

Venue: PYRAMID 1
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1515-1630 hr

Symposium 2B: Recent advances in blood cancers

S2B-1. The diagnosis and treatment of natural killer cell malignancies

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Natural killer (NK) cell malignancies are uncommon diseases. Previously known as polymorphic reticulosis or angiocentric T-cell lymphomas, they are classified by the World Health Organization as NK/T cell lymphoma, nasal type, and aggressive NK-cell leukemia. They are prevalent in Asia and South America, but exceptionally rare in western countries. Pathologically, NK-cell lymphomas show a polymorphic neoplastic infiltrate with an angioinvasive and angiodestructive pattern. Lymphoma cells are characteristically CD2+, surface CD3-, cytoplasmic CD3+, and CD56+. Cytotoxic markers such as TIA-1, granzyme B and perforin may also be expressed. T-cell receptor gene is germline in configuration. There is almost invariable infection of the lymphoma cells by Epstein-Barr virus (EBV), which is present in a clonal episomal form. Clinically, they can be divided into nasal, non-nasal, and aggressive lymphoma / leukemia subtypes. Most nasal NK-cell lymphomas present with stage I/II disease, and frontline radiotherapy is the most important key to successful treatment. Many stage I/II patients treated with radiotherapy fail systemically, implying that concomitant chemotherapy may be needed. Chemotherapy is indicated for advanced nasal NK-cell lymphoma, and the non-nasal and aggressive subtypes. However, treatment results are unsatisfactory, which may partly be due to the expression of high levels of P-glycoprotein in the lymphoma cells. Therefore, stratification of patients according to risk factors may be important in the overall treatment strategy. The International Prognostic Index and other prognostic indices have been found to be predictive of outcome. Quantification of circulating EBV DNA is a reliable surrogate marker of lymphoma load, which is useful in the monitoring of treatment outcome. Combination chemotherapy with drugs unaffected by P-glycoprotein has shown promise in the treatment of advanced and refractory diseases. The role of high dose chemotherapy with hematopoietic stem cell transplantation is unclear, as the optimal conditioning regimen remains undefined.

S2B-2. The bone marrow differential count: uncertainties and unknowns

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The bone marrow (BM) differential count is a critical parameter in the management of patients with the myelodysplastic syndromes (MDS) and leukaemias. It is expressed as a percentage of the total nucleated cell count in the routine, manual BM nucleated differential cell count (NDC). The NDC is subject to wide variability due to errors of imprecision, inaccuracy and uncertainty, as well as the inevitable dilution of the BM aspirate by peripheral blood nucleated cells (PBNC). Imprecision arises from sampling errors and the non-random distribution of cell types in smears, whereas inaccuracy arises from observer variation in the recognition of BM cells. Virtual slides may enable BM quality assurance exercises to improve accuracy. A partial nucleated differential count (PNDC) that enumerates only immature haemopoietic cells is independent of PBNC dilution and can be determined in dilute BM samples. It alters the disease category in a significant proportion of BM aspirates with MDS and has the potential to better stratify MDS to improve clinical outcomes and treatment.

S2B-3. How curable is the low grade indolent lymphoma?

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The discussion of this disease entity will be confined mainly to the more lymph node base disease that include the Follicular Center cell tumour (all the three grades), the Diffuse small cell Follicular Center Lymphoma, Marginal zone B cell lymphoma, Small Lymphocytic Leukemia/ Lymphoma, Lymphoplasmacytic Lymphoma, Lymphoepithelioid Lymphoma, and some of the Cutaneous/ Periphery T cell Lymphoma. According to the Follicular Lymphoma International Prognostic Index (FLIPI), five parameters have been identified that divided the patient group into three, which is the Low, Intermediate and the High risk groups. The significant parameters are the age of patient (over vs below 60 years old), stage of disease (III- IV vs I and II), Hb levels ($>12\text{gm/dl}$ vs $<12\text{gms/dl}$), numbers of nodal involvement (<4 vs >4 regions), and the blood LDH level (above and below normal level). Patients with high risk disease (those with more than 3 adverse factors) have median survival of slightly over 5 years, and the 35.5% chance of surviving 10years, indicating that the disease is lethal in a significant proportion of the patients with a supposedly indolent disease. Past strategies relying mostly on cytotoxic agents have seen mixed results in inducing remission but no real improvement in prolonging the survival of the patient population as a whole. Three European Phase III high dose Autologous Myeloablative treatment vs Conventional dose chemotherapy yielded one positive result (GLSG 64.7 vs 33.3%, 5 years EFS, $p<0.0001$), one borderline (GOELAMS 60 vs 48%, 5 years EFS, $p=0.05$) and one negative result (GELA 45vs 36%, 7 years EFS, $p=0.5$). The adequacy of the follow up period might be debatable, nevertheless the findings implied that cytotoxic drugs on its own often failed to eradicate residual disease and induced cure in majority of patients with Indolent Lymphoma. The introduction of anti- CD 20 antibody Rituximab in 1995 and subsequently radioactive tagged anti- CD20 antibody (Zavelin) provide novel agents that can be added to the chemotherapy. The combination appeared to synergize the therapeutic efficacy of the chemotherapy in the treatment of Indolent Lymphoma. This combination has produced higher remission rate and more durable remission period in most trials, however the follow up periods are often relatively short when compared with the natural history of the Indolent Lymphoma (Hiddemann et al, Marcus et al, Herold et al, salles et al, Hochster et al). Nevertheless it marks a departure from the past strategy, and showing the possibility of novel approach that confirms the evolutionary improvement in the results of the treatment. Future new direction in my opinion is shown by three important recent developments that could provide significant change to the way Indolent Lymphoma is being managed. First is the use of microarray technology that revealed the genotypic differences among what seemingly looked like homogenous group of disease. Secondly, is the uncovering of Hepatitis C virus in the pathogenesis of the Indolent Lymphoma and the positive response the disease shown when treated with antiviral agent in some of these patients. Lastly is the confirmation on the importance of the microenvironment in the progression of the lymphoproliferative process. This will no doubt opening up new therapeutic targets that could potentially has profound effects on the outcome of the treatment. The evolutionary change that mirrored our understanding on the pathobiology of this lymphoproliferative disorder has set a promising path towards an ultimate cure for this prevalent illness.