LETTER TO EDITOR


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I studied with great interest the article of Henderson and Feigelson (1). The authors wrote that ‘there is a scientific basis for association between risk of breast cancer and serum androgens, as androgens could provide a large pool of substrate for conversion to estrogens via the action of aromatase in breast tissue’ (1).

I partly agree with the authors because some recent data suggest that, apart from the mechanism mentioned, the association of androgen with breast cancer is independent of estrogen. Xie et al. (2,3) have shown that testosterone affects the stroma of the gland, probably through a paracrine action of epithelial cells, and hence, the stroma may promote carcinogenesis in a reciprocal fashion, shortening the latency time of carcinogenesis in mammary gland. In vitro studies (4) on some human breast tumor cell lines also support the role of androgens in breast carcinogenesis via stimulation of cell proliferation as direct activation of estrogen receptor alpha. Analysis of DNA sequence from exon 1 of the androgen receptor gene suggests that enhanced transcriptional activity of the gene might promote breast cancer progression (5). It is extremely important that recent epidemiological study (6) has shown that the association of androgen with breast cancer in postmenopausal women is independent of estrogens. This study, in conjunction with past epidemiologic studies (1 and references 36–39 therein), investigated postmenopausal women. Only two papers (7,8) favored a role of androgen in breast cancer of premenopausal patients.

At the Cancer Research Centre in Moscow, Russia, we divided into two groups: <35 years old (637 ‘young’ patients) and 36–45 years old (595 ‘middle-aged’ patients) (9–12). Overall survival for the young patients was statistically significantly lower than that of the middle-aged patients. To explain these data, the possible role of sex hormones was investigated in the blood serum of 60 young and 60 middle-aged patients, and in two groups of healthy women (50 subjects in each) of corresponding age. We showed that steroid hormone concentration in plasma depended on the phase of the menstrual cycle and that the basal level of secretion of estradiol was similar in all groups. In the follicular phase of the menstrual cycle, the level of testosterone in the young patients was significantly higher than in all other groups (controls and middle-aged patients), but in the luteal phase, the level of testosterone was increased significantly only in comparison with the young control group. In the middle-aged patients, in the follicular and ovular phases, the level of testosterone was decreased compared with the corresponding middle-aged control group.

Our results support those obtained by Grattiola (7) and Secreto (8), and also suggest an association of breast cancer with hyperandrogenia in premenopausal patients. Unlike their results, we found that hyperandrogenia only associates with younger premenopausal breast cancer patients (<35 years of age) (9–12).

In conclusion, some epidemiologic and experimental studies provide evidence for a causal relationship between both pre- and postmenopausal hyperandrogenia and the risk of breast cancer. These data also suggest that association of androgen with breast cancer is independent of estrogen, but the impact of androgen on breast cancer, of course, warrants further investigation (particularly in young patients because of the poor prognosis compared with older patients) just to define the strategy of chemoprevention and treatment of this cohort of patients.

References


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