394 SUCCESSFUL DIAGNOSIS OF LYMPHOMA FROM CORE BIOPSES

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Background: Current BCSH guidelines recommend excision biopsy as the method of choice for diagnosis of lymphomas unless the node or mass is within an inaccessible area. Many case series have shown that diagnostic yield from core biopsies is extremely variable.

Method: We audited 2 patient groups with a final diagnosis of lymphoma, who underwent core biopsy by experienced operators using US or CT guidance at our institution. The first group, 55 new patients at a single centre knee lump clinic and the second, 52 new patients from a single intervention radiologist’s biopsy list. The nature of the final diagnostic biopsy and, where known, the size of the core was documented. Reporting was performed by a single specialist lymphoma pathologist.

Results: Of the 55 patients in group 1, 16 had Hodgkin lymphoma (HL) and 29 non-Hodgkin lymphoma (NHL). Seventy one percent (39/55) of initial core biopsies were diagnostic. Of these 15/39 had a final diagnosis of HL (8-NS, 5-MC, 2-other) and 24/39 had NHL (11-DLBCL, 8-FL, 2-CLL/SLL, 1-LPL, 1-MCL, 1-MLL). Within the non-diagnostic group 13/16 had a final diagnosis of HL (7-NS, 2-MC, 1-other) and 5/16 had NHL (2-FL, 1-MCL, 1-DLBCL, 1-PTCL); 14/16 required excision biopsy for final diagnosis. The median size of cores (169 needle) was 5mm in non diagnostic group and 17mm in the diagnostic group.

Of the 52 patients in group 2, 10 had HL and 42 NHL. Eighty five percent (44/52) of initial core biopsies were diagnostic. Biopsy sites included 12 extranodal, (5-lung, 1-small bowel, 1-thyroid, 1-liver, 2-soft tissue, muscle, 1-parotid) and 40 nodal (14-cervical, 22-deep abdominal, 3 mediastinal, 1-auxiliary). Within the diagnostic group 6/44 had HL (4-NS, 2-MC) and 38 had NHL (20-DLBCL, 9-FL, 3-MZL, 1-PTCL, 1-ALCL, 1-LPL, 2-PTLD, 1-CLG NHL). Within the non-diagnostic group 4/8 had a final diagnosis of HL (3-NS and 1-MC) and 4 had NHL (2-FL, 1-DLBCL, 1-PTCL). All 8 with non-diagnostic cores were re-biopsied: 5 excisional and 3 repeat core biopsies. The median size of cores was 13mm in the non-diagnostic group and 23mm in the diagnostic group. There was no morbidity incurred from any biopsy performed.

Conclusion: Core biopsy, especially of deep tissue masses, is a reasonable, safe approach to diagnosis of lymphoma and can avoid the need for anaesthetic and laparotomy. Operator expertise and adequate sample size, however, are essential to obtain a high diagnostic yield as in our series (83/107, 78% of cases). Diagnostic failure mainly arise in with node fibrosis in NSHL and when core specimens are small.

395 ARE THERE ANY SIGNIFICANT VARIATIONS IN THE CLINICAL OR HISTOLOGICAL PRESENTATION OF LYMPHOID PATHOLOGIES OVER THE COURSE OF TIME?

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Introduction: Little data is available concerning variations in the clinical characteristics of lymphoid pathologies at presentation. We decided to investigate whether any variations in these aspects had occurred in our environment during the last few years.

Materials and Methods: The GOTEL group database is an archive of all new lymphoid malignancies diagnosed at the Cancer Institute Hospital. All serum from the patients were separated and stored at -20°C after informed consent. All the histopathology samples were reviewed according to the WHO classification by expert hematopathologists. Recombinant His-tagged TRIM68 protein was made with cell-free system, Protemist®BDT, and adsorbed to 96-well plates. Serum were diluted at 1:100 with PBS (-), and put into the 96-well plates. After washing, goat anti-human (H-L) antibody was added, and the absorbance was determined at 450nm.

Results: Serum was collected from 254 patients (DLBCL 104 cases; FL 57 cases; MALT 9 cases; MCL 8 cases; BL 4 cases; CLL/SLL 2 cases; SMCL 2 cases; IL 15 cases; ATLL 4 cases; MM 21 cases; ALCL 3 cases; NK/T 3 cases; PTCL 10 cases; ATL 3 cases; AML 6 cases; CML 1 case; and other cancers 3 cases). Mean absorbance at 450nm (OD450) in DLBCL, MCL, B-LBL, CLL/SLL, SMCL, ALCL, MCL, NKT, and ATLL was higher than other hematological malignancies and others visited and were treated at the Cancer Institute Hospital. All the patients were separated and stored at -20°C after informed consent. The histopathology samples were reviewed according to the WHO classification by expert hematopathologists. Recombinant His-tagged TRIM68 protein was made with cell-free system, Protemist®BDT, and adsorbed to 96-well plates. Serum were diluted at 1:100 with PBS (-), and put into the 96-well plates. After washing, goat anti-human (H-L) antibody was added, and the absorbance was determined at 450nm.

Conclusion: Serum anti-TRIM68 autoantibody in lymphoid malignancies, especially aggressive lymphomas, was detected higher than other hematological malignancies and cancers. Serum anti-TRIM68 autoantibody may be as an indicator of aggressive or advanced lymphoma.

396 WITHDRAWN

397 HIGHER LEVEL OF SERUM ANTI-TRIM68 AUTOANTIBODY AS AN INDICATOR OF AGGRESSIVE OR ADVANCED LYMPHOMA

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Background: TRIM68 (Tripartite motif-containing protein 68) is a member of ring finger proteins, and E3 ligase for ubiquitination. It is also known as u56, whose autoantibody was detected in patients with AIDS, SLE, and Sjögren syndrome. Recently, incidence of DLBCL is increasing in the AIDS patients after developing HAAT therapy. To clarify relationship between development of lymphoma and anti-TRIM68 autoantibody, we examined if anti-TRIM68 autoantibody is detectable in lymphoma patients without AIDS.

Patients and Methods: From September 2008 to June 2010, 254 patients with hematological malignancies and others visited and were treated at the Cancer Institute Hospital. All serum from the patients were separated and stored at -20°C after informed consent. All the histopathology samples were reviewed according to the WHO classification by expert hematopathologists. Recombinant His-tagged TRIM68 protein was made with cell-free system, Protemist®BDT, and adsorbed to 96-well plates. Serum were diluted at 1:100 with PBS (-), and put into the 96-well plates. After washing, goat anti-human (H-L) antibody was added, and the absorbance was determined at 450nm.

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Conclusion: Serum anti-TRIM68 autoantibody in lymphoid malignancies, especially aggressive lymphomas, was detected higher than other hematological malignancies and cancers. Serum anti-TRIM68 autoantibody may be as an indicator of aggressive or advanced lymphoma.

398 FOLLICULAR LYMPHOMAS WITHOUT BCL2 REARRANGEMENT ARE HETEROGENEOUS CONCERNING THE HISTOLOGICAL GRADING AND GENETIC FEATURES

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Background: Follicular lymphoma (FL) is genetically characterized by BCL2/18q21 chromosomal translocation with one of the 3 immunoglobulin chain loci. The resulting upregulation of this anti-apoptotic oncogene is considered as an important genetic event in FL lymphomagenesis although not sufficient. However, ~15 FL are reported with a BCL2 germline (BCL2-G) status, mainly in grade 3B with a diffuse pattern. Alternative genetic events have been identified in FL with BCL2 rearrangement. The latter is also detected in ~20% of FL with BCL2 rearrangement and is linked with a worse prognosis. TNFRSF14 has been recently identified as a candidate gene.

An analysis was made of all the clinical variables collected, comparing their behaviour during the different diagnostic periods. Neither the period, gender, ECOG stage, LDH, ß2 microglobulin, Hodgkin’s or non-Hodgkin’s type neoplasia, B Lymphoma versus Hodgkin’s, NK or T nodal or extra-nodal origin, median age at diagnosis nor histological type by region of origin, showed any statistically significant differences in their distribution over the course of time.

Conclusion: In our experience, there are no significant variations in the clinical presentation or histological type in lymphomas diagnosed over the course of time in Spain.
Material: We report a series of 9 BCL2-G typical FL further characterized for BCL6/3q27,IGH/14q32,TNFRSF14/1p36.33 and mir34a/1p36.23 loci by FISH. The cases were selected after a morphologic review which excluded 2 borderline cases with marginal zone lymphoma. All 3 cases of DLBCL suspected to be transformed FL.

Results: The median age was 61 [56-58] yr-old. Sex ratio (M/F): 5 /1. The main site was nodal in 6 cases (inguinal: 3) and extra-nodal in 3 cases (bladder, pancreas, duodenum). It is noteworthy that the 5 patients with available data had previous toxic exposition (4 professional exposures and 1 previously treated cancer). There was no prevalence for grade 3 (4 gr 1, 2 gr 2a, 3 gr 2b, 1 unknown). The FLIPI was relatively low (4 professional exposures and 1 previously treated cancer). There was no bone marrow or GI tract. Four NOS patients died of lymphoma one month after progression, before any treatment. The other patients received chemotherapy and one of them died of sepsis. Currently five patients are alive, four in continuous CR (two in each group).

Discussion: In this series, BCL2-G FL appear to be relatively heterogeneous concerning morphological aspect (grade) and genetic characteristics. Previous toxic exposition was seen in most of the patients with available data. Higher resolution genomic studies are under process to identify common oncogenic pathways.

400 THE HISTOLOGIC SUBTYPE OF LARGE B-CELL LYMPHOMA PROGRESSION IN SPLENIC MARGINAL ZONE LYMPHOMA PATIENTS INFLUENCES CLINICAL COURSE AND PROGNOSIS

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Background: Splenic marginal zone lymphoma (SMZL) is an indolent extranodal B cell lymphoma which transforms to high-grade lymphoma in 10% of cases. The histological progression is usually represented by a diffuse large B cell lymphoma, not otherwise specified (DLBCL-nos), but, more rarely, it shows features of T-cell/histiocyte-rich large B cell lymphoma (TCIRBLC).

Aim: To retrospectively compare epidemiological, clinical, prognostic features and outcome of SMZL patients progressing to DLBCL-nos or to TCIRBLC.

Patients and Methods: From January 1995 to December 2010, 79 patients with SMZL were consecutively seen at our Institute. Their median age was 66 years. Twenty-two were in an advanced stage and 17 had B symptoms. Twelve patients (15.2%) progressed to high-grade lymphoma. Historically, five of them were classified as TCIRBLC, seven as DLBCL-nos. Clinical characteristics and outcome data of both groups were compared.

Results: Median age at diagnosis was 60 years in the TCIRBLC cases, and 73 in the NOS cases (p=0.01). Male/female ratio was 1.4 and 1.3, respectively. All patients had Ann Arbor’s III-IV stage. The NOS cases had more frequent B symptoms (43% vs 20%), high-risk IPI (66% vs 50%) and high-risk SMZL prognostic score (Arcaini, Blood, 2006) (57% vs 40%). HCV infection rate was similar (16% and 20%). Treatment prior to progression included splenectomy in all TCIRBLC cases and in 3/7 NOS cases. Two NOS patients received alkylating agents +/- rituximab and two were managed expectantly. Median time from diagnosis to transformation was significantly longer in TCIRBLC cases than in NOS cases (55 vs 18 months) (p = 0.031).

Conclusion: As previously reported, the TCHRLBC variant of SMZL progression represents a distinct clinicopathological entity, developing in younger patients, later during the course of disease, with less severe SMZL at diagnosis and with a better prognosis.
central regions of the genome. In contrast, regions with low CCND1 expression were centromeric, with breakpoints falling as far as 300 kb from the transcription start of the gene. The breakpoints were not localized to specific genomic regions. A total of 24 breakpoints were observed, with 14 falling within 210 kb from CCND1 and the remaining 10 distributed throughout the genome.

Conclusion: Flow cytometric (FC) assessment of T-cell receptor Vβ chains (TCRVβ) is a well described method for assessing T-cell populations in patients with suspected T-cell lymphomas. Most studies have been performed on blood samples with clonal T-cell populations, with a focus on minimal residual disease detection. This method might be used for fast and reliable identification of a T-reg phenotype. Both patients had a very poor clinical course with relapsed and refractory disease. Further research is needed to identify similar cases of PTCL with a T-reg phenotype, which may represent a distinct clinicopathological entity.

408 UTILITY OF FLOW CYTOMETRY USING T-CELL RECEPTOR Vβ INTERROGATION IN THE CHARACTERISATION OF T-CELL LYMPHOMAS

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Introduction: Flow cytometric (FC) assessment of T-cell receptor Vβ chains (TCRVβ) is a well described method for assessing T-cell populations in patients with suspected T-cell lymphomas. Most studies have been performed on blood samples with clonal T-cell populations, with a focus on minimal residual disease detection. This method might be used for fast and reliable identification of a T-reg phenotype. Both patients had a very poor clinical course with relapsed and refractory disease. Further research is needed to identify similar cases of PTCL with a T-reg phenotype, which may represent a distinct clinicopathological entity.

409 CYTOTOXIC MOLECULE (CM)-POSITIVE LYMPHOMA: CLINICOPATHOLOGIC AND IMMUNOHISTOCHEMICAL CLASSICAL HODGKIN LYMPHOMA, HODGKIN-LIKE ANAPLASTIC LARGE CELL LYMPHOMA AND NODAL PERIPHERAL T-CELL LYMPHOMA

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Background: Cytotoxic molecules (CM) are apoptosis-inducing molecules found in aruzpheric cytoplasmic granules of T lymphocytes. Detection of CM expression (granzyme B, TIA1 and perforin) is essential to the diagnosis of some mature T-cell lymphomas. We retrospectively analysed clinical and laboratory data of sequential biopsies from 32 patients with CM-positive T-cell lymphomas. In our small series, we noted resolution of the TCRβ chain rearrangement studies by PCR which were concordant in 100% of cases. Imaging was available for 7 patients; 2 had disseminated lymphohenopathy (ATLL and MF).

Results: Four patients who underwent chemotherapy had a repeat assessment of TCRβ by FC and were negative following treatment.

Conclusions: TCRβ interrogation by FC was often the first study to suggest a T-cell disorder, especially in patients with peripheral blood lymphohenopathy, indicating further studies are required to establish a diagnosis. We argue that this is a useful addition to the range of tests available for the diagnosis of T-cell disorders. In our small series, we noted resolution of the TCRβ chain rearrangement studies by PCR which were concordant in 100% of cases. Imaging was available for 7 patients; 2 had disseminated lymphohenopathy (ATLL and MF).

Patients and Methods: To characterize CM+ CHL, we clinicopathologically profiled 32 patients with CM+ CHL in comparison with 439 with CM-negative (CM-) CHL. Further, we clinicopathologically compared these 32 patients with CM+ CHL, 21 with CM+ HD-like ALLC, and 55 with CM+ nodal PTCL-NOS.

Results: H-RE cells of CM+ CHL patients had the prototypic immunophenotype of CD15+ CD30+ fascin+, with positivity for Epstein-Barr virus in 38% of cases. All CM+ CHL tumor cells were positive for Pax5. No difference in clinical parameters was seen between CM+ and CM- CHL. Notably, survival curve for CM+ CHL was significantly inferior to that for CM- CHL (P = .0003). Nodal PTCL-NOS was characterized as follows: 63% of patients had a performance status greater than 1 (P = .004), 79% were at an advanced clinical stage (P = .013), and 72% had serum lactate dehydrogenase levels higher than normal (P < .001). Immunophenotypically, CM+ CHL and CM+ nodal PTCL-NOS were positive for CD3epsilon in 7% and 83% (P < .001), CD3 in 9% and 40% (P = .007), CD15 in 71% and 4% (P < .001) and CD20 in 97% and 51% (P < .001) of patients, respectively. Interestingly, like other CM-positive T-cell lymphomas, CM+ CHL showed a poor prognosis. Survival curves of patients with CM+ disease somewhat overlapped in the two years after diagnosis.

Conclusion: The histological and immunophenotypic features of CM+ CHL were generally within the boundaries of the CHL category, but differed from typical CHL in its aggressive clinical behavior. The question of whether CM+ CHL should
be categorized as Hodgkin lymphoma or T-cell lymphoma requires further consideration, and novel therapeutic approaches should be explored.

410 PREDICTIVE VALUE OF TUMOUR BURDEN COMBINED WITH MOLECULAR, HISTOMORPHOLOGICAL AND CLINICAL PARAMETERS IN ADVANCED STAGE CLASSICAL HODGKIN LYMPHOMA

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Introduction: In advanced stage Hodgkin lymphoma (HL), treated with more aggressive therapies, data of prognostic value of bulky disease are less consistent than in early stage HL. Furthermore, in combination of macroscopic measurement of tumor mass with molecular, histomorphological and other clinical variables might increase the predictive value of tumor burden.

Material and Methods: In a cohort of 100 advanced stage cHL pts treated with ABVD (1997-2005) we analyzed the prognostic relevance of voluminous tumor mass and their correlation with molecular (Bcl-2, Survivin, Bax, NFkB, Ki-67 and active caspase 3 expression determined by immunohistochimistry), histomorphological (eosinophilic tissue infiltration, morphologic atypia of HRS cells, clusters or sheets of the HRS cells, total involvement of the lymph node by the neoplastic and inflammatory cells, presence of coagulative necrosis, sclerotic bands within the lymph node) and other clinical variables (IPS, extranodal involvement, elevated sedimentation rate (>50mm/h and ≥3 involved sites) at diagnosis. The median follow up was 7 years. Significance was tested according to response rate and overall survival (OS).

Results: Patients with mediastinal bulky disease had significantly decreased EFS (p=0.05). Shorter OS was associated with voluminous tumor burden (p=0.001). There was statistically significant correlation between bulky disease and high Bcl-2+ at threshold of 50% of labeled tumor cells (p=0.01), clusters or sheets of the HRS cells (p=0.001), morphologic atypia of HRS cells (p=0.05), sclerotic bands within the lymph node (p=0.019) and elevated ESR>50mm/h (p=0.042). Additionally, there was positive correlation with tissue eosinophilia, but it was not statistically significant (p=0.07).

Multivariate analysis revealed bulky disease as significant predictor for OS (p=0.003).

Conclusion: Advanced stage cHL pts with voluminous tumor mass, high Bcl-2+, cohesive clusters or sheets of the HRS cells and morphologic atypia of HRS are at a higher risk and could benefit from other, more intensive therapeutic approach.

411 CLINICAL RELEVANCE OF HISTOLOGICAL VARIABLES IN ADVANCED CLASSICAL HODGKIN LYMPHOMA

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Introduction: Although the outcome of Hodgkin lymphoma (HL) has been significantly improved, identification of new prognostic factors might help in better stratification of patients (pts) towards more effective treatment.

Material and Methods: In a cohort of 100 advanced cHL pts treated with ABVD (1997-2005) we analyzed the prognostic relevance of pathomorphologic features such as tissue infiltration by eosinophils (>50% of all cells or clusters in at least 5 HPF), morphologic atypia of HRS cells (>25% of bizarre and highly anaplastic HRS cells with pleomorphic nuclear features and highly irregular nuclear outline), cohesive clusters or sheets of the HRS cells (sheets of >20% cohesive HRS cells), total involvement of the lymph node by the neoplastic and inflammatory cells (no focal residual secondary follicles), presence of coagulative necrosis (large areas of necrosis) at diagnosis. The median follow up was 7 years. Significance was tested according to the response rate and overall survival.

Results: Lower complete remission rate was associated with atypia of HRS cells (p=0.001), total involvement of the lymph node (p=0.021) and cohesive clusters or sheets of the HRS cells, (p=0.037). Decreased OS had pts with tissue eosinophilia (p=0.013), atypia of HRS cells (p=0.000), total involvement of the lymph node (p=0.002) and cohesive clusters or sheets of the HRS cells (p=0.004).

Multivariate analysis revealed that tissue eosinophilia was significant predictor for OS (p=0.02).

Conclusion: Advanced stage cHL pts with tissue eosinophilia are at a higher risk and could be eligible for more effective therapeutic approach.