Editorial Note on Acute Myeloid Leukaemia in the Elderly

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Editorial

Acute myeloid leukaemia (AML) is a clonal disorder which is characterized by differentiation blockade and rapid proliferation of myeloid primitive cells (hematopoietic stem cells (HSC), lymphoid/myeloid progenitors, and myeloid precursors) as a result of regular hematopoiesis programmes trans-formation. It is the most prevalent acute leukaemia in adulthood, and its frequency increases with age, with 3 to 4 occurrences per 100,000 people worldwide each year. The median age at AML diagnosis is estimated to be over 60 years old. The disease, known as blasts, is characterised by the accumulation of undifferentiated myeloid cells in the bone marrow (BM) (>20 percent) and peripheral blood of patients, resulting in altered hematopoiesis associated with anaemia, thrombocytopenia, neutropenia, and immunodeficiency. AML was initially classified into cytomorphological subtypes based on the affected myeloid lineage (monocytes, red blood cells, platelets, and granulocytes) and maturation stage (myeloblastic, promyelocytic, erythrocytic, myelomonocytic, monoblastic, monocytic, and megakaryocytic).

However, a molecular classification based on the cytogenetic changes found in leukemic blasts has been adopted. There were some abnormal karyotypes with chromosome translocations, duplications, or deletions, as well as different patterns of mutations affecting genes involved in hematopoietic cell proliferation and differentiation. Although 50% of patients have a normal karyotype, the combination of mutations associated with an aberrant karyotype can be complicated. The treatment prognosis of such AML patients can be classified into three groups: favourable, intermediate, and unfavourable. There are six types of AML, according to the World Health Organization (WHO): those with recurrent genetic abnormalities, those with myelodysplastic syndrome-related features, those that are therapy-related, those that are not otherwise specified, those that are myeloid sarcoma-associated, and those that are myeloid proliferations related to Down syndrome.

Adult's first-line treatment for AML consists primarily of chemotherapy agents (particularly cytarabine and anthracyclines–doxorubicin and daunorubicin) or allogeneic hematopoietic stem cell transplantation (all o-HSCT). In patients younger than 60 years old, intensive chemotherapy induction and consolidation phases result in 50% complete remission (RC) (5% blasts in the BM). Clinical responses are more unsavoury in patients over the age of 60, with poor overall survival. When present, cytogenetic abnormalities (mutations and/or gene fusions) can aid in the detection of residual leukemic cells known as Minimal/Measurable Residual Disease (MRD) after treatment. This latter, however, is not always predictive of disease progression, and relapses can occur in 50% of cases between 2- and 48-months post-chemotherapy. Allo-HSCT is a treatment option for relapsed and refractory AML. However, high-risk mortality (30%) due to acute Graft-versus-Host Disease (aGvHD) in transplanted recipients complicates its use even further. Given the 5-year overall survival rates for AML patients (30%), there is an urgent need to develop new therapeutic strategies.

This exploration of molecular and cellular mechanisms which enable cancer cells to evade immune surveillance has paved the way for immunotherapy. Because this pathology primarily affects the elderly, this review will concentrate on cell lymphopoiesis and peripheral response during AML and ageing. We discuss how leukemic cells can exacerbate age-related thymic involution and peripheral T-cell senescence, as well as the current strategy and challenges in developing immunotherapy-based approaches for treating AML patients.

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