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Letter to the Editor

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Controversies in the Management of Ischemic Cerebrovascular Accidents in Patients With Non-Promyelocytic Acute Myeloid Leukemia

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To the Editor

Acute myeloid leukemia (AML) is the most common acute leukemia in adults and is an aggressive disease, characterized by the uncontrolled expansion and proliferation of poorly differentiated cells of the myeloid lineage [1, 2]. Hyperleukocytosis, defined as a white blood cell (WBC) count of > 100×10^9/L, can be the result of an excessive production of undifferentiated myeloid blasts and can occur in up to 13% of patients with AML [3]. It is associated with an increased risk of leukostasis, which is considered a hematologic emergency [4]. Elevated blood viscosity and the inability of leukemic white cells to properly deform to adequately traverse microcirculation results in obstructive thrombi and impaired perfusion, particularly in organs with extensive microvasculature, such as the brain [5, 6]. Furthermore, high oxygen consumption and demand promote local tissue hypoxia, resulting in acute cerebral infarctions [5].

Thrombotic evens in AML can occur in up to 15% [7]. The pathophysiology of ischemic strokes in AML patients differs markedly compared to non-cancer patients and can be multifactorial, depending on both the characteristic of the disease and its treatment [7]. Leukemic cells are known to produce and secrete pro-inflammatory cytokines, promoting a pro-thrombotic and hypercoagulable state, and through direct interaction with the endothelium contributing to endothelial dysfunction and thrombosis [6, 8]. In fact, chemotherapy-induced cell lysis can result in the release of pro-coagulant factors, increasing the risk of thrombotic evens in AML patients [8]. Further risk factors for thrombotic events include co-morbidities, age, sex and the use of hematopoietic growth factors [8].

While the management of ischemic strokes in non-cancer patients with fibrinolytic therapy has proven beneficial within the therapeutic window of 4.5 h [9], the management of acute ischemic strokes in AML patients with leukostasis poses a challenge, since there are no guidelines or recommendations on the optimal approach in the acute setting.

Due to bone marrow failure, many AML patients may have thrombocytopenia. One major concern for the administration of aspirin or fibrinolytic therapy in those patients is the increased risk of intracranial bleeding [10, 11].

Recommended approaches to leukostasis in AML patients include the administration of cytoreductive therapies consisting of hydroxyurea or cytarabine or the mechanical removal of leukemic cells via leukapheresis [3]. However, none of those modalities have been investigated for the management of acute ischemic strokes in AML patients in the acute setting.

Hydroxyurea and cytarabine may take several days to reach their maximum effects, and thus, may not be suitable in the setting of acute life-threatening leukostasis, considering the fact that the therapeutic window for the management of ischemic strokes lies within 4.5 h [11]. Moreover, rapid count reduction may also place patients at increased risk of tumor lysis syndrome and consequent renal failure [12].

The use of leukapheresis for the management of leukostasis in the setting of acute ischemic strokes has not been evaluated and its use is center-dependent and may not be available in every hospital.

While literature has shown that the use of antithrombotic agents for the prevention of thrombotic events in thrombocytopenic AML patients with atrial fibrillation can be safe, little is known about the use of fibrinolytic and anti-thrombotic agents in the management of ischemic strokes in the acute setting.

The paucity of literature addressing this issue indicates the necessity of more research to determine the optimal therapeutic strategy in this high-risk patient population. Considering the high overall mortality, it is imperative to balance the benefits of thrombolysis versus the hemorrhagic risk due to the underlying disease- and chemotherapy-induced thrombocytopenia [8].

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Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Author Contributions

RB wrote the manuscript; RK read and approved the manuscript.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Abbreviations

AML: acute myeloid leukemia; WBC: white blood cell

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