solid tumors simultaneously with the effusion or during the course of disease. Almost 100% of these cases are HIV+, the tumor cells are HHV8+, and more than 2/3 of the cases are EBV+. The malignant cells resemble immunoblasts and sometimes they show plasmacytoid differentiation. Half of the patients express CD45R (LCA) and 20% express CD20 (pan-B). They can also express CD38, a marker of plamocytes. The present discussion about PEL is the finding of several solid tumors with similar characteristics, HHV8+, but without effusion during the whole course of disease. Knowles, Chadburn and Cesarman's group support the idea that these cases are inside the PEL spectrum and that they should be classified as extra-cavitary variant of the PEL. On the other hand, the plasmablastic lymphoma, EBV+ and HHV8- described originally from the oral mucosa, which is a solid tumor with no effusion, has been found in other sites like nasal and paranasal sinuses, testicle, bone and anorectal regions and a few are HHV8+. Morphologically, the plasmablastic lymphoma is very similar to PEL. The malignant cells have plasmablastic differentiation (an immunoblast with plasmacytoid differentiation), in other terms they are similar to immunoblasts, large cells with vesicular nucleus and a prominent nucleolus that usually do not express normal B cell markers such as CD20, but express plasmacytoid differentiation markers such as CD38. Even the immunocytochemical profile is similar to PEL. The situation is complicated by a recent publication of HIV patients with multiple mieloma developing extramedular solid tumors with plasmablasts of similar morphology to PEL and plasmablastic lymphoma. In conclusion, patients with AIDS can present lymphomas with plasmablastic differentiation, associated or not to HHV8, generally EBV+ that sometimes present with cavitary effusion, some other times are solid tumors or even mixed. If they are part of the spectrum of the same lymphoma or distinct entities, it is not quite clear. With the present knowledge, I believe that it is too soon to classify these lymphomas, before more is known about them. To designate a solid tumor as a solid variant of effusion primary lymphoma, looks to me farfetched and does not contribute to clarify the disease. The role of HHV8 and EBV in the genesis of these lymphomas with plasmablastic differentiation need further studies.

Aggressive Non-Hodgkin's Lymphoma – Therapeutic Considerations of Pre Rituximab Era

Carmino Antônio de Souza

Lymphomas have been known as one of the most responsive malignancies to chemotherapy. They are frequently subdivided on Hodgkin's Disease (HD) and Non-Hodgkin's Lymphoma (NHL). Lymphomas are heterogeneous clonal malignancies that have been classified in different ways. For the REAL classification, each disease is defined as a different entity based on the morphology integration, immunephenotypic and genetics aspects, clinical behavior and the original cell. Most patients with localized disease, stage I and II (*Ann Arbor Classification*), cure with conventional doses of chemotherapy (CTX) or CTX + radiotherapy (RTX) - 75% of 5 years disease-free-survival (DFS). Those with advanced disease (stage III and IV) have less favorable results, the complete remission rate (RR) is nearly 50%, but only 2/3 of the patients will be free of disease. The long term DFS for these patients is around 40 to 50% with polichemotherapy. Regimens with antracyclines, specifically CHOP (cyclophosphamide (CY), doxorubicin, vincristine, e prednisone), have been the main approach for aggressive lymphomas since 1970. 70 to 80% of the patients will respond to CHOP. The long term cure rate with CHOP is around 35% and there are no evidences that second and third generation regimens are more efficient. FISHER, in 1993 did not find difference in the survival and response rates comparing CHOP, m-BACOD, Promace-Cytabom and MACOP-B, although the CHOP protocol was cheapest and less toxic. GORDON, SERTOLI e COOPER also did not show that regimens like m-BACOD, MACOP-B, e ProMACE-MOPP, have better results than CHOP on the treatment of intermediate and high grade lymphomas. It is generally accepted that patients with intermediate and high grade lymphomas that relapse after initial therapy have a reserved prognostic and the additional

chemotherapy rarely induces a second long term remission. Relapses of lymphoma will occur in 40% of the cases, after induction therapy; refractory disease is seen in 10 to 20% of the patients. Rescue therapy with CTX including cytostatic agents, normally not used as first line therapy was introduced as an attempt to rescue these patients. Salvage therapy with chemotherapy regimens like DHAP (dexamethasone, cytarabine, cisplatin); ESHAP (etoposide phosphate, methylprednisolone, cytarabine, cisplatine); IMVP-16 (mesna, ifosfamida, metrotrexate, etoposide phosphate) gives complete remission rates ranging from 10 to 37%, but 2-years survival of 25%. A review of approximately 700 young patients with advanced diffuse large cells lymphoma, treated with rescue chemotherapy in 29 different trials, showed a 2-years DFS lower than 5%. In 1987, PHILIP said that the experience acquired with Burkitt Lymphoma showed that these lymphomas still could be responsive to CTX with intensified doses. The combination of large dose CTX and rescue with bone marrow autologous transplant was considered promissory. This multi-institutional study included 100 patients with primarily refractory lymphomas, with sensitive or resistant relapse. The DFS was 0% at the primarily refractory group, 14% at the resistant relapsed group, and 36% at the sensitive relapsed group.

The Role of the Autologous Transplant

The objective of the high dose therapy with support of bone marrow autologous transplantation or peripheral progenitor cells is to overcome the resistant tumor cell, through cytotoxic drugs in mieloablative dosage. Several clinical studies with relapsed or refractory aggressive lymphomas have been done using high dose CTX and rescue with bone marrow autologous transplant or peripheral blood progenitor cells (PBPC). These studies demonstrate benefits with patients with chemo sensitive disease. Most studies used BEAM protocol as induction and PBPC infusion as rescue. The global survival rates, for 2 to 5 years, ranged from 60% to 30%. 2-years and 5-years DFS ranged from 51% to 27% and the event-free-survival ranged from 48% to 26%. These studies presented mortality rates associated with the procedure, ranging from 2.5% to 15% and this still shows high relapse rates after transplantation (35% to 57%). Some controlled, prospective and randomized studies compared the ASCT results and conventional CTX as rescue therapeutic at “slow” responders, with no significant differences in terms of survival rates. In 1995, PHILIP proved the superiority of the ASCT strategy as compared with DHAP protocol, for chemo sensitive patients, as a rescue therapy. The authors demonstrated survival rates of 53% for ASCT and 32% for DHAP rescue (p=0.038).

Prognostic Factors

Many prognostic factors has been identified, and associated to the treatment used for lymphomas. In 1993, the International Non-Hodgkin’s Lymphoma Prognostic Factors Project proposed a system of international prognostic index (IPI). It was studied the clinical characteristics of 3,273 patients with large cells, immunoblastic and mixed diffuse lymphoma, treated with doxorubicin regimens. The risk factors considered independent and adjusted by the age were: lactic dehidrogenase (LDH), “Performance Status” (according WHO) and stages III and IV (Ann Arbor) (SHIPP et al, 1993). This classification system is extremely helpful for a better therapeutic indication, following the disease risk. The IPI divides patients at diagnosis in four risk groups: low, intermediate-low, high-intermediate, and high, with global survival rates projected, in 5 years, from 73%, 51%, 43% e 26%, respectively, independent of age. For patients with less than 60 years, survival rates of 83%, 69%, 46%, e 32%, respectively. For patients with more

than 60, the global survival rates were 56%, 44%, 37%, and 21%. The increased experience with the autologous transplant for the Non-Hodgkin's lymphomas treatment has identified prognostic factors for this therapeutic modality result. These factors are useful in determining the transplant situation, as so the selection of the patients that will benefit most with the procedure. The sensitivity to treatment before the transplant is the most important factor associated with the transplant results, for relapsed or refractory aggressive lymphomas patients. In 1987, PHILIP demonstrated the importance of autologous transplant as salvage treatment of aggressive Non-Hodgkin's lymphomas. Patients with sensitive relapsed tumors have significantly higher survival rates than those with resistant (3-years DFS 36% vs. 14%; $p<0.003$). The complete remission with initial CTX was the most important factor for the result after the transplant (3-years DFS, 30% vs. 0%; $p<0.001$). Another important prognostic factor is associated with the previous treatment extension. In 1993, VOSE demonstrated that patients receiving more than three CTX schemas before the transplant have worst results, in terms of global response and survival rates. Other adverse prognostic factors include high LDH levels, number of extra-nodal disease and presence of bulky tumor masses.

Research Nurse: New Duties Related to Clinical Trials. Experience of Clinical Research in Oncovirology in Bahia/Brazil

Milena Bastos, Estela Luz

The clinical research can be defined as all investigation processes involving human beings to search new knowledge about drugs, procedures and methods solving problems to prevent, diagnose or cure diseases. This relates ultimately with human protection. Ethics in research field matured enormously in the last 50 years, mainly after the II World War with the landmark Nuremberg Code. After this, followed 7 declarations from 1964 to 2000 from the WMA Declaration of Helsinki - Recommendations guiding physicians in biomedical research involving human subjects; Belmont's Report (1979) and the Common Rule; Code of Federal Regulations / ICH Guidelines (2000). In Brazil, there are 3 main ethics declarations: MS/RDC/196/96, 251/97 and 292/99. All those follow the international principles in research ethics. After implementation of that rules, Brazil has received an increasing support on clinical research, which has required an insertion of different professionals in the different parts of the studies. As a result, the research nurse figure is growing mostly because of their vision of the subject with singular requirements moreover their high clinical and administrative skills. Legislation, however, is not following the pace of changing and no specific rules are found in Brazil for the research nurse, differently from the US allows to the research nurse a wide range of clinical activities, including prescriptions of specific drugs. The research nurse must have good knowledge of clinics, managerial vision, logistic skills and to be a clever trader. Besides that, they must have a profound knowledge on research ethics and the scientific methodology helping the researchers to improve the study design and documentation. Their present formal activities ranges from monitoring, manager, study coordinator, data / drug controller to clinical assistant. In Bahia, in the last 3 years, we began to study patients with virus related malignancies, involving teams from infectious diseases, hematology and pathology departments. We as research nurses have centralized our activities in link the national and international institutions involved; locate possible patients after medical suspicion; speed diagnosis and patients acceptance of their pathology, comforting them; compile data of clinical and laboratory history; speed treatment; and in the maintenance of data and specimen bank.