1459 POSTER

HE4 Levels in Endometrial Cancer Patients − Potential Role as a Tumour Biomarker

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Background: Endometrial cancer (EC) is the most common gynaecologic malignancy in the western world. To date, no good marker for EC management is available and CA125, often used in clinical practice, has limited utility. The purpose of this study was to investigate the diagnostic impact of preoperative serum HE4 in EC patients and its relationship with clinicopathologic characteristics.
Material and Methods: The study included 193 EC patients [35 well- (G1), 89 moderately- (G2) and 69 poorly- (G3) differentiated, representatives of all histotypes and stages], 14 patients with endometrial hyperplasia with focal areas of endometrial carcinoma (Hy/EC) and 125 women with normal endometrium (NE) as healthy controls. Pre-operative serum samples were analyzed for HE4 and CA125 levels by a chemiluminescent microparticle immunoassay on automated ARCHITECT instrument (Abbott Diagnostics Division, Chicago, IL).
Results: sHE4 values were significantly higher in EC patients (median = 79.9, mean = 116.0, range 6.5–1348.4), regardless of tumour stage and differentiation grade, compared with NE (median = 39.0, mean = 41.4, range 21.6–84.5) and with Hy/EC (median = 42.6, mean = 47.8, range 24.7–138.9), both $p < 0.001$. Instead, no difference in sHE4 levels was detected between NE and Hy/EC ($p = 0.3475$). The areas under the receiver operating characteristic curves (ROC-AUC) were determined for HE4, CA125 and in combination for discrimination of NE and EC. HE4 had a significantly higher ROC-AUC when compared with CA125 in all EC ($p < 0.0001$), regardless of tumour stage and differentiation grade. ROC-AUC deriving from HE4 and CA125 combination was not significantly increased when compared with HE4 alone ($p = 0.2533$). High sHE4 levels significantly correlate with adnexal involvement, deeper myometrial invasion (M2 vs M0/M1), lymph nodes metastasis, higher stage (>I vs I), lymphovascular invasion, positive peritoneal cytology, higher grade (G2/G3 vs G1), presence of cervical invasion (all $p < 0.01$). No significant difference was detected among different histotypes ($p = 0.638$).
Conclusions: This study highlights that HE4 is secreted at higher levels in serum of EC patients compared with NE controls and it is more sensitive and specific compared to CA125 in distinguishing malignant disease, regardless of tumour stage and grade. sHE4 levels could be associated with a more aggressive tumour phenotype and could be clinically useful in identifying high-risk EC patients for a more aggressive adjuvant therapy.

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A Novel Lectin Array-based Technology for Non Invasive Cancer Diagnosis via Serum Samples − a Proof of Concept in Gastric Cancer

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Background: Cancer development is associated with glycosylation alterations of glycoproteins. The aberrant glycoproteins may be detected in malignant cells and secreted or released into blood. We have developed a novel lectin array-based platform that can be utilized to detect unique glycosylation patterns of proteins. Binding of a glycoprotein to the array results in a characteristic fingerprint, highly sensitive to changes in its glycan composition. The results are analyzed by software that uses bioinformatic tools.
Using this technology, we performed a study aimed to identify the presence of gastric cancer via serum samples. Gastric cancer is a common cause of cancer-related death worldwide. It is difficult to diagnose and causes only non-specific symptoms. Therefore, invasive approaches such as endoscopic observation and biopsy are necessary for diagnosis.
Materials and Methods: A cohort of 120 gastric cancer patients and 150 healthy controls were tested using the lectin array (LA) technology. The LA was composed of 30 different lectins, printed in triplicates. 15 μl of serum were depleted from the 14 most abundant proteins, labeled fluorescently and coupled with the LA overnight at 37ºC. LA slides were scanned by a laser scanner and the results were interpreted by the software.
Results: The LA assay was capable to distinguish between samples from gastric cancer patients and controls in a sensitivity and specificity of 80 and 85%, respectively. Several lectins were selected as predictors enabling to differentiate between gastric cancer patients and healthy controls. The LA was equally capable of detecting the disease in samples from early and advanced-stage gastric cancer.
Conclusions: The current study demonstrates the feasibility of using a lectin array-based technology for non-invasive detection of gastric cancer via serum samples, showing high sensitivity and specificity (80 and 85%, respectively). Aberrant glycosylation is well documented to occur in all types of human cancers. The LA provides an easy means to exploit this observation and to translate it into a clinical assay applicable to clinical diagnostics laboratories. The promising results of the current study need to be validated in a large controlled clinical trial. Nevertheless, they imply that this technology can be potentially used as an adjunct diagnostic test for patients suspected for having gastric cancer and provide a proof of concept to its cancer diagnostics potential in general.

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Hyponatremia (hNa) in Cancer Patients (pts): an Underestimated Problem

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Background: Among biological abnormalities occurring in cancer pts, hNa is often neglected; despite it can bring some severe neurological disorders (such as confusion or coma). Exact prevalence is not known. Etiological investigations are often limited and clinical care not always optimized.
Methods: We conducted a prospective 3-month survey including all the pts consulting at Emergency Service in our institution (a French comprehensive cancer center), whatever the reason of the consultation was and undergoing some blood tests including Natremia (Na). hNa was defined as Na <136 mM/l, severe hNa, as Na <129mM/l: in that case the pt was hospitalized for further investigations and treatment. Anti-diuretic hormone (ADH) level was determined and an hypocorticism was check by performing cortisolaemia dosage and ACTH stimulation test. Biological dehydration was defined as urinary urea/plasma urea > 10.
Results: 1190 pts were included: 32 pts were found with hNa (2.7%), with a mean Na=127±3.6mM/l, (Na ⩽120:3pts, 120 <Na ⩽129:16pts; 130 ⩽Na <136:13pts). Tumour types were predominantly colo-rectal (31%), lung (15%) and gynecologic cancers (12%), 77% pts had metastatic, and 74% progressive disease; 80% receiving chemotherapy, while 22% were treated with targeted therapies. Seventy two % had some biological dehydration. After adequate care (re-hydration for 92% pts) Na improved in all patients: mean Na (mM/l) after 3 days was 132±4.3, after 6 days 134±4.7. Twenty eight % pts had no symptom of clinical or biological dehydration. Hypocorticism could be considered in 21% of pts as basal cortisolaemia was 480±37nM/l and after stimulation 790±217nM/l. All ADH levels were in normal range. One third pts with hNa died within a mean of 32 days (6 to 84 days) after diagnosis of hNa.
Conclusion: hNa in cancer pts is not a rare occurrence. Prevalence can be estimated to 2.7% in ES. In 60% of the cases hNa was considered as severe, leading to pts hospitalization. Dehydration is the main cause of hNa, as it concerned 2/3 pts. Functional hypocorticism could be considered in 21% pts. Of note, hNa seems to be associated with poor prognosis, but this need to be addressed in further study.

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BRCA 1/2 Mutation Carriage in Healthy Women and Patients With Breast Cancer is Associated With Elevated Serum Thymidine Kinase 1 Activity

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Background: The BRCA1 and BRCA2 tumour suppressor genes are involved in the regulation of cellular proliferation and DNA repair. Mutations in these genes confer greater risk of developing breast and ovarian cancer. In this study we explored thymidine kinase 1 (TK1), a pyrimidine metabolic pathway enzyme essential in the salvage DNA synthesis and repair processes.
Patients and Methods: Serum TK1 activity was determined with a high sensitive DiviTum (Biovica) ELISA assay in 5 groups of women, namely, control subjects from healthy blood donors (Group 1, n = 120), healthy carriers of BRCA1/2 mutation (Group 2, n = 67), healthy carriers of BRCA1/2 mutation who underwent preventive bilateral salpingo-oophorectomy (Group 3, n = 33), primary breast cancer (BC) patients non-carriers (Group 4, n = 66) and primary BC patients carriers of BRCA1/2 mutation (Group 5, n = 17).
Results: There was no correlation between serum TK1 activity and age in the control group ($R = 0.07$). The enzyme activity in women from each of the Groups 2−5 was found to be significantly higher than in women