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Perspective

The Pathological Features of *FLT3* Alterations in Individuals with Acute Myeloid Cells

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DESCRIPTION

AML is a deadly and aggressive illness. *FLT3* mutations are linked to a poor prognosis in AML, which results in over 100,000 AML-related fatalities and about 120.000 new cases annually worldwide. A retrospective analysis was conducted on 149 patients, ages 20-95, who received an AML diagnosis in our clinic and had *FLT3* mutations. In 87.2% of these instances, relapse/refractory illness was discovered, and in 25.5%, *FLT3* mutation. 35.2% of cases with mutation-positive results had a *FLT3-TKD* mutation and 65.8% had a *FLT3-ITD* mutation. 38 patients in our study who had recently been diagnosed with *FLT3* mutations were treated with chemotherapy and *FLT3* inhibitors, such as sunitinib, sorafenib, and midostaurin; of these patients, 76.3% (n:29) had received midostaurin. Individuals with *FLT3-TKD* mutation had a greater death rate than those with *FLT3-ITD* mutation. Patients who got both midostaurin and chemotherapy had a 2.0-fold increased risk of death compared to the control group, which was primarily made up of patients who had relapsed or were resistant to treatment. All patients had a cumulative death rate of 66.4% and a median overall survival of 44.8 months. Higher mortality was linked to increasing age (HR: 1.03; p<0.001), having a *FLT3* mutation (HR: 1.82; p=0.007), and having relapse/refractory disease (HR: 23.66; p=0.002). Patients who received allogeneic stem cell transplantation had a reduced mortality risk (HR: 0.19; p<0.001). The existence of the *FLT3* mutation had a negative impact on survival when the survival rate was examined in relation to the mutation (HR: 1.82). The hematological system's unchecked clonal expansion of myeloid stem cells gives rise to the tumor known as Acute Myeloid Leukemia (AML). Adult AML is a frequent cancer. According to data from the American Cancer Society (ACS), there were 20.240 new cases of AML in the US in 2021 (11,230 male cases and 9010 female cases). Numerous factors have been found to influence the prognosis in AML. Among them include advanced age, high-risk molecular markers, and high-risk cytogenetic profile. A poor prognosis has been linked to the presence of *FLT3* and *TP53* mutant status, which are regarded as high-risk molecular markers. Additionally, the prognosis for individuals with refractory or relapsing (R/R) AML is dismal, and remission is extremely difficult to achieve in these people. Making the best possible treatment decisions for AML also heavily depends on knowing the prognosis. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) has become the primary curative therapeutic strategy for individuals with a dismal prognosis. AML is a bone marrow malignancy where clonal proliferation of myeloid cell progenitors occurs. The increase of immature blastic cells in the bone marrow during the early stages of hematopoiesis might because symptoms linked to anemia and thrombocytopenia. The most common signs of bone marrow failure include fever, hemorrhage, and malaise. Compression and pain are other symptoms that may arise from blastic cell infiltration into different organs. In affluent nations and among Caucasians, people of advanced age are more likely to be diagnosed with AML. All age groups are affected by the disease, even though the typical age of onset is about 70. The disease has a significant mortality rate; it is predicted that 11.540 deaths in the US would result from it in 2022. Clinical trials are required to improve treatment because the current chemotherapy regimens intended for the treatment of AML are only effective in a limited percentage of patients. Studies on CNS involvement in AML are scarce in comparison to ALL. According to a study on CNS involvement in AML, patients with *FLT3* mutations showed higher levels of CNS involvement and higher LDH levels. In our investigation, patients with FLT3 mutations showed greater CNS involvement (15.7% *vs* 0.3%; p=0.004) than patients without mutations. Patients with CNS involvement had a greater death risk (HR: 2, 13; p<0.001). We propose that CNS positive has a negative impact on AML patient's prognosis.

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