TUMOR MARKERS

ESSAY

Submitted for Partial Fulfilment of
The Master Degree of
(GENERAL SURGERY)

BY

FAYEZ ADLY AZIZ

M.B., B. Ch.

Supervised By

Prof Dr

ABDEL-MEGUID EL-SHINNAWY

Professor of General Surgery

AIN SHAMS UNIVERSITY

Dr.

MOHAMED ABD EL-MONAIM

Lecturer of General Surgery

AIN SHAMS UNIVERSITY

1986

Central Library - Ain Shams University

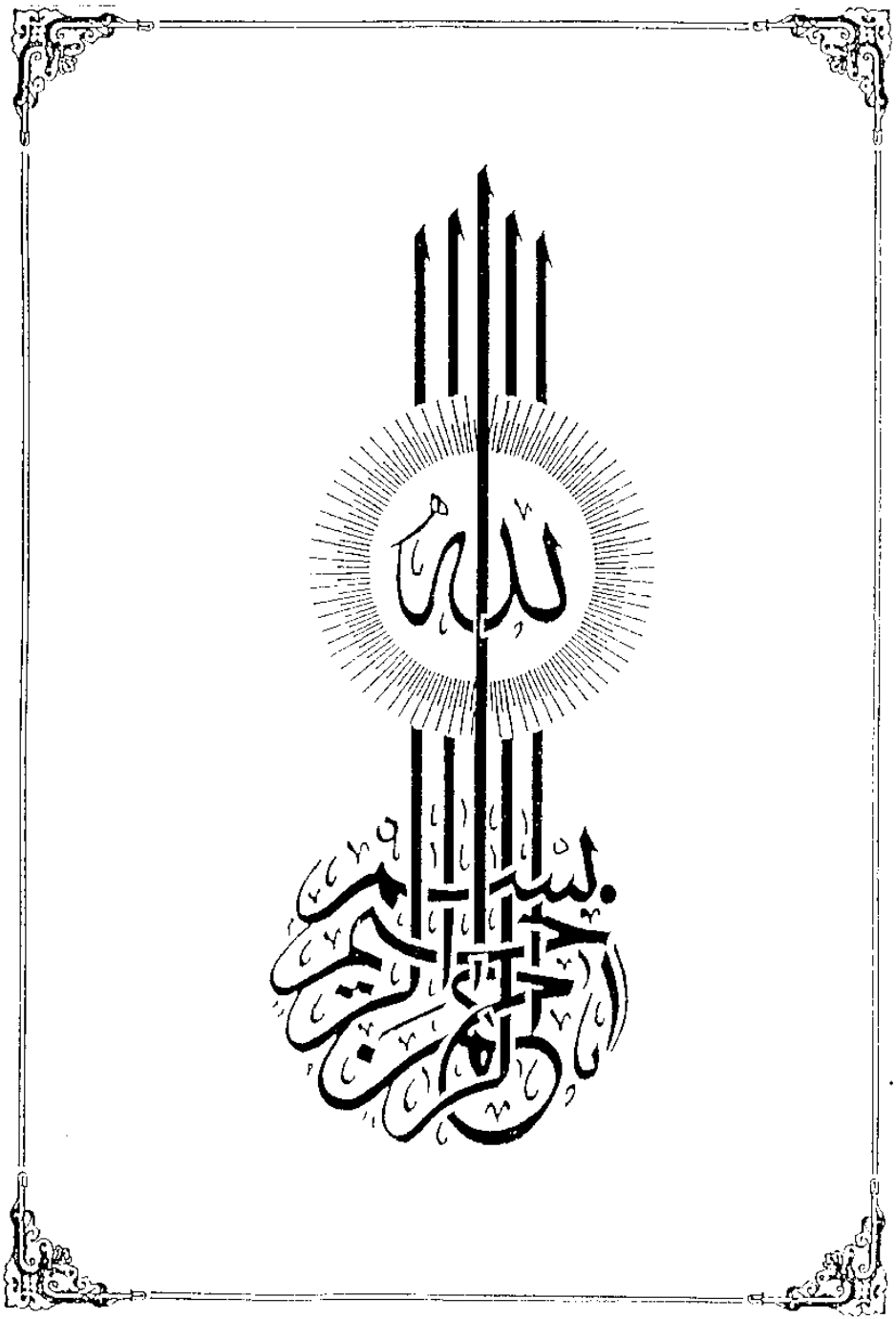
ACKNOWLEDGEMENT

I would like to express my deepest appreciation and gratitude to Professor Dr. **ABDEL-MEGUID EL-SHINNAWY**, *Professor of General Surgery, Faculty of Medicine, Ain Shams University, for his valuable supervision, guidance and encouragement.*

I wish also to acknowledge with my cordial thanks to Dr. **MOHAMED ABD EL-MONAIM**, *Lecturer of General Surgery, Faculty of Medicine, Ain Shams University, for his valuable assistance and advice.*

** **
*

Central Library - Ain Shams University



Central Library - Ain Shams University

CONTENTS

Central Library - Ain Shams University

Central Library - Ain Shams University

TUMOR MARKERS

Central Library - Ain Shams University

TUMOR MARKERS

1) Introduction :

The physical examination and standard diagnostic radiologic procedures have serious limitations in the early detection and localization of small tumor mass. Aneoplasm of one cubic centimeter, a realistic limit of clinical screening, has already completed approximately 30 doublings or two thirds of its growth. It contains one bilion cancer cells, and viable cells are likely to have been shed into the blood stream or lymphatic system. Despite an "early" diagnosis and surgical removal, the patient may have many undetected microscopic metastases. In patients with advanced stages of disease, particularly with intra-abdominal malignancy, it is often difficult to assess disease progression and response to treatment.

Research has therefore been directed toward the identification of tumor-specific products in body fluids that might have three potential applications in clinical practice :

1) early diagnosis of malignancy.
2) the pre- or post-operative assessment of prognosis.
3) early diagnosis or recurence or distent metastase.

Central Library - Ain Shams University

An ideal tumor marker not only should signal the presence of microscopic tumor but also should define the site and morphologic type of malignancy.Unfortunately the available markers have not attained such a high degree of sensitivity and specificity. The problem of sensitivity has been addressed by the use of radioimmunoassays that can measure nanogram quantities of antigen. The problem of specificity has been more difficult to resolve. The use of normally occuring hormones enzymes, proteins or oncofetal antigen requires that the blood concentration of these materials must be present in excess of the establised normal range. Attention has more recently been directed toward the placental hormones, which are not normally found in the blood of adult males and non pregnant females.

2) Definition of Tumor Markers :

Tumor markers are substances made by tumors, or are at least closely associated with the presence of tumors, that can aid in the diagnosis of cancer and in assessment of tumor burden. Many of the clinically useful tumor markers have been detected by immunologic assays.

Central Library - Ain Shams University

In recent years there has been growing interest in the clinical application of immunologic assays for the evaluation of patients with cancer. This has been due to recent advances in radioimmunoassays, and other highly sensitive immunologic techniques which allow measurement of picogram or nanogram quantities of antigens. In addition, immunologic assays can be exquisitely specific and in some instances, can be discriminant between molecules with differences in single amino acid or suger. Such procedures have provided the basis for discrimination of various types of neoplastic cells from normal cellular materials.

Measurement of tumor markers has important implication for the diagnosis and management of cancer, and also for basic understanding of the biology of human tumors.

3) Classification of Tumor Markers :

Avariety of substances may be useful as tumor markers some are normally present in the tissues of the fetus and then either disappear or are greatly reduced in amount by the end of gestation or shortly after birth. These have been termed oncofetal antigen

Central Library - Ain Shams University

or embryonic antigens. Other tumor markers may be normally produced by the placenta. Some tumor markers may be characteristic of cancers of a particular tissue or organ and, some may be present in some normal adult tissues but may be functionally or quantitatively altered in tumors or may be released in higher concentrations into the circulation of cancer patients. Antigen of oncogenic virus, or at least antigens cross-reactive with viral patients, may also be detectable in some human tumors. Most tumor markers are characterized only by their immunologic properties, but some have functional activities or are variants of normal functional products. There include hormones, enzymes and metal-binding, and secretory protiens. In addition to detection of tumor markers by their antigenic specificities, assays have been developed recently for the general detection of circulating antigen antibody complexes, and a considerable number of cancer patients have been found to have elevated levels. Such assays would detect elevated levels of complexes, regardless of the antigens to which the antibodies are directed.

It should be obvious from the large number of examples of possible human markers listed in (Table 1) that

Central Library - Ain Shams University

a high level of effort is being expended in this area of research. However, it is important to note that only a few of these have been definitively shown to have place in clinical oncology. This is largely a reflection of the difficulties involved in satisfactory transfer of technology from the research laboratory to the bedside.

Central Library - Ain Shams University

Table 1 : Types of human tumor markers.

Type of antigen	Examples	Tumor mainly associated with	References
I- Oncofetal antigens	1. Carcinoembryonic antigen (CE.A)	Gastrointestinal tract but also other carcinomas.	(Gold et al., 1965), (Zamcheck et et al., 1972).
	2. Alpha-fetoprotein (AFP)	Hepatoma, testicular germ cell tumors.	(Abelev et al., 1971), (Waldman et al., 1974).
	3. Fetal sulfoglycoprotein antigen (F.S.A.)	Gastric cancer	(Hakkinen et al., 1969).
	4. Pancreatic oncofetal antigen.	Carcinoma of pancreas	(Banwo et al., 1973), (Gelder et al., 1979).
	5. Gamma fetoprotein	variety of cancers	(Edynak al al., 1972).
	6. Beta-oncofetal antigen (BOFA)	variety of cancers	(Fritsche et al., 1975).
II- Placental antigen s	1. Human chorionic gonadotropin (h.c.G)	Choriocarcinoma , nonseminomatous testicular tumors, other tumors.	(Brounstein et al., 1973), (Vaitukaitus et al., 1976).
	2. Human placental lactogen (hPL)	Choriocarcinoma , other tumor.	(Rosen et al., 1979).
	3. Placental alkaline phosphatase (Reganisoenzyme)	Gynecologic and other tumors.	(Nathanson et al., 1971).
	4. Pregnancy B_1-globulin.	Choriocarcinoma	(Tatarinov et al., 1977).
	5. Placental pyruvate kinase.	Variety of cancers	(Fottrell et al., 1976).

Central Library - Ain Shams University

Type of antigen	Examples	Tumor mainly associated with	References
III- Tissue or organ associated antigens.	* Cervical cancer antigens.	* Carcinoma of cervix.	(Kato et al., 1977).
	* Ovarian cancer antigens.	* Carcinoma of ovary	(Bhattacharya et al., 1979)
	* Breast cyst fluid protein.	* Breast cancer.	(Haagensen et al., 1977).
	* Lungtumor antigens	* Lung cancer	(McIntire et al., 1979).
	* Colon specific antigen (C.S.A.P.)	* Colorectal cancer	(Pant et al., 1977).
	* Zinc glycoant marker (ZGM)	* Gasterointestinal cancer	(Pusztaszeri et al., 1976).
	* Leukemia associated antigens.	* Acute leukemia	(Greaves et al., 1979), (Herberman et al., 1977).
	* Prostatic acid phosphatase	* Carcinoma of prostate.	(Foti et al., 1977).
	* Nonhistone nuclear antigens.	* Variety of cancers.	(Chiu et al., 1977).
IV- Ectopic hormones.	* Calcitonin.	* Medullary carcinoma of thyroid	(Heath et al., 1979). (Tashjian et al., 1974).
	* "Big" A.C.T.H.	* Lung cancer.	(Wolfsen et al., 1977).
	* Parathormone.	* Lung cancer.	(Heath et al., 1979).

Central Library - Ain Shams University

Type of antigen	Examples	Tumor mainly associated with	References
V- Isoenzymes	* Lactic dehydrogenase (LDH)	* Breast cancer.	(Blair et al.,
	* Alkaline phosphatase.	* Variety of cancers	(Carey et al., 1976). (Higashino, 1975).
VI- Antigens of oncogenic viruses.	* Herpes simplex virus (HSV) non virion antigens.	* Carcinomas of cervix and of head , neck.	(Nahmias et al., 1979)
	* Epstein Barr virus (EBV) associated antigens.	* Burkitts lymphoma nasopharyngeal carcinoma.	(Klein et al.,
	* Mouse mammary Tumor virus.	* Breast cancer.	(McCoy et al., 1978). (Muller et al., 1972).
	* Mason pfizer monkey virus.	* Breast cancer	(Yeh et al., 1975).
	* Murine and non-human primate leukemia virus.	* Acute leukemia	(Herberman et al., 1977)
VIII- Normal antigens or their variants.	* Ferritin	* Leukemia, lymphoma breast cancer	(Marcus et al., 1975). (Mori et al., 1976).
	* Casein	* Breast cancer.	(Hendrick et al., 1974).
	* Ceruloplasmin	* Variety of cancers	(Linder et al.,
	* Immunoglobulin	* Multiple myeloma, Waldenstroms macroglobulinemia.	(Linder et al.,

Central Library - Ain Shams University

Type of antigen	Examples	Tumor mainly associated with	References
	* Blood group substances.	* Variety of cancers	(Davidsohn et al., 1979). (Springer et al., 1974).
	* Lactoferrin	* Lung cancer.	(Veltri et al., 1976).
	* Tissue polypeptide antigen (TP.A)	* Variety of cancers	(Bjorklund et al., 1976).
VIII- Antigen antibody.		* Variety of cancers.	(Theofilopoulos et al., 1976).

Central Library - Ain Shams University