Regenerating blasts masquerading as relapse in a patient with ALL following G-CSF therapy

TO THE EDITOR: Granulocyte colony-stimulating factor (G-CSF)-associated blastocytosis with a lack of an associated left shift poses a challenge for accurate assessment of the underlying disease [1]. In particular, blastocytosis after chemotherapy for acute leukemia may mimic a recurrence of underlying leukemia. Only a few cases of myeloblastosis in AML or ALL or of leukoerythroblastosis in AML after G-CSF therapy have been described anecdotally in the literature [2-4]. Herein, we report a case of myeloblastosis in ALL within 2 days of G-CSF administration masquerading as early relapse, causing a diagnostic dilemma. This was compounded by a striking lack of telltale evidence that G-CSF treatment was effective, such as increased granulation and a left shift.

A 25-year-old man diagnosed with common acute lymphoblastic leukemia antigen (CALLA) positive, precursor B-cell ALL (Fig. 1A) completed his first phase of induction chemotherapy with methotrexate, cyclophosphamide, and cytarabine. His day 36 bone marrow showed 2.8% blasts with positive minimal residual disease (MRD) (0.046%). To accelerate recovery from persistent neutropenia, he was treated with G-CSF; an adequate response was noted, with

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Fig. 1. (A) Diagnostic blasts with a high nucleocytoplasmatic ratio and scant agranular cytoplasm (Giemsa stain, ×1,000). (B) Regenerating blasts are larger with moderate granular cytoplasm (Giemsa stain, ×1,000). (C-F) Immunophenotyping showing the regenerating blasts positive for CD45, CD34, CD13, and CD33 and negative for CD19 and CD10.
a total leukocyte count (TLC) of 2.9×10^9/L. On day 70, he completed his second phase of induction chemotherapy and was started on G-CSF therapy for severe neutropenia (TLC: 0.76×10^9/L). On day 73, his peripheral blood smear showed marked leukopenia with a predominance of lymphocytes and 2% blasts without any left shift or increased granulations. This lack of prototypical G-CSF response along with previous MRD positivity and presence of 2% blasts led to a suspicion of relapse, and bone marrow examination was advised. Marrow aspirate showed hypocellular marrow with 14% blasts, and focal areas showed up to 25% blasts (Fig. 1B), along with a lack of a maturing myeloid component, which suggested relapse. Trephine biopsy, in contrast, showed hypocellularity with only a few scattered CD34 positive blasts. This necessitated flow cytometric evaluation, where the blasts showed negativity for B lymphoblastic markers and expressed myeloid markers, including CD13, CD33, and CD34, suggesting that they were regenerating myeloblasts (Fig. 1C-F). No further therapy was administered and the patient was kept on close hematological follow-up. The counts recovered after 4 days, with the typical responses of a left shift and increased granulation. Follow-up marrow examination after complete recovery of blood counts, 10 days after discontinuing G-CSF therapy, revealed cellular marrow elements with 4% blasts (regenerating) and negative MRD (<0.01%).

Post-G-CSF blastocytosis is a problematic and confusing issue that is difficult to differentiate from disease recurrence and hemopoietic recovery. In our case, there were regenerating blasts (>20%) in the bone marrow, with an absence of telltale G-CSF-induced changes, such as presence of immature granulocytes, monocytosis, or prominent granulations on peripheral smear. To conclude, the regenerating blast percentage may increase after G-CSF therapy to >20%, without concomitant increases in other mature myeloid precursors.

The lag time before complete response to G-CSF therapy may be as long as 10 days, as seen in our case, posing potential problems in management and a challenge in therapeutic decisions. A careful morphological assessment of the blasts at the time of diagnosis, aided by awareness of these G-CSF-associated aberrant patterns and flow cytometric characterization can help guide management decisions.

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TO THE EDITOR: t(16;21)(p11.2;q22) is a non-random chromosomal translocation that occurs in acute myeloid leukemia (AML), myelodysplastic syndrome that evolves to AML, blast crisis of chronic myelogenous leukemia, and rare cases of Ewing’s tumors [1]. AML cases harboring t(16;21)(p11.2; q22) are associated with poor prognosis and a high relapse rate. This translocation produces a fusion gene between the FUS (fused in sarcoma) gene on chromosome 16 and the ERG (erythroblast transformation-specific related) gene on chromosome 21. The FUS gene is highly related to the EWSR1 (Ewing sarcoma breakpoint region 1) gene, and the FUS protein is an RNA binding protein. On the other hand, the ERG gene encodes an external transcribed spacer (ETS) family transcription factor. In the chimeric protein, the N-terminal FUS transactivation domain fuses to the C-terminal DNA binding ETS domain of ERG. The fusion protein seems to function as a transcriptional activator [2].

However, the occurrence of t(16;21) in acute lymphoblastic leukemia (ALL) is very rare. To our knowledge, it has been reported in only 13 ALL patients, including 10 adults and three children [3-6].

We herein describe the case of a 6-year-old boy who was admitted to our hospital owing to parotid enlargement and cranial nerve VII palsy. Physical examination revealed...