Elevated Levels of Prostate-Specific Antigen in Serum of Women With Fibroadenomas and Breast Cysts

Prostate-specific antigen (PSA) is a valuable serum marker for diagnosis and monitoring of prostate cancer. In males, the reference range is about 1-2 ng/mL, and values above 3-4 ng/mL are indicative of either prostate cancer, benign prostatic hyperplasia, or prostatitis. Women have no prostate, and levels of PSA in female serum should be very low or undetectable. Many recent reports, however, confirm that PSA is produced in the female breast (*1*). A relatively large study examined the levels of PSA in female serum and confirmed that, among serum samples from 1064 women, the highest concentration observed was 0.9 ng/mL. The median PSA in normal women is about 0.002 ng/mL (*2*). Women with hyperandrogenic syndromes may have levels up to 0.6 ng/mL.

We here report on two female patients with fibroadenomas (C-191 and C-231) and two female patients with breast cysts (C-57 and C-157), all of whom exhibited the highest PSA levels in serum among a total of 200 women with benign breast diseases. Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an abortion, confirming that these are all genotypic women. The total PSA levels measured by two different assays described elsewhere (*3*) (an in-house assay and a commercial assay; Immulite PSA; Diagnostic Products Corporation, Los Angeles, CA) were 4.8 ng/mL (C-57), 14.1 ng/mL (C-157), 55.1 ng/mL (C-191), and 7.7 ng/mL (C-231). The agreement between the two assays was ±10%.

It is well-known in the literature that the predominant form of PSA in male serum is PSA bound to α_1-antichymotrypsin (PSA-ACT) (*4*). Only 10%-20% of PSA, on average, represents free PSA with a molecular mass of 33 kd. We fractionated the serum PSA of the serum samples from the four women by using high-performance gel filtration liquid

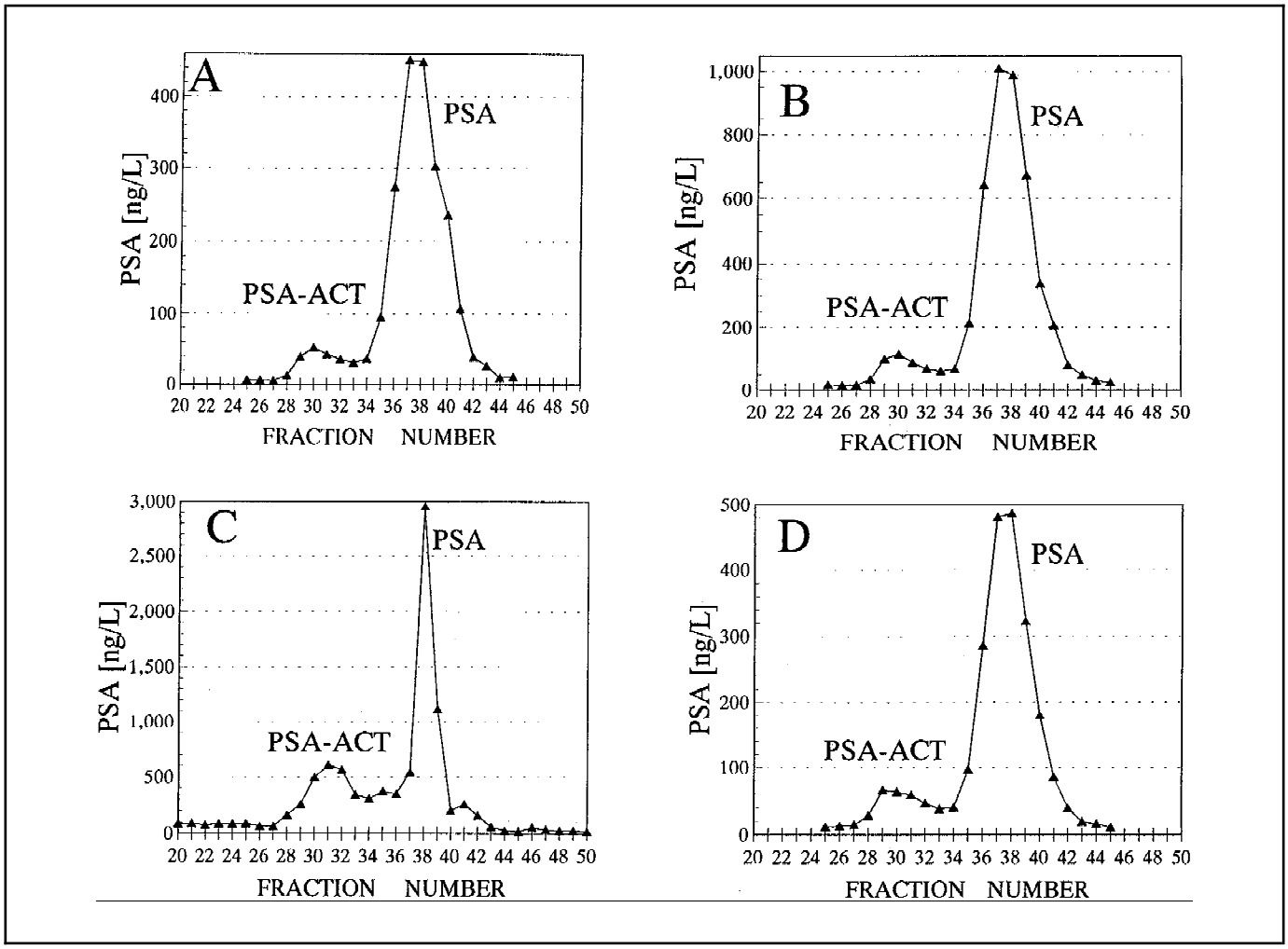

Fig. 1. Molecular forms of prostate-specific antigen (PSA) in the serum of the four women. The complex of PSA with α_1-antichymotrypsin (PSA-ACT) has a molecular mass of approximately 100 kd. Free PSA has a molecular mass of approximately 30 kd, and it is the predominant form in all sera. Patients C-57 **(A),** C-157 **(B),** C-191 **(C),** and C-231 **(D)** are shown.

chromatography and found that more than 80% of the total PSA is free PSA (Fig. 1).

These data lead us to the following conclusions: 1) The serum PSA of some women with fibroadenomas or breast cysts could reach levels higher than those seen in serum of male patients with prostate cancer. The PSA values presented here are the highest ever reported for female serum. We speculate that this PSA is produced and released by the hyperplastic breast tissue, since this tissue contains more PSA than normal or cancerous breast tissue (*5*). We further speculate that, in fibroadenomas or cysts, there may be increased leakage of PSA from the tissue to the serum, a situation that is similar to that seen in prostate cancer. 2) The molecular forms of PSA in the serum of female patients with fibroadenomas or cysts are very different from those in the serum of male patients with prostate cancer. In the latter, PSA-ACT predominates; in the former, PSA-ACT is a minor component (Fig. 1). 3) Female serum should not be regarded as a PSA-free biologic fluid anymore. PSA levels higher than those seen in serum of prostate cancer patients can be seen in some female patients with fibroadenomas or cysts.

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Notes

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