

Common WBC Disorders in the Elderly

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Population of older people is progressively increasing throughout the world. Aging is associated with marked increases in a number of diseases, especially neoplasms. The overall outcome of elderly with malignancy is worse than that of younger patients due to more comorbid illness, less able to tolerate intensive cytotoxic chemotherapy and increased risk of systemic infections. Acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), myelodysplastic syndromes (MDS), multiple myeloma (MM) and diffuse large B-cell lymphoma (DLBCL) comprise common WBC disorders in the elderly. The incidence of these diseases increasing with age and the median age of them are mostly above 60 years.

Clinical symptoms related to AML are caused by bone marrow failure and tissue infiltration. High-dose chemotherapy and aggressive therapeutic options such as hematopoietic stem cell transplantation (HSCT) those are effective in treating younger AML are not always beneficial to most elderly. Combination of anthracycline and cytarabine as induction, followed by consolidation with difference dose cytarabine are mostly used, however, long term survival is still disappointed. Elderly patients with good performance status are candidates for more intensive treatment (including nonmyeloablative HSCT) and are likely to get better survival. For patients unfit to intensive therapy, low-intensive therapy (e.g. low dose cytarabine) appears to be superior to palliative treatment.

MDS are characterized by pancytopenia, dysplasia in myeloid series, and ineffective hematopoiesis. Although inevitable, progression to AML varies between different risk groups. Allogeneic HSCT is the only way to cure MDS but is usually unfit to elderly patients. Less intensive chemotherapy, blood transfusion with iron chelation, infection control and life quality improvement seem to be the optimal strategies in physically unfit elderly. Few novel agents are recently used in MDS. Hypomethylating agents, 5-azacytidine (Vidaza®) and decitabine (Dacogen®) are able to prolong time to AML progression and overall survival in high-risk MDS. Lenalidomide (Revlimid®) is effective for del5q syndrome.

The incidence of CLL in Western countries is higher than that in Taiwan. Although regarding as indolent disease, their clinical features are extremely variable. Recent advance in chemo-immunotherapy and novel agents demonstrated excellent outcome in CLL. However, physician should decide the timing of treatment initiation cautiously and assess the physical fitness and comorbidity before intervention. The treatment goals may vary from long-lasting remission to symptomatic palliation. The importance of response rate and quality of life should be weighed equally.

MM should be suspected in elderly who have unexplained anemia, renal insufficiency and bone pain. Treatment of MM has changed substantially due to novel drugs development but should

be initiated only in symptomatic patients. Induction with 2- or 3- drugs regimen followed by autologous HSCT is now widely used among younger and physically fit elderly patients. In unfit and frail patients, frontline therapy has shifted from traditional melphalan and prednisolone (M+P) to M+P plus new agents, such as thalidomide (MPT), bortezomib (MPV) or lenalidomide (MPR). Bisphosphonates such as pamidronate and zoledronic acid are widely used to reduce bone events, however, patients should receive dental evaluation before therapy to avoid osteonecrosis of jaw.

Today, rituximab plus CHOP (R-CHOP) regimen is standard of care in DLBCL treatment. LNH-98.5 study recently demonstrated 10-year PFS and OS was 36.5% and 43.5% respectively, which are much better than pre-rituximab era. Before initiation of R-CHOP, physicians should be aware of the comorbidities and organ dysfunctions which may render elderly more susceptible to toxicities. Supportive care, such as G-CSF and infection prophylaxis play important roles to reduce treatment related morbidities. There is no standard treatment for unfit and frail patients. Less toxic regimens should be considered.