194 The distinctive biology of diffuse large B-cell lymphoma (DLBCL) in adolescents and young adults (AYA)

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Background: DLBCL is a generic term for a clinically and biologically heterogeneous group of tumours. Depending on a gene expression profiling of DLBCL has revealed a molecular subtypes that include germinal center B cell-like (GCB) and activated B cell-like (ABC or non-GCB). Less than half of adult patients with DLBCL can be cured by conventional CHOP-type chemotherapy. The remainders have tumours that are either refractory to currently available treatment or have a relapses. The prognosis of paediatric DLBCL mostly GCB has improved since short intensive multi-agent chemotherapy regimens like NHL-BFM 90 was introduced. We hypothesized that adolescents and young adults with the GCB DLBCL may benefit of such treatment. The purpose of this study was to determine the efficacy of intensive BFM-like therapy for AYA with DLBCL.
Materials and Methods: From 10.1998 to 04.2008, 28 (m-14, f-14) patients (pts) with de novo DLBCL were treated with 6 chemotherapy cycles similar to those in NHL-BFM 90 for B-NHL. Before 2006, 18 pts received a modified treatment cycles with the reduction of methotrexate (1 g/m^2/36h instead 5 g/m^2/24h). Since 2006, 10 pts received therapy on a national paediatric protocol B-NHL 2004M. This protocol differed from BFM by adding rituximab 375 mg/m2 on the first day of each cycle and reduction of methotrexate doses only in the first 2 cycles (1 g/m^2/24h instead 5 g/m^2/24h). Tumours were classified as GCB or non-GC based on three markers – CD10, BCL6, and MUM1 (Hans, 2004).
Results: Median age pts was 21.0 years (range, 15−38). 24 (86%) pts were diagnosed in advanced (III-IV) stages. The molecular subtypes of DLBCL were evaluated for 16 pts: 8 (50%) classified as GCB and 8 (50%) – non-GCB. Complete response achieved 8 (100%) pts with GCB and 5 (63%) pts with non-GCB ($p > 0.05$). 5-years event free survival was 1.0 (SE 0.0) vs. 0.50 (SE 0.18) respectively ($p = 0.046$). 5-years overall survival was 1.0 (SE 0.0) vs. 0.50 (SE 0.23) respectively ($p = 0.071$). Median follow-up was 3.4 years. The GCB and non-GCB group did not differ in their international prognostic index scores, presence of bulky disease and frequency of Rituximab treatment.
Conclusions: AYA with immunohistochemically determined GCB-type DLBCL have an improved prognosis as a result of intensive BFM-like therapy recalling those of children in contrast to non-GCB. The classification of DLBCL as GCB or non-GCB most likely reflects biologic differences, which might influence therapeutic decisions in this age group.

195 Telocytes – players of the pancreatic stromal puzzle

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Background: We showed previously the existence of an Interstitial Cajal Like Cell (ICLC) among the acini in the exocrine human pancreas. We prefer now to name these cells "telocytes" because they are different from the classical Interstitial Cells of Cajal. The features by which they differentiate the most are their very long and thin prolongations, visible only by electron microscopy.
Telocytes are present in the instertitial space of a variety of organs, both cavitary and non-cavitary, networking within themselves and with local cell populations.
Material and Methods: Histologically normal areas of human pancreatic body, remote of primary disease, were obtained from archived paraffin-embedded tissue of patients that had undergone surgical procedures for a non-neoplastic disease.
To identify pancreatic telocytes (TC) we used routine light microscopy, non-conventional light microscopy (less than 1 μm semi-thin sections of Epon-embedded specimens cut by ultramicrotomy and stained with Toluidine blue), transmission electron microscopy (TEM), and immunocytochemistry.
Results: The results showed that TC can be recognized by TEM, as a small cell body having long thin moniliform processes, with dilatations that accomodate mitochondria and endoplasmic reticulum, as well as caveolae.
Two-dimensional reconstruction from serial photos suggest a network-like spatial distribution of TC. TC represent roughly 3.3+0.5% of all pancreatic cells, and seem to establish close spatial relationships with: capillaries (43%), acini (40%), stellate cells (14%), nerve fibres (3%).
Most of TC (88%) have 2 or 3 long processes (tens of μm) emerging from the cell body. Immunocytochemistry revealed that TC are CD117/c-kit and CD34 positive. We found TC positive (40−50%) for smooth muscle α-actin or S-100, and, occasionally, for CD68, NK1 neurokinin receptor and vimentin. The reactions for desmin and chromogranin A were negative in TC.
Conclusions: The various types of network partners of TC in pancreas suggest the idea of an integrative role of TC, a role in modulating/coordinating the function of the whole organ, but the very way in doing so remains still unknown.
An interesting direction of research for understanding the *pancreatic fibrosis* might be the *interactions of TC with pancreatic stellate cells*, and to consider *some stromal pancreatic tumours,* as extra GIST (by analogy with GIST) as a diagnostic contingency.

196 Factor score of multidrug resistance in treatment locally advanced rectal

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Background: To explore a problem of multidrug resistance treatment locally advanced rectal cancer by using neoadjuvant chemotherapy combining with ozonotherapy.
Materials and Methods: 11 patients with locally advanced rectal cancer conduct transanal testing of tumour that followed by neoadjuvant system of polychemotherapy with ozone therapeutics. By stages: $T_4N_2M_0$. Morphologically in most cases observed adenocarcinoma in various level differentiations in 7 and mucinous carcinoma in 4 patients. All patients carried system polychemotherapy by scheme of FOLFOX-4. Chemotherapy course conducted two-times.
Results: Re-examination of prevalence neoplastic process testifies that in 6 patients' educed stabilizing neoplastic process, in 2 − involution of tumour that allows leading apparent radical operation in 6 patients, cytoreductive in 4 patients and in 1 patients find out progression of neoplastic process. At determining p53 hyper expression until treatment it found out in 9 patients (++), bcl-2 hyper expression found out only in 1 patient. After conduction chemotherapy course found out, that expression P53 is missing in 7 patients; bcl-2 hyper expression was without change.
During morphologic researches of bioptic material from tumour medical pathomorphosis I level find out in 2, II level in 3, III level 1 patient. Indices of glutathione S-transferase decrease from 6.3±0.48 till 4.62±0.52%. Indices of tumour necrotic factor-α (TNF-α) increase from 3.4±0.74 to 4.82±0.46 pg/ml.
Conclusion: Usage testing of tumour enables conduction to neoadjuvant course of treatment locally spread process without prior operation. Leadthrough polychemotherapy system with ozone therapeutics decreases ghost effects of chemotherapy, while as results in suggestive involution of tumour, which increases possibility of carrying out radical and cytoreductive operation. Also it decrease in blood level of expression glutathione S-transferase marker P53 and increase of TNF-α that contributes sensitization of tumour cells to chemotherapy and increase apoptotic index, after history in colorectal cancer patient.

197 The COX-2 promoter polymorphism −765 G>C is associated with poor prognosis in hospitalized patients

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Background: It has been reported that COX-2 gene plays a crucial role in the genetic predisposition to many diseases although there is no information about its role in prognosis of hospitalized patients. COX-2 overexpression is known to be an important mechanism in carcinogenesis and myocardial infarction. Our study investigates the role of the COX-2 765 G>C promoter polymorphism as a prognostic factor for the hospitalized patients.
Material and Methods: We performed the single nucleotide polymorphism (SNP) of 100 patients who died during hospitalization as well as 100 control patients, using real-time PCR and sequence analysis. Posthumously performed autopsies on them, indicating the cause of death and then collected tissue for research.
Results: We found that the C allele was present in 14.8 % of the patients died at hospital, whereas in the control group it was present in 41% of cases. There was statistically significant difference in the presence of the C allele in patients hospitalized at hospital compared to the control group ($p < 0.001$), with the G allele being associated with poor prognosis.
Conclusions: In summary, we have shown that COX-2 765 G allele promoter polymorphism is significantly associated with poor prognosis in patients who arrived to hospital when compared to the normal control group. Although several differences have been identified in these patients compared to control, the exact mechanism by which COX-2 765G allele impacts on prognosis is yet to be elucidated.