DIAGNOSTIC PRACTICE

Prostase, hK2 May Be More Accurate Biomarkers For PCa

Presently, invasive and expensive biopsy is only reliable way to make a definitive Dx

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Although widely used as a diagnostic guideline for prostate cancer (PCa), an elevated level of serum prostate specific antigen (PSA) is not specific to the disease, nor is the antigen a true marker of the disease, a leading researcher reported during a session at Urology Update in Toronto.

"PSA is not only produced by cancerous tissue, but also by normal and hyperplastic tissue," said Dr. Elephthorios P. Diamandis, "and the normal and hyperplastic tissue produce significantly more PSA than cancerous prostatic tissue."

The professor of medicine at the University of Toronto and head of the division of clinical biochemistry at Mount Sinai Hospital said PSA levels rise in PCa cases because the disease produces more malignant cells, destroys the gland's architecture, and diffuses additional amounts of the antigen into the circulation.

"Increases in PSA in the circulation are not due to overproduction by the tumor cells," he emphasized. "In fact, there are recent reports in the literature speculating that tissue PSA may be an anti-carcinogenic molecule, that is, a tumor suppressor not only for the prostate but also for breast tissue."

Serum PSA is also elevated in benign prostatic hypertrophy (BPH) and prostatitis, and is only a marker of cancer, he added. There is no biochemical test that can distinguish between PCa and BPH; an invasive and expensive biopsy is still the only reliable way to make a definitive diagnosis.

"The problem with biopsy," Dr. Diamandis said, "is that for every five you perform on suspicious patients, only one will reveal a cancer, the others will be biopsies for nothing. What we need today is a non-invasive way to discriminate between BPH and prostate cancer."

Until a more definitive method is developed, several other modalities can be utilized. One is to calculate the percentage of free prostate specific antigen (FPSA), but this measurement is effective only within a range of 4-10(/L of total PSA. There is an inverse relationship between the per cent of FPSA and the probability of cancer; the lower the percentage, the higher the probability.

"If the per cent of FPSA is greater than 25, the probability of cancer is only about 5%," Dr. Diamandis said. "We use this modality to spare some patients the necessity of a biopsy.

"But be careful, because the cutoff is different with different biochemical methods. You should ask your biochemist what the optimal cutoff is with the per cent FPSA method you use. And please remember that the FPSA is a relatively weak test because it doesn't really discriminate efficiently."

New biochemical tests for PCa are expected to be introduced shortly. One, the human glandular kallikrein (hK2) molecule located next to the PSA gene on chromosome 19, is expected to be in use later this year. Although it is no better than PSA as a biomarker for PCa, it may have some value in identifying younger men with very mild elevations of PSA who are at high risk of developing the disease.

"PSA levels of 2.5, 3, and 3.5 are not normal for most relatively younger patients and the literature says that about 15% have prostate cancer," he said. "But we don't biopsy them because there are so many of them. This hK2 marker is supposed to tell you which patients have a higher than 15% chance of having cancer, and who should be biopsied when the hK2 is elevated."

Candidates for biopsy are men with a high hK2/FPSA ratio, because they are most likely to have a cancerous prostate.

The search is on for other kallikrein molecular relatives of PSA that may be useful biomarkers for cancer, Dr. Diamandis said. The Human Genome Project may uncover other valuable markers, and multianalysis may provide yet another method.

"We may have five weak tests, but if we put all of them together we may come up with a final predictive value that is much more powerful than each of the five alone," he said. "Now people are not talking about five [tests] but about tens and hundreds and sometimes thousands of multiple analyses in one shot."

The most recent potential biomarker is prostase, a gene that appears to be expressed preferentially in PCa; if its potential is realized, prostase may be used within the next three or four years as another diagnostic option in PCa.

Even with the imperfect tools clinicians have today, there is reason to be optimistic about the treatment of PCa, Dr. Diamandis concluded.

"My own belief is that nobody should die of prostate cancer in the new millennium, because with what we have we actually can do a very good job treating and monitoring patients with prostate cancer."