40 from German children. The expression of EBV gene products was studied by in situ hybridization for EBER. EBV positive tumor cells were found in 87% (47/54) pediatric BL. An unexpected expression of latent membrane protein (LMP) -1 of EBV was observed in the neighborhood of Schistosoma mansoni granulomas and scars. The frequency of EBV infection was higher in pediatric (87%) than in adulthood HL (55%) in the same area (p <0.005). The EBV-infection was related more frequently to LNH occurring in AIDS patients than in immunocompetent patients (p=0.002). The overall EBV infection rate in Bahian and German tonsils was similar (50 per cent of Bahian and 45 per cent of German tonsils). However, a significantly higher number of EBER-positive lymphoid cells were found in the germinal centers (GCs) of 8/20 EBV-positive tonsils from Brazil, while only 3/18 tonsils from Germany displayed a few EBER positive cells (1-9 cells/GC; mean: 0.5 cell/GC per case) in this compartment (p <0.007). In addition, in two cases the EBV-infected GC cells in Bahian samples expressed an oncogenic protein, the EBV-encoded latent membrane protein (LMP)-1, findings not present in German samples. In conclusion, we shown a high frequency of EBV-associated lymphoma in pediatric and AIDS patients and therefore EBV-infection may play a major role in the lymphomagenesis in these groups. Since BL and HL are derived from GC cells, the similar rate of EBV-infection in pediatric BL and HL corroborate the hypothesis that the pattern of EBV-infection in GC may be related to the development of these lymphomas in developing areas. This study was supported by CNPq, Brazil and Deutsche Forschungsgemeinschaft.

**Burkitt non-Hodgkin Lymphoma in Childhood**

José Henrique Barreto

Burkitt’s Non-Hodgkin Lymphoma (B-NHL) has a high incidence at Equatorial Africa. It is endemic and associated with the Epstein-Barr Virus (EBV) infection. AIDS pandemic has increased the incidence of this neoplasia that has a close relationship with the EBV infection. In New Guinea the Burkitt’s Lymphoma is highly associated with EBV and this association seems to be similar to those found in some regions of Latin America, which has similar socioeconomics and climatic conditions. An example of that is the Bahia State (and other regions of the Northeast) that shows a higher frequency of Burkitt’s lymphoma associated to EBV than Southeast Brazilian states and Argentina. In the Brazilian Northeastern Region Burkitt’s lymphoma seems to have an intermediate frequency between sporadic and endemic types. The high incidence of abdominal presentation of Burkitt’s lymphoma (as opposed to the jaws presentation, in North of Africa) suggests common mechanisms that still need to be elucidated. The high incidence of Burkitt’s lymphoma in children is similar to those found in other reports. Apparently a better immunologic control as the child grows decrease the number of EBV infected cells, target of neoplastic transformation.

The treatment in the majority of the Brazilian centers is in accordance to the Brazilian Cooperative Group for Childhood Lymphomas Treatment, protocol NHL 2000. In prognostic terms, is expected that clinical remission of 90% of low risk B cells NHL and 70% to 80% for the high risk B cells NHL. From January 2000 to September 2004, 76 NHL patients between 0 and 19 years old were evaluated. The mean age was 8.1 years (range 2-16yrs). There were 49 male and 27 female patients. 14 patients were white and 11 black 51 mixed. 39.5% of the patients came from the rural areas. 44 (57.8%) have B-NHL, 17 (22.4%) T lymphomas, 9 (11.4%) large-cells anaplastic lymphomas, 5 (6.6%) large-cells diffuse lymphomas and 1 (1.3) nasal angiocentric lymphoma. The most frequent symptoms were abdominal pain (23), followed by increased abdominal volume (14) and cervical tumors (14). Other related symptoms were abdominal tumor (7), dispnea (6), cough (3) and vomiting (3). There were other less frequent symptoms related. The most affected region was abdomen (45; 59.2%), cervical (11; 14.5%), mediastine (13; 17.1%). Others were: nose, inguinal, mallar, oropharynx, paravertebral and testicle (1
case each). The presence of bone involvement was observed in 23.7% of the patients and 3.9% presented CNS involvement. Time to diagnosis ranged from 1 to 210 days (mean = 47.1 days). The mean LDH was 2,014 U/mL (range 91U to 36,599U). 51 patients had immunophenotyping, 23 confirmed B (Burkitt’s) NHL, 13 T NHL patients, 2 T anciocentric NHL patients (one nasal e one testicular), 2 mediastinal diffuse large cell NHL patients (B), 4 abdominal diffuse large cell NHL patients (B), 7 large cell anaplastic lymphoma patients (T). 51 (67.1%) patients are alive and with no evidence of disease, 22 (28.9%) were dead, 2 (2.6%) alive (but with short follow-up) and 1 patient was lost of follow-up. The causes of deaths were: progressive disease (13; 59.1%), sepsis (7; 31.8%) and deep venous thrombosis and cardiogenic shock (1; 4.5% each).

Treatment of B Non-Hodgkin’s Lymphoma in Children: The Experience of Multicentre Studies and Brazilian National Cancer Institute’s Experience

Claudete Klumb

Pediatric lymphomas are the third most common neoplasm in children and adolescents. Unlike lymphomas in adults, childhood non-Hodgkin’s lymphomas (NHL) are diffuse, aggressive neoplasms with a tendency to widespread dissemination. The outcome in childhood lymphoma non-Hodgkin’s (NHL) has improved steadily over the past decade through the incremental development of multiagent chemotherapeutics regimens. At present, 80-90% of children are cured with intensive risk-adapted chemotherapy. The most recent era advance is chemotherapy directed toward both stage and histology, an approach that has been validated in randomized multicenter clinical trials. Nevertheless, in developing countries there are many obstacles to treatment of childhood lymphomas. The most important are late diagnosis, low socioeconomic status and under-nourishment. In developing countries patients with these conditions may be at increased risk for therapy-related toxicity, including life-threatening infections.

In more recently trials, Patte et al. and Reiter et al., reported higher long term EFS in children with advanced stages of B-NHL using short intensive multiagent chemotherapy. However, the application of these regimens in developing countries may result in severe and life-threatening toxicity. Previously, our group reported 86.7% (SE=0.87) and 64% (SE=0.78) pEFS for children with early and advanced stage of non-lymphoblastic lymphoma, respectively. At that time, our results confirmed that a short duration therapy was effective to treat most children with non-lymphoblastic lymphoma in Brazil. Our following objective was to treat non-Hodgkin’s B cell lymphoma in children with manageable toxicity-related morbidity without detriment of survival results. Between January 1998 to April 2003, 53 consecutive patients (age ≤ 16 years), from National Cancer Institute, Brazil were stratified by risk factors (Stage and LDH level) and treated with BFM 86/90 (Berlin-Frankfurt-Münster) based protocol with reduction of methotrexate dose from 5 mg/m² to 2mg/m². The mean age of patients was 6 years (range: 1 to 16 years). Seventy 2% of patients had lymphomas classified as Burkitt type; 11% as diffuse large cell lymphoma, 6% as Burkitt-like lymphoma, and 11% were not classified. At a median follow-up time of 35 months 44 patients (83%) survive in complete remission. The event free survival for all patients was 78% (SE= 0.07), 100% (SE=0.0) for stage I/II patients, and 74% (SE= 0.08) for stage III/IV disease. Six patients suffered from initial treatment failure, 1 patient relapsed, all of whom died. There was only one death for sepsis related to treatment. This strategy was very effective for the treatment of B-NHL in setting of a developing country. Our results were comparable to BFM 90 study and other contemporary groups and represent an advance of the cure rates in childhood B-NHL from Brazil. However, despite dramatic improvements in the treatment of childhood NHL, approximately 20% of patients either do not achieve a complete remission, or develop recurrent disease. The identification of clinical and biologic features that are predictive of treatment failure may help in the development of more effective therapeutic strategies.