The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Volume 343:890-891 September 21, 2000 Number 12

Elevated Serum Prostate-Specific Antigen Levels in a Woman with Metastatic Breast Cancer

To the Editor: Prostate-specific antigen (PSA) is a protein produced almost exclusively by the prostate. Although various tissues in females have been found to produce very small amounts of PSA, serum PSA levels in females are quite low and are measurable only with ultrasensitive PSA immunoassays.[1] In a study of 1064 women, the highest serum PSA levels were less than 1 μg per liter, and only 1.5 percent of the women had levels that were higher than 0.1 μg per liter; the median value was 0.002 μg per liter.[2] Significantly higher values have been reported in women with benign breast diseases.[3] PSA is a hormonally regulated protein, and administration of the synthetic progestin megestrol acetate in women with metastatic breast cancer may induce the production of PSA.[4] Elevated serum PSA levels appear to have prognostic value in such patients.[4]

I report here on a woman who received a diagnosis of unilateral breast cancer in 1977, at the age of 48 years, and was treated with radical mastectomy. Twenty years later, the patient received a diagnosis of cancer in the remaining breast, and she was treated with simple mastectomy. Axillary-node examination revealed metastasis, and a lung mass was detected along with further metastasis to the spine, skull, and ribs. The patient was treated first with tamoxifen and then with megestrol acetate. Treatment with megestrol acetate was initiated at a single dose of 160 mg per day. Eight months later, while the treatment was still being given, a serum sample was obtained for this analysis.

Serum total and free PSA were measured with two commercial immunoassays (Roche Elecsys and DPC Immulite 2000), with identical results. The tests were performed because of a recent report of induction of PSA in patients receiving megestrol acetate.[4] The total PSA level was 16 μg per liter, and the free PSA level was the same (free PSA, 100 percent). The serum sample was further fractionated on a gel-filtration column, along with a serum sample from a male patient with a similar total PSA value. As expected, the serum from the male patient contained PSA that was predominantly bound to α_1-antichymotrypsin, whereas the sample from the patient with breast cancer contained predominantly free PSA.

The patient with breast cancer had further metastasis, to the central nervous system. A sample of cerebrospinal fluid contained 10.0 μg of total PSA per liter. It has been reported that the concentration of total PSA in cerebrospinal fluid in men and women is normally less than 0.4 μg per liter.[1]

The serum PSA level in this woman far exceeded the level in normal men (<4 μg per liter) or even in men with localized prostatic carcinoma (generally <10 μg per liter). This finding suggests that with hormonal stimulation by the androgenic progestin megestrol acetate, serum PSA in women can reach levels that are about 8000 times as high as normal levels in women. To my knowledge, the PSA level in this woman was among the highest values reported in women and was unique in that PSA was present entirely in its free form. The free form of PSA may have value for the diagnosis of breast cancer.[5] Furthermore, PSA in cerebrospinal fluid may be a biomarker of breast cancer that has metastasized to the central nervous system. Research in animals suggests the possibility of using PSA as a target for imaging in patients with breast cancer.[1]

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