History and evolution of endocrine therapy of breast cancer

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The first recorded observation that carcinoma of the breast would respond to hormonal manipulation was written by Beatson slightly over 100 years ago when he reported that surgical oophorectomy induced a remission in a patient with metastatic breast cancer. Oophorectomy remained the most effective therapy for metastatic pre-menopausal breast cancer for the first half of the 20th Century. The synthesis of cortisol and other adrenocortical hormone analogues in the 1950's & 1960's made possible the expansion of ablative endocrine surgery to include adrenalectomy and hypophysectomy. This "major endocrine ablation" technique allowed post-menopausal patients with metastatic breast cancer to benefit from hormonal therapy. In large series reporting the results of major endocrine ablations, an average of 30-35% of all patients achieved substantial clinical remissions in their disease. The discovery of hormonal receptors in breast cancer tumor cells and the widespread applications of biochemical and histochemical receptor testing of pathologic breast cancer specimens in the 1970's - 1980's allowed clinicians to predict with 90% certainty which patients would respond to endocrine treatments. This development substantially reduced major surgical procedures in patients who had little chance of responding. The discovery that estrogen receptor blockade with the drug tamoxifen could achieve the same result as adrenalectomy and hypophysectomy in post-menopausal women led to another revolution in the care of patients with metastatic breast cancer. Tamoxifen and other estrogen receptor blocking agents, effectively replaced surgical hormonal ablative treatments in the last third of the 20th Century. The development of clinically useful blockers of the aromatase pathway of estrogen synthesis in the adrenals, as well as agonists to block pituitary stimulating hormones, made the possibility of total estrogen blockade by non-surgical methods a reality. Algorithms for the use of these agents in clinical situations will be presented, and the recent expansion of synthetic estrogen receptor modulators (SERMS) to be used in breast cancer prevention strategies will be discussed.

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