is contradictory to recent reports on CK7 negativity of BSCC. Low expression rate of BSCC for CK19 contrasts with invariable expression in conventional SCC, and limits the diagnostic utility of CK19 mRNA detection in this peculiar entity.

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Application of infrared microspectroscopy and chemometrics for diagnosis of colon cancer

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Background: Nowadays the application of attenuated total reflectance - Fourier transform infrared (ATR-FTIR) microspectroscopy in the detection of cancer is a newly emerging diagnostic field, which has shown great potential. The applicability of advanced chemometrics techniques such as principal component analysis (PCA), linear discriminant analysis (LDA) and soft independent modeling class analogy (SIMCA) and their capability in interpreting the complex environmental data have been discussed.

Materials and methods: Totally 80 Formalin-fixed, parafin-embedded tissues from patients were prepared from the histopathology division of Shahid Rajaee Hospital. ATR-FTIR studies were performed by a Nicolet® instrument. All spectral studies were performed 4000-400 cm^{-1} wavenumber region. The measured sites' area was about 50×50 μm^2. Number of 49 scans and 16 cm^{-1} were optimized. Spectroscopic data were processed in total spectral region by this software. Resolution was set as the optimum condition. In order to apply the chemometrics methods, PCA and SIMCA techniques were performed by MATLAB® version 7.1 software.

Results: Two intensive signals at 1660 cm^{-1} and 1540 cm^{-1} which are due to amide I and amide II respectively, are indicative of protein structure. Spectral features due to stretching vibrations of $PO2^-$ from the nucleic acids and the C–O stretching vibrations from the carbohydrate residues in the glycogen (or collagen) are found in 1240 and 1250 cm^{-1}. PCA is an approach that can simplify the data interpretation by reducing the variable dimension of the spectral data matrix down to a very small number of orthogonal principal components that summarize nearly all of the variance in the original data matrix. SIMCA is sensitive to the quality of the data used to generate the principal component models. As a result, there are diagnostics to assess the quality of the data, such as the modeling power and the discriminatory power. After application of cross-validation 3 PCs for each class of sample (normal and cancer) were foundAfter application of principal components in the model, Q as a residual error for prediction the model was 7×10^{-4} and 1.4×10^{-3} for cancerous and normal class in calibration set respectively. In SIMCA, an unknown spectrum is identified as a specific group (or other group) by comparing the F-distribution with the 95% confidence interval. Sixty unknown samples (26 normal and 34 cancer) were predicted by SIMCA model. In the prediction step, 4 cancer tissue samples were predicted to be normal wrongly. The accuracy, sensitivity and specificity of the model were 93.3 and 88.2% and 100% respectively.

Conclusions: It was tried to demonstrate that ATR-FTIR microspectroscopy in combination with chemometric methods can reliably distinguish malignant colon tissues from healthy ones. It is important to be explored a noninvasive and rapid method for detection of colon cancer biopsies. High accuracy, sensitivity and specificity were obtained in the research.

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Urine carcinoembryonic antigen levels are more useful than serum levels for early detection of Bilharzial and non-Bilharzial urinary bladder carcinoma: observations of 43 Egyptian cases

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Background: Both urinary bilharziasis and urothelial neoplasia are associated with increased production of tissue carcinoembryonic antigen (CEA).

Patients and methods: Urine and serum CEA were determined in 43 patients with urinary bladder carcinoma including 22 post bilharzial and 21 nonbiharzial cases, in addition to 10 normal control cases.

Results: A significant increase was detected in both urine and serum CEA levels with bladder carcinoma compared to control cases. Urinary CEA was significantly elevated in 86% of bilharzial, versus 62% in nonbilharzial bladder carcinoma. Only 10.5% of control cases had urinary CEA elevation. The mean urinary CEA in bilharzial, was higher than that of nonbilharzial carcinoma, but the difference was not statistically significant. There was a definite relationship between urine CEA and the stage of malignancy; the higher the stage, the higher the level of urine CEA. No relationship could be detected between the stage of malignancy and serum CEA, or between the grades of malignancy and urine or serum CEA levels.

Conclusion : Urinary CEA is more useful than serum CEA in the early detection of urotherlial carcinoma particularly if provoked by bilharziasis. Its level is also correlated with the tumor stage.

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Effectiveness of COX2 inhibitor treatment in patients with dysplastic oral leukoplakia

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Background: Oral premalignant lesions include leukoplakias, which develop along epithelial surfaces that have been chronically exposed to carcinogens such as tobacco and alcohol. These lesions are markers for field cancerization because patients with oral premalignancy can develop squamous cell carcinoma at the site of the lesion as well as at other sites in the upper aerodigestive tract. Approximately 6% of all oral leukoplakias become malignant. An effort is being made to identify surrogate endpoint biomarkers (SEBs) for HNSCC. Objective: Study effectiveness of COX2 inhibitor treatment in patients with dysplastic oral leukoplakia, and also analyze COX2 as potential SEB in leukoplakia tissue samples by means of qPCR. Materials and Methods: Expression levels of COX2 gene, in 24 unique freeze samples from 24 patients with leukoplakia, were measured. From each patient, 3 samples were obtained: opposed lateral oral mucosa, leukoplakia mucosa before and after treatment with COX2 inhibitors. As control, a pool of healthy human oral mucosa from healthy donors (n=4) was used. qPCR experiments were performed on a LightCycler 480 Instrument (Roche) using LightCycler 480 SYBR Green I Master (Roche). A constitutively expressed gene, HPRT, was used as internal control. Results: The highest levels of COX2 expression were obtained in leukoplakia samples not only before treatment with COX2 inhibitors but also after it. 41.66% of samples showed lower COX2 expression levels in leukoplakia samples after the treatment and 37.5% of samples showed higher expression levels after it. Only 20.84% of samples showed higher expression levels in opposed lateral oral mucosa from patient. COX2 expression was always lower in the pool of healthy human oral mucosa from healthy donors than in opposed lateral oral mucosa from patient, which can be explained by means of the "field cancerization" phenomenon. Conclusions: Real Time PCR assays confirmed that COX2 is up-regulated in premalignant oral epithelial lesions, indicating that COX2 may contribute to carcinogenesis. 41.66% of patients treated with COX2 inhibitors showed a decrease in COX2 expression levels. The results showed a correlation with clinical response to treatment with COX2 inhibitors (Celecoxib). Therefore COX2 could represent an attractive SEB to target to in leukoplakias. Support: S. Díaz Prado is beneficiary of an Isidro Parga Pondal contract from Xunta de Galicia (Spain).

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Ki-67 and survivin immunostaining for evaluation of cervical precancer lesions

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Background: Numerous molecular biomarkers have been suggested for early verification of cervical precancer. Ki-67 immunostaining is usually used as pattern of cellular proliferation. Survivin, a novel member of the family of apoptosis inhibitors, plays an important role in cell cycle regulation. Aim of this study was to examine whether a combination of immunostaining for Ki-67 and survivin could be used to evaluate the further progression of cervical intraepithelial neoplasias (CIN) to cervical cancer (CC).

Materials and methods: The study included 30 CIN cases, 14 squamous-cell CC stage 1A (microcarcinomas) and 16 invasive CC cases. High risk HPV (HPV16 and 18) were demonstrated in 83% of CIN and 80% of CC cases, correspondently. Ki-67 and survivin were used for immunostaining of paraffin sections with monoclonal (MIB-1) and polyclonal antibodies correspondently. To detect an early genetic abnormality in cervical pathogenesis the loss of heterozygosity at 6p21.3 (HLA region) was tested

with microsatellite markers TNFa, D6S273, D6S291 in DNA samples prepared from the serial tissue sections.

Results: Low Ki-67 nuclear expression was found in 45% of CIN1-2 and 25% of CIN3 lesions. Namely, less then 30% of cells in lower two thirds of the epithelium thickness were Ki-67 positive. The rest of CIN lesions revealed Ki-67 nuclear expression in 60-90% of cells in all layers of cervical epithelium. Expression of Ki-67 in microcarcinomas varied from 30% to 90% of cells while invasive SCC had 50-70% of stained nuclei. Survivin expression increased with the severity of CIN lesion, reflecting the reduction of apoptosis. Thus survivin expression was detected in 25% of CIN1, 50% of CIN2 and 67% of CIN3. Cytoplasmic expression of survivin was found in 70% of CC. Only few CIN cases (22%) were negative for Ki-67 and survivin that correlated with the retention of microsatellite heterozygosity at 6p21.3. We suppose these CIN lesions may regress with apoptosis.

Conclusions: The obtained results suggested that the combination of immunostaining for Ki-67 and survivin might be helpful in early diagnostic of cervical lesions and evaluation of further CIN progression.

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Informative comprehension of detection of chimeric genes PAX3/7-FKHR in prognostically unfavourable forms of rhabdomiosarcomas in children

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Background. Alveolar rhabdomyosarcoma (ARMS) is an aggressive soft tissue malignancy of children. Most ARMS patients express PAX3-FKHR or PAX7-FKHR gene fusions resulting from t(2;13) or t(1;13) translocations, respectively. The availability of them in tumor correlates with sensitivity to cytostatics and efficacy of the treatment. These markers can be detected also in bone marrow (B?), that is a feature of micrometastases or minimal residual disease.The objective of the work is to determine informative comprehension of detection of expression of chimeric gens PAX3-FKHR and PAX7-FKHR in cells of tumor and BM in prognostically unfavourable forms of rhabdomyosarcomas (RMS) in children. Materials and methods. Tumor tissue and BM, obtained during the treatment (from 3 aspirates per one examination), from 26 childhood RMS patients, aged 3-11. The treatment of patients was carried out in accordance with protocols: Protocol EpSSG RMS 2005 for non-metastatic embryonal and alveolar RMS; CWS-96 for metastatic (IV stage) and recurrent RMS. Choice of protocol was based on determination of PAX3-FKHR and PAX7-FKHR fusion status. Fusion status was determined using the real-time RT-PCR method. Results. Chimeric genes in cells of tumor have been detected in 11 patients that evidence on belonging of these tumors to RMS of alveolar type (aRMS), which are of unfavourable prognosis and require different from embryonal RMS protocols of polychemotherapy (PCT). At a moment of making out a diagnosis in 8 of 11 patients with aRMS chimeric transcripts PAX3-FKHR and PAX7-FKHR in BM were detected that evidence on IV stage of disease. In 1 patient they were detected in all 3 points of BM. During a year from diagnosis and beginning of the treatment 5 of 8 patients of this group died. After course of PCT in two patients chimeric genes in BM were not detected, that evidence on the efficacy of the treatment. Conclusions. High sensitivity of real-time RT-PCR assays are capable of identifying PAX3-FKHR and PAX7-FKHR fusion status both in tumor and submicroscopic metastatic disease in sites such as the BM. Our study has demonstrated the clinical utility of fusion gene detection in differential diagnosis, prognosis, and minimal disease monitoring, as well as allows determine the rate of achieved remission.

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Prognosis and recurrence pattern of patients with cervical carcinoma and pelvic lymph node metastasis

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Objective to investigate the prognostic risk factor(s) and pattern of disease relapse of patients with cervical carcinoma and pelvic node metastasis. Methods 124 cases of FIGOIB1~IIA cervical carcinoma with pelvic node metastasis treated from January 1991 to December 2001 were selected for this study. Prognosis and recurrence were retrospectively analyzed using the clinico-pathological data. Results The over all 5 year survival and disease-free survival (DFS) was 63.3% and 61.4% respectively. Overall recurrence rate was 39.5% (49/124). Intra-pelvic relapse (25/41, 61.0%) was significantly more frequent than extra-pelvic relapse (13/41, 1.7%, P=0.008).Multivariate analysis identified involvement of common iliac node as independent prognostic factor (P=0.035). According to this factor, node-positive patients could be divided into low risk group (without common iliac node involvement, 104 cases) and high risk group (with common iliac node involvement, 20 cases). The DFS were 69.4% and 24.5% respectively, and the difference was significant (P=0.003). Intra-pelvic relapse was observed in 22.1% of low risk and 25.0% of high risk group respectively, the difference was not significant (P>0.05), however extra-pelvic relapse was seen in 7.7% of low risk and 40.0% of high risk group, and the difference was significant (P<0.001). Conclusions Common iliac node involvement is the significant factor that influences the prognosis of patients with cervical carcinoma and pelvic node metastasis. According to this factor, survival and recurrence pattern differs significantly. These findings provide important reference for individualized modification and investigation of treatment mode.

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Clinical and pathological features of primary lymphoma of bone

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Introduction: Primary lymphoma of bone (PLB) is a rare disease, first described by Oberling in 1928. Even today the diagnosis of PLB can be difficult due to the relatively non-specific clinical signs and ambiguous radiographic features. Here we have reviewed the patients presenting with PLB, their clinical features, especially the relation between clinical stages and patients' outcome.

Patients: In this study, PLB was defined as follows. 1) Malignant lymphoma presenting a single or multiple bone lesion(s) with or without invasion to surrounding soft tissue. 2) There is no evidence of visceral or nodal involvement at the time of first diagnosis after the several radiographic screening, including whole body CT scanning, gadolinium scintigraphy.

According to the definition, we have experienced 17 cases of PLB from 1991 to 2005 in National Cancer Institute, Japan. All patients were diagnosed as PLB with needle and/or open biopsies. There were eight males and eight females varied 8 to 73 years old (Median 41 years old) at the time of diagnosis. The median follow-up period was 7.2 years (8 month to 11 years). The affected bone lesions were as follows. Femur and ilium: 5cases, thoracic vertebrae, sacrum and tibia: 3 cases, lumber vertebrae and rib: 2 cases, skull and humerus: 1 case. There were no specific radiographic images on PLB, except for the occasional extensive abnormal bone marrow signal on MRI whereas plain X-ray images were negative. Histopathologically, there were 11 cases of diffuse large B cell lymphoma, 3 cases of anaplastic large cell lymphoma (K1-lymphoma) and lymphoblastic lymphoma (precursor B cell type) and low grade B cell lymphoma (unclassified) accounted for the rest of two cases. Clinical stages (Ann Arbor) at the diagnoses, Stage IE: 9cases, stage IV: 7cases.

Result and Conclusion: All cases were treated with the combination of systemic chemotherapy(including anti-CD20 antibody; rituximab)with or without local radiotherapy. Surgical treatments were performed in 6 cases; laminectomy and instrumentation of thoracic vertebrae 2 cases, osteosynthesis of pathological fracture 3 cases, total hip arthroplasty 1 case. Overall survival rate was 81% (13/16). (Mean survival time; 46 months) Overall survival rate of stage IV was 71% (5/7), relatively good outcome compared to that of the historical control of stage IV patients including nodal or visceral involvement. These clinical outcomes might suggest the possibility of specific biological features of lymphoma cells only with skeletal involvement.

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Assessment of vascularity in gastric malignant tumors

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Introduction: Assessment of angiogenesis is possible nowadays by various methods: imaging methods, molecular biology and pathological exams. A high value of vascularity index is correlated with an advanced disease, thus the angiogenesis assessment could offer important preoperative parameters.

Method: In our study we proposed to assess the vascularity index in gastric adenocarcinoma using imaging method comparing to pathological markers (microvessel density, CD34, VEGF).

We included 8 patients with gastric cancer assessed by endoscopic ultrasound with color Doppler, power Doppler and pulse Doppler possibilities. We computed the vascularity index using a custom-made application based on the free ImageJ open-source software. The ROI