Role of Tumour Necrosis Factor in the Aetiology of Lipid Abnormalities and Cachexia in Breast Cancer Patients

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The present study was undertaken to investigate:
1. The association between hyperlipidaemia and stage of the disease in breast cancer.
2. The frequency of TNF alpha and CA 15.3 in breast cancer.
3. The possible role of insulin and/or TNF alpha on any serum lipid abnormalities and cachexia observed in these patients.

Fasting blood samples were collected from 55 patients with histologically proven breast cancer who were attending the Al-Thawra University Hospital, Sanaa, Yemen. Another 55 fasting blood samples were also collected from age-sex matched control. All samples were analysed for triacylglycerol, total cholesterol, HDL-cholesterol, LDL-cholesterol, glucose, insulin, CA 15.3 and TNF alpha. Patients with known diabetes, thyroid disease, hyperlipidaemia or evidence of infected sepsis were excluded as patients with weight loss.

The results showed that serum triacylglycerol levels increased significantly with increasing stage of the disease, but total cholesterol, HDL-cholesterol and LDL-cholesterol were found to decrease significantly with increasing stage of the disease.

Glucose and insulin levels showed a significantly low levels in late stages of the disease (III and IV) than those of the early stages (I and II). TNF alpha levels tended to increase significantly with increasing stage of the disease. It appeared to be a more sensitive indicator than CA 15.3 for disease progression in breast cancer.

The study of hormones antagonizing insulin action (cortisol, glucagon, TSH and Growth Hormone) is recommended to assess the possible role of these hormones together with TNF alpha in the development of cachexia seen in cancer patients.

Evaluation of Superoxide Dismutase (SOD) Levels in Ovarian Neoplasms: Relationship to Cancer Antigen 125 (CA125) and Patients Survival

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This study was carried out on 27 patients with ovarian cancer, 28 patients with benign ovarian lesions and 30 normal females who were chosen as a control group. Serum samples and tissue specimens were obtained from the patients admitted to the obstetrics and gynecology department at Ain Shams University hospitals. Staging of the ovarian cancer was evaluated during surgery and all cases were diagnosed by histopathological examination. Demographic data showed that 70% of cancer patients were above the age of 45 years and 60% of them were postmenopausal. The results obtained from this study demonstrated a significant increase of serum and mitochondrial levels of SOD as well as serum levels of CA125 among cancer patients compared to those for the benign and normal groups (P<0.01). Interestingly enough, SOD levels gave higher sensitivity and specificity values in stage I cancer patients compared to CA125 (92%, 95%, VS 73%, 68%, respectively). These findings might indicate the potential usefulness of SOD as a biological marker in the early detection of ovarian cancer. Furthermore, optimal debulking was associated with significantly increased levels of SOD compared to those who had suboptimal or interval debulking. Thus monitoring of SOD levels may be a useful tool to predict the feasibility of performing optimal debulking. This study also investigated the coexpression of TNF-a and SOD in patients with ovarian cancer biochemically and by immunohistochemistry (IHC). The data indicated a significant increase of both markers compared to benign and normal groups. The survival outcome of the patients was analysed using Kaplan-Meier curves and the log-Rank test. A nonsignificant increase in the probability of survival was associated with increased TNF-a levels alone. However, survival was significantly increased when both TNF-a and SOD levels were increased. To the best of our knowledge, this is the first report in the literature to demonstrate the prognostic significance of this molecular pathway (Trid-a-SOD interactions). The latter induces apoptosis in ovarian cancer cells and hence improves the survival. Based on these findings, a gene therapy model may be hypothesized as a future perspective.

Telomerase Activity, and Tissue Polypeptide Specific Antigen (TPS) in Egyptian Breast Cancer Patients

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Breast cancer is the most common malignancy among Egyptian women. The aim of this study is to evaluate the role of both telomerase and TPS assessment in diagnosis of breast cancer. The study included 40 patients with breast cancer, and 20 patients with benign breast diseases. Telomerase activity was assayed using the qualitative TRAP assay in the breast tissues, and TPS was measured in sera of the patients by EIA. Telomerase positivity was 15% in benign group versus 60% in malignant group (P=0.0029). It was significantly correlated to stage of the disease, and lymph node status (P=0.01). However, it had no significant relation to any of the patient's age, tumor size, or grade of the tumor. Mean rank of TPS was significantly higher in malignant than benign groups (P<0.001), and in telomerase positive than telomerase negative patients (P<0.001). In malignant group, mean rank of TPS was significantly higher in late stages (III & IV), than in early stages (I & II) (P<0.002), in lymph node positive than negative patients (P<0.003), and in grade 3 than grade 1 & 2 (P<0.01). ROC curve was utilized to choose the best cutoff for the TPS (88 U/L). At this cutoff, the sensitivity was 95%, and the specificity was 70%. Chi square analysis showed a significant correlation between TPS, and telomerase positivity (P<0.001). At a higher cutoff (129 U/L), TPS positivity was significantly correlated to stage, lymph node status in addition (P<0.01). We can conclude that telomerase positivity and TPS might be used as additional markers for diagnosis and management of breast cancer.

Mutations in K-ras and c-erbB2 expression in pancreatic cancer samples from archival tissue samples

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Propose: K-ras mutations occur in 80% of pancreatic cancers. c-erbB2 expression vary between 19 to 82%. Both genes are perspective targets of anticancer therapies. Materials and methods: Detection of K-ras codon 12 point mutations were determined by mutant enrichment PCR followed by restriction analysis, c-erbB2 expression was evaluated by immunohistochemistry in 32 paraffin-embedded tumour samples (28 exocrine pancreatic carcinomas, 3 neuroendocrine tumours and 1 carcinoma of Vater ampulla). Correlation with overall survival and other clinical characteristics was performed. Results: In exocrine pancreatic cancer samples, K-ras mutations have been found in 56% (13/23) cases and c-erbB2 overexpression in 21.4% (6/28). In 5 cases of K-ras analysis no DNA amplification occurred. No K-ras mutation or c-erbB2 overexpression was found in 3 neuroendocrine tumours. c-erbB2 overexpression was strongly correlated with shortened overall survival (Breslow: p=0.184). Other analyses did not reach statistical significance.

Conclusion: We conclude that overexpression of c-erbB2 gene, but not K-ras mutation, is strongly associated with shortened survival of exocrine pancreatic cancer patients. Acknowledgement: Supported by grants IGA MZ CR 4953 - 3, LF1-206019-2