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A - EVALUATION OF THE ACTIVITY OF THE REGIONAL REFERENCE CENTRE FOR HYPOPHARYNX, LARYNX, HEAD AND NECK CANCER AND URINARY BLADDER DURING 1978

by

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1. Studies on the aetiological factors in bladder cancer

Under this heading we take the liberty to review the activities started before the establishment of the Centre in order to complete the picture.

(i) Tryptophan metabolism

Tryptophan metabolism in schistosomal and non-schistosomal patients with bladder cancer and with other, different urological diseases (1964-1970).

These studies have revealed that the endogenous carcinogenic metabolites of tryptophan, which were found in the urine of non-schistosomal bladder cancer patients were also found in schistosomal bladder cancer patients. It was concluded that the high excretion of levels of these carcinogenic metabolites in bladder cancer patients, as compared with others, with different benign urological diseases, may play a role in the induction of cancer bladder.

(ii) Effect of cigarette smoking on tryptophan metatolism - 1970

Tryptophan metabolism was found to be altered in cigarette smokers, and increased amounts of tryptophan carcinogenic metabolites were found in the urine of cigarette smokers.

(iii) Effect of some hormones on tryptophan metabolism (1974-76)

Some natural and synthetic hormones e.g. Oestradiol 17-B, Progesterone, Stilbsterol and others, and especially those used as contraceptive pills, may induce abnormal excretion levels in some carcinogenic tryptophan metabolites.

B-Glucuronidase

(iv) Studies on B-Glucuronidase activity in schistosomal and non-schistosomal cancer patients, and others with different benign urological diseases (1965-1970).

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The results of these studies showed that the activity of B-Glucuronidase increased in the urine of patients with bladder tumours either associated with schistosomiasis or free from its infestation. The urinary tract may cause an increase in urinary B-Glucuronidase activity, especially in schistosomal bladder cancer patients. It was concluded that urinary B-Glucuronidase plays a part in induction of bladder cancer by the hydrolysis of the soluble esters of tryptophan metabolites and releasing the less soluble carcinogenic bases.

2. Studies on Urinary non-specific alpha esterases

(i) The biochemical method for measuring the activity of urinary non-specific alpha esterases was modified and restandardized, using Sigma chemical products: alpha-naphthyl acetate and Fast Garnet GBC. The time of incubation is fifteen minutes and the absorption readings are now measured after thirty minutes of addition of Fast Garnet GBC. Moreover, the enzyme unit is expressed as μ moles of alpha-naphthyl produced/ minute. The method of calculation was also modified to express the real activity of urinary enzymes.

All these modifications lead to the same conclusions previously found for using the urinary alpha-esterase activity as a preliminary screening test for bladder cancer. The previous suggested limit of urinary enzyme activity (150 units), is lowered to 50 units, after these modifications, as a limit to discriminate between patients with bladder cancer and those with other urological diseases.

(ii) Studies on the enzyme kinetics and the separation of these enzymes are still in progress and under investigation.

(iii)A pilot field study is being conducted at Montazah Schistosomiasis Dispensary to predict the administrative difficulties when applied on a large scale, and to make cost/benefit evaluations.

(iv) Suggested research activity for 1979

(a) effect of sex, age, smoking, haematuria, pyuria and bacterial infection on urinary enzyme activity;

(b) studies on some other biological markers in a comparative study and the possible combination between these parameters and urinary alpha-esterases, in order to increase the sensitivity and specificity of the esterases method.

These markers are:

(1) Fibrenogen Degradation Product (FPD).
(2) Urinary acid and alkaline ribonucleases and deoxyribonuclease.
(3) Urinary muramidase activity.

The non-specific alpha esterase in breast and thyroid tumours

As it is appreciated that a rise in the levels of alpha-esterase enzymes is not specific to bladder cancer, but may be high in other types of cancer, a basic study was started in the pathology department to determine the activity in other organs. We started with thyroid and breast tissue. Although this histochemical study may be useful in pathological diagnosis, it can be useful as a screening test only in those organs from which secretions or discharged changes can be collected and examined, e.g. cervix, bronchus, etc.. Studies of these may be the subject of further report.

Thyroid tumours

The non-specific esterase activity was studied in tissue sections of benign and malignant thyroid tumours (histochemically), using alpha-naphthyl acetate as substrate and a dye diazo fast blue.

The reaction representing the enzyme activity in both benign and malignant tumours was markedly increased as compared with sections taken from normal tissue. However, the reaction was still much higher in malignant than in benign tumours and was higher in papillary than in follicular carcinoma. Anaplastic carcinoma and medullary carcinoma of the thyroid were exceptions. The non-specific esterase activity in the former was very weak and was moderate in the latter.

It was thus concluded that this technique may be of value in diagnosing thyroid neoplasia, follicular and papillary, in cases which are histologically doubtful.

Breast tumours

The non-specific esterase activity was demonstrated in the different types of breast malignant tumours, scirrhous, medullary, colloid, tubular and non-infiltrating ductal and lobular carcinoma.

In all types the non-specific esterase activity was higher than in normal breast spithelium. There was no significant difference between the different types of tumours. However, the enzyme activity was higher in tumours associated with lymph node metastasis than in those with no lymph node metastasis. Hence it was deduced that this enzyme plays a role in invasiveness and spread of breast cancer.

Localization of carcinoembyronic antigen (CEA) in cancer bladder using immunoperoxidase technique

It was proved that the plasma and urine CEA levels were found to be influenced by different diseases, not only malignant diseases, but also in many other gastro-intestinal diseases, such as pancreatitis, liver diseases as well as in many urological diseases. For this fact, we applied the immunoperoxidase for localization of CEA in tumour cells themselves, specially localization of CEA in cancer bladder had not been tried before.

Thirty-six bladder tissue specimens were examined. Some specimens with different schistosomal lesions, and other with cancer bladder. At the same time ten normal bladder specimens were used as a control. Our studies showed a positive reaction in CEA by I.P. technique, in schistosomal and non-schistosomal cancer bladder cases, including squamous cell carcinoma, transitional cell carcinoma and adenocarcinoma.

Our results on schistosomal squamous metaplastic lesions showed positive immuno-peroxidase reaction for CEA, while schistosomal proliferation of metaplastic lesions produced a negative I.P. Depending on these results, we considered squamous metaplasia a precancerous lesion, which gives importance to these techniques.

The detection of CEA in tissue by I.P. is a good indicator for the presence of malignancy at the cellular level. Thus we suggest detecting the CEA not only in the sera of bladder cancer but also in the tissue.

Value of CEA in sera of bladder cancer cases as a diagnostic and prognostic test

Encouraged by the value of the test in colonic cancer, cases with cancer bladder treated by surgery and/or radiotherapy are studied for the value of CEA as assessed before and after treatment. This was compared with the values in normal controls and cases with schistosomal cystitis but with no malignant tumour.

Twelve cases treated by cystectomy and two with radiotherapy were studied - only one treated surgically showed significant levels compared to the controls. This case showed a raised value of CEA antigen preoperatively: 11.3 ng/ml. Result was reduced to 6.3 ng/ml postoperatively.

Further work is in progress as the numbers are now too small to obtain significant results.