EDITORIAL

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The human prolactin in breast cancer – a boon or a bane?

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The role of prolactin (PRL) in breast carcinogenesis remains unsettled controversy to be explored and remains an important area in research. PRL is responsible for the proliferation and maintenance of ductal cells within the human breast by activating the expression of genes necessary for proliferation. Hankinson's demonstrated the raised levels of PRL and subsequent raise of breast cancer in postmenopausal women. Clevenger and his colleagues confirmed the synthesis of PRL within the breast tissue through autocrine/paracrine stimulating loop mechanism. Probably this local secretion of PRL plays an important role in the growth of breast carcinoma by altering expression of PRL or its receptors [1].

Meanwhile, literature suggests that PRL levels may influence human breast cancer but no clear correlation between the circulating PRL levels and the etiology or prognosis of the disease, which was proved by using ergot drugs and sectioning of pituitary [2, 3]. To prove this concept, another cohort of women with advanced breast cancer was given a combination therapy of bromocriptine, to diminish circulating PRL levels, and a stomatostatin analog to block human chorionic gonadotrophin action. Patients with above combination therapy showed no evidence of disease progression [4]. This confirms the combination of anti-prolactin and anti-growth hormone could be tried as therapeutic trial in breast cancer patients.

Berenblum proposed a two-step theoretical mode to establish the relationship of PRL and its role in breast malignancy in mice. Variation in the level of PRL secretion would alter the architecture of breast epithelium by influencing its metabolism. Later the transformed epithelium may initiate or inhibit the tumor formation. In this way, the PRL directly stimulate the mitotic activity of the transformed epithelium or indirectly through the ovarian estrogen [5]. Goodman and Bercovich hypothesized that PRL may have the potential for direct prevention and treatment of breast cancer [6]. Nouhi and his co-workers (2006) proved the anticancer role of PRL by suppression of tumor invasion. It was supported by elevated levels of prolactin and recurrence free survival rate of breast carcinoma followed by hormone replacement therapy [7].

Recently, it was shown that PRL-stimulated Stat5 pathway

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plays a complex role in breast cancer and as well as opposite actions, may oppose its progression, in line with the evidence that PRL may act against angiogenesis in tumors, suppress invasion, support adhesion and inhibit epithelial transition and cell proliferation, as shown in animal and in vitro models. Study represents the first quantitation of PRL receptor (PRLr) in breast carcinoma by immunoblot analysis and indicates that PRLr and estrogen receptor (ER) expression are associated. As ER-positive tumors have a favorable prognosis in comparison with ER-negative tumors,a similar association may hold for PRLr expression. Similar to the ER-negative breast cancers, PRLr-negative breast cancers may have seized the growth regulatory signaling factors associated with the PRLr or mutated the PRLr itself. Altered receptor growth control has been hypothesized to contribute to the unfavorable prognosis associated with ER-negative tumors; a similar argument could also be made for the PRLr negative breast cancers [8].

The relevance of extrapolating the tumorigenesis data obtained in animal models to humans has always been questioned by earlier research. Bioassays and endocrinal mechanisms of PRL-mediated breast carcinomas in mice and rats were relevant and follow the same in humans [9].

Therefore, literature survey reveals that, there is no consistent concept about the role of prolactin, anti-prolactin hormones on breast cancer. Although the effect of anti-prolactin drugs have been studied to analyze their role in breast cancer in some study, till date no single study has proven the efficacy of combined therapy of anti-prolactin and growth hormones in limiting cancer progression.

Abbreviations

Estrogen receptor (ER), Prolactin (PRL), Prolactin receptor (PRLr), Signal Transducer and Activator of Transcription 5 (Stat5)

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