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Letter to the Editor

Four Years Long-Term Follow-Up of Patient with Atypical Chronic Myeloid Leukemia Post Haploidentical Transplant with TBF Conditioning

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Dear Editor,

Atypical chronic myeloid leukemia (aCML) is a rare subtype of myelodysplastic syndrome/myeloproliferative neoplasm overlap syndromes (2016 WHO classification) with a high rate of transformation to acute myeloid leukemia and poor survival. aCML is a disease of the elderly with an estimated incidence of 1-2% of BCR-ABL1 positive CML. Clinical presentation includes splenomegaly and leukocytosis with granulocytic dysplasia [1, 2].

Diagnostic criteria is defined by: leucocytosis (WBC count ≥ 13.10^9/L) due to increased neutrophils and their precursors (≥10%); dysgranulopoiesis; hypercellular bone marrow (BM) with granulocytic proliferation and dysplasia; minimal or absent absolute basophils (< 2% of leucocytes) or monocytosis (< 10% of leucocytes); less than 20% blasts in the blood and BM; the absence of rearrangement of BCR-ABL1, PDGFRA, PDGFRB, FGFR1 or PCM1-JAK2 and not meeting criteria for Polycythemia Vera, Essential Thrombocythemia or Primary Myelofibrosis [2-4].

Currently, no standard of care has been clearly defined for the treatment of aCML. Adverse prognostic factors include: age >65 years, female gender, leukocytosis >50.10^9/L, peripheral blood myeloid precursors (≥10%) and the presence of SETBP1 mutations. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the only curative option, particularly in younger patients with high-risk disease features at the time of diagnosis [5-9].

We describe here a 42-year-old man who was seen in consultation in June 2016 for pallor and splenomegaly, leukocytosis of 39.10^9/L, platelet count: 82.10^9/L and haemoglobin of 10.8 g/dL. Morphologic evaluation of peripheral blood smear noted a myelemia with 54% of myelocytes, and metamyelocytes without basophils or monocytes. BM analysis revealed hypercellularity, granulocytic hyperplasia and dysplasia. Polymerase chain reaction for BCR-ABL1 was negative and cytogenetics analysis by FISH showed trisomy 22 and no Philadelphia chromosome. Abnormal-related mutations were not done. He was diagnosed as aCML and was given hydroxyurea. The evolution was marked by the fall of the WBC and the complete reduction of the size of the spleen. No HLA-matched related donor was identified and 18 months after diagnosis (December 2017), the patient received haploidentical allo-HSCT using his brother as the donor. He received G-CSF mobilized peripheral blood stem cell as a graft (CD 34 cell counts: $6.41x10^6$/kg) after TBF myeloablative conditioning regimen with associated thiotepa 5 mg/kg on days -6 and -5 (total dose 10 mg/kg), fludarabine 50 mg/m^2 on days -4,-3, and -2 (total dose 150 mg/m^2), and busilvex 3.2 mg/kg on days -4,-3, and -2 (total dose 9.6 mg/kg). GVHD prophylaxis consisted of post-transplant cyclophosphamide (PTCy) 50 mg/kg on day +3 and +5, cyclosporine given from day 0 to day +180 and MMF (15 mg/kg q12h) from day +1 to day +28. Time required to achieve a granulocyte

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count greater than $0.5x10^9$/l was 15 days. No complications noted: severe infection, cytomegalovirus reactivation, acute or chronic graft versus host disease. The patient remained free of disease after 4 years of follow-up (December 2021), healthy, complete clinical, immunologic and hematologic recovery, and fully donor chimerism without signs of aCML. Allo-HSCT is considered as the only curative option for aCML. No case was reported in the data available for haploidentical transplantation with PTCy, certainly due to the low disease incidence.

Conflicts of Interest

None.

Ethical Approval

None.

Consent to Participate

Informed consent has been obtained from the patient for publication of this report.

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