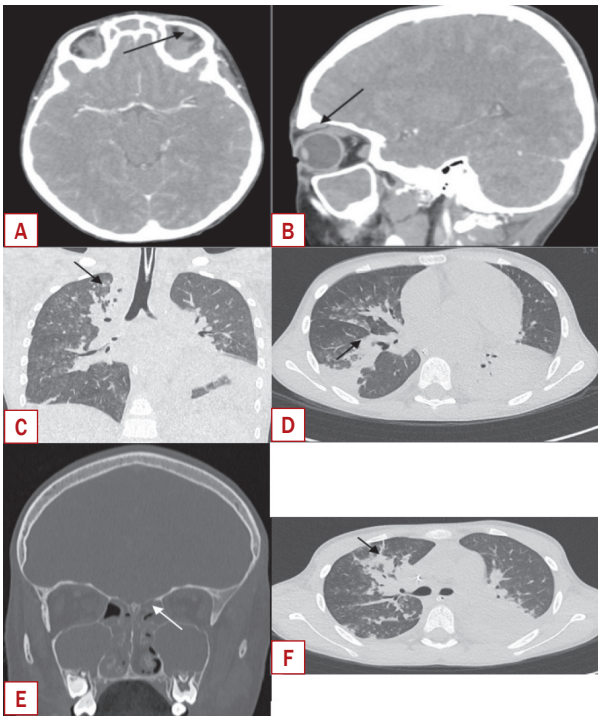

Figure 1 A–F: CT scans performed. **A, B.** Head CT scan after administration of contrast agent, cerebral window, transverse and sagittal section. Along front parts of left orbital roof, there is a soft tissue lesion measuring 13 mm × 10 mm × 4 mm (ap × ds × cc); **C, D and F.** CT scan of chest, pulmonary window, frontal section, transverse sections. Pneumonic densities with preserved air bronchogram throughout lower lobe of left lung. Bronchopneumonic densities in upper lobe of left lung. Scattered bronchopnemonic densities and ground glass changes in right lung. Right pleural cavity without fluid. Fluid in left pleural cavity. Endotracheal tube in trachea. Probe in stomach; **E.** CT scan of head, frontal section, bone window. Airlessness of paranasal sinuses and thickening of mucous membranes with obstruction of ostium-ductal complexes

Article information and declarations

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None.

Authors' contributions
ET — literature search, manuscript preparation. JC — manuscript preparation. DG — manuscript preparation. KAW, MS — critical review. MD — patient care, critical review. KJP — radiological images and descriptions. KD — idea, critical review.

Conflict of interest
The authors declare no conflict of interests.

Ethics statement
The authors declare that informed consent for publication was not obtained, as published data does not allow for patient identification.

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