10. Prostatic Cancer

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Prostatic Acid Phosphatase

Sensitivity and Specificity of Kits The first enthusiastic reports on the diagnostic potential of a radioimmunoassay (RIA) to measure prostatic acid phosphatase (PAP) have not been borne out by subsequent studies [1]. A number of commercial RIA and immunoradiometric (IRMA) kits are currently available and all suffer from the same general problems; i.e. they are insufficiently sensitive to detect minimal disease and are occasionally abnormal in patients with benign prostatic hypertrophy. Enhanced sensitivity of such kits is generally associated with reduced specificity while attempts to increase specificity result in diminished sensitivity.

Stability of Serum Samples;

Interfering Substances

PAP deteriorates very rapidly at room temperature and following freezing and thawing [2]. This creates a problem if measurement of the enzyme is to be undertaken at a regional laboratory.

Acidification of the

samples will stabilize the enzyme if it is to be measured by conventional colorimetric techniques, but this treatment interferes with the antigen-antibody reaction and yields spurious results by RIA or IRMA. More work is needed in this area. We have observed that hyperlipemia leads to defective pellet formation in some of the kits. Wildly abnormal results occur as a consequence. It is not clear what level of triglyceridemia begins to interfere with the test. Until further information becomes available, it is suggested that blood samples should be taken with the patient in a fasting state.

Monitoring Treatment

Although the test is routinely used to help stage patients, it suffers from the pitfalls mentioned above. Its main use lies in monitoring treatment, although here also lack of sensitivity and specificity remains a problem. Moreover, if the tumor is undifferentiated, it may no longer secrete the enzyme.

Efforts have been made to enhance the capacity to detect metastases in prostate cancer. One of these involves the measurement of PAP in bone marrow. Initially, this procedure was thought to be useful. Careful study

of a larger series of patients, however, indicated that the technique adds little to what can be deduced by measurement of the enzyme in peripheral blood [3]. PAP can be detected histochemically. This may be helpful sometimes in differentiating metastatic adenocarcinomas of undetermined origin [4].

Prostate-Specific Antigen

This marker for prostate cancer has recently been described by the group at Roswell Park. Immunohistochemical detection of prostatic cancer has been demonstrated and an enzyme-linked immunosorbent assay has been developed for measuring the antigen in human blood. As with the analysis for PAP, measurement of prostate-specific antigen (PSA) lacks sensitivity and specificity. It appears that PAP and PSA are distinctly different substances and a combination of the two procedures has been used to increase their effectiveness in detecting prostatic cancer while minimizing nonspecificity. This is an interesting observation, now requiring further corroboration [5].

The use of PSA as a prognostic indicator and in predicting recurrence is currently the subject of limited investigation, but is nevertheless generating widespread interest [6–10]. Whether the same PSA is being studied by different groups is not clear. Furthermore, concurrent sequential determinations of PAP appear, at times, to be neglected in these studies, so that the degree of concordance between the two markers during monitoring of therapy is rather difficult to ascertain. This kind of data may be required in order to establish the degree of tumor heterogeneity in the individual case and to recognize the emergence of hormone-resistant clones. A better understanding of the biology of the tumor may facilitate individualization of therapy.

Other Markers

In the absence of tumor-specific antigens and as long as markers for the common epithelial tumors lack sensitivity and specificity, reliance has to be placed on a host of ancillary techniques to facilitate diagnosis and to monitor treatment. Prostate cancer is no exception. The following is a partial list of nonspecific biochemical tests that have been investigated in this connection: total alkaline phosphatase and alkaline phosphatase isoenzymes [11]; creatine kinase BB [12]; lipid-bound sialic acid [13]; lactic dehydrogenase isoenzymes [14]; urinary hydroxyproline [15]; prostacyclin [16]; polyamines [17], and hemoglobin F [18].

Except for the widespread and acknowledged use of total alkaline phosphatase determinations, the precise role that the foregoing tests play in facilitating diagnosis, staging and monitoring treatment of prostatic cancer still remains to be determined. Parenthetically, the same can be said for the usefulness of these and other tests for most epithelial tumors. There is a desperate need for the development of a collaborative system to evaluate the great variety of tests alleged to be useful in cancer detection and management.

Hormone Receptors

Attempts are being made to devise tests for hormone-binding proteins in carcinoma-tous prostatic tissue in order to ascertain

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whether the tumor may be responsive to endocrine manipulation [19]. This has turned out to be considerably more difficult than quantitating estrogen and progesterone receptors in breast cancer. The problem appears to lie primarily in the heterogeneity of the primary lesion and the difficulties inherent

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in obtaining tissue from metastatic sites. 8

9 Plasma Hormone Levels in Monitoring Response to Treatment

Plasma testosterone levels are sometimes measured as a means of evaluating the response of patients to hormone manipulation.

13 Care must be taken to ensure reproducibility

at low testosterone levels where one reaches 14

the limits of method sensitivity. Glucocorticoids are sometimes used to help relieve pain

in patients with metastatic disease and to 16 reduce levels of adrenal androgens. Measurement

of androstenedione and dehydroepiandrosterone sulfate can be undertaken to help

18 monitor the adequacy of treatment. Assay of

these substances does not constitute a problem. 19

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