PAP, CGA, CEA, and NSE Biomarkers – Importance in Prostate Cancer Diagnosis

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DISCLAIMER: Please recognize that I am not a Medical Doctor. I have been an avid student researching and studying prostate cancer as a survivor and continuing patient since 1992. I have dedicated my retirement years to continued research and study in order to serve as an advocate for prostate cancer awareness, and, from a activist patient's viewpoint, to voluntarily help patients, caregivers, and others interested develop an understanding of prostate cancer, its treatment options, and the treatment of the side effects that often accompany treatment. There is absolutely no charge for my mentoring – I provide this free service as one who has been there and hoping to make your journey one with better understanding and knowledge than was available to me when I was diagnosed so many years ago. Readers of this paper must understand that the comments or recommendations I make are not intended to be the procedure to blindly follow; rather, they are to be reviewed as my opinion, then used for further personal research, study, and subsequent discussion with the medical professional/physician providing your prostate cancer care.

Below is an explanation that should be easy to understand the role of biomarkers PAP, CGA, CEA, and NSE to better understand the extent of a patient's prostate cancer. These relate more to the Nature of PC but are also tied into extent since if elevated indicate that the PC is active and likely in distant sites. Please take note that drugs prescribed to the patient should be checked to see if they may be distorting the levels of any of these biomarkers. This same consideration should be investigated with an abnormal level increase with most any test.

PAP, CGA, NSE, and CEA are important biomarkers for patients with validated GS 4+3/7, 8, 9, and 10. Internationally recognized Medical Oncologist Stephen B. Strum, who has specialized specifically in prostate cancer research and treatment since 1983, remarks: "I have advocated testing of the above markers but I see this recommendation has been abused to where it is being routinely tested by a number of physicians despite a validated GS of 6 or (3,4). I have rarely (can't think of one case) seen elevations of these markers in such instances, especially when the GS

has been validated by an expert. These markers are most useful in THE CONTEXT of high Gleason scores such as (4,3) or higher (4,4), (4,5), (5,4) or (5,5).This includes:

PAP (Prostatic Acid Phosphatase - concern if over 3.0 - Indicates the disease may not be organ-confined - a possible lymphatic spread of the disease)

CGA (Chromogranin A - concern if over 14.3 U/l - A progressive increase in serum CGA indicates an aggressive clone of PC cells that has an increased tendency to metastasize to lymph nodes, liver and lungs). (My Note: Since CGA is more often measured in ng/ml, according to http://emedicine.medscape.com/article/2114314-overview the normal range of CGA is <36ng/ml).

NSE (Neutron-Specific Enolase - concern if over 12.5 ug/L - Identifies a possibly more aggressive PC)

CEA (Carcinoembryonic antigen - concern if over 4.0 ug/L - Identifies PC that may be more aggressive or possibly AIPC)

(Best to always have repeat tests performed by the same laboratory since methods of testing can vary)

(Further described below)

Definitions:

Prostatic Acid Phosphatase (PAP) (Normal range 0-3.5 ug/L) -The PAP should be a part of your baseline PC evaluation. However, as with PSA, the PAP may also be elevated due to the trauma caused by the prostate biopsies. Therefore, you need to wait at least five weeks after the biopsy procedure before testing for PAP unless this test was ordered prior to the diagnostic biopsies. Ideally, both PSA and PAP testing should not be done for at least 48 hours after any sexual activity involving ejaculation, 48 hours after DRE, or 48 hours after riding a bicycle.

Most physicians and patients consider the PSA and PAP to be simply "blood tests." However, the biologic reality is that PC cells elaborate numerous chemical substances that are vital to their growth and well-being and are often related to

their function. Many of these cell products are enzymes important to the growth and spread of the cancer. PAP and PSA are just two of many enzymes that should be regarded beyond that of merely representing commercial laboratory tests. The results of PAP and PSA testing add to the biologic "profile" that an astute patient-physician team uses to accurately decipher the real status of the patient's disease. A PAP level within normal range is indicative the PC may not have migrated and is still confined to the area of the prostatic bed and not beyond the lymph nodes. Here is a April 2008 report in PubMed regarding The Importance of the serum Prostatic Acid Phosphatase (PAP) Test to Determine Cause-Specific Survival in Patients: **http://www.ncbi.nlm.nih.gov/pubmed/18242384?dopt=Abstract**

CHROMOGRANIN A (CGA) (Normal range is <36ng/ml) according to http://emedicine.medscape.com/article/2114314-overview - The plasma CGA level is used to help identify patients with an aggressive form of PC. In such patients, the CGA elevations should be documented as progressively increasing and not just a sporadic or stable elevation.
This is not as complicated as it may sound. Prostate tissue, both benign and malignant, is comprised of at least four different cell types: basal cells, epithelial cells, neuroendocrine cells and stromal cells. CGA testing involves the measurement of blood levels of chromogranin A, a protein synthesized by the neuroendocrine cell type (i.e. of neurogenic origin with endocrine functions) found in prostate cancer. Neuroendocrine cells in PC are not dependent on androgens as are the epithelial cells (also called luminal cells), which are the cells most commonly involved in PC growth. Serial CGA testing can help track the patient's response to treatment, especially if serum PSA and/or PAP expression is low. Low PSA levels may be seen despite significantly high tumor volumes in situations where the PC has mutated to an aggressive cell type; this is characterized by a high Gleason score of 8-10. In fact, obtaining a full baseline set of biomarkers in situations associated with such an aggressive picture often reveals elevation(s) in plasma CGA.

CARCINOEMBRYONIC ANTIGEN (CEA) (Normal range <4.0 ug/L) - a fetal antigen or protein that may be expressed by PC that is aggressive and often androgen-independent).

When a progressive increase in any of these biomarkers is documented, there is

invariably evidence of mutated aggressive PC. These findings should always be placed in context with the rest of the clinical and pathological picture.