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Uterine pathology of Tamoxifen-treated Breast Cancer patients

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Abstract

Both Breast and Uterus are highly sensitive to hormonal influences, normally related to their reproductive functions. Due to abundant Receptors in their tissues, hormones are capable of eliciting profound changes of breast and uterine tissues, including neoplasms. Prevention and therapy of Breast and Endometrial Cancers using hormones as an adjuvant therapy is successful but challenging as there are side effects to be avoided. Tamoxifen (Tam) is a non-steroidal synthetic triethylene estrogen derivative used successfully in the adjuvant therapy and prophylaxis of breast cancer. It binds to Estrogen Receptors(ER) in a manner similar to estradiol inducing a binding of Tam-ER complexes to the nuclear DNA resulting in a decrease of available unbound ER, exerting an antagonistic, antiestrogenic effect on breast tissue. Its effect on the uterus is more complicated as Tam acts both as an antagonist and an agonist of Estrogen. In the uterus the agonist effect is manifested by endometrial polyps, hyperplasia, leiomyomas, adenomyosis and occasional neoplasia. In the largest study published so far, endometrial tissue (from biopsies and Hysterectomies) from 700 patients treated with Tam for Breast cancer, 64% showed normal cycling or inactive/atrophic endometrium ; 24% had endometrial benign polyps with cystic glandular and/or mild hyperplastic glands, displaying a different histologic pattern from endometrial polyps seen in patients not treated with Tam; in 4.7% of cases, frankly malignant changes were identified, the majority serous carcinoma of high grade, less than one third low grade endometrioid carcinoma. The malignant endometrial tissue was found in polyps, not associated with hyperplastic or atypical glands as it is most often seen in endometrioid carcinoma of patients not treated with Tam. Endometriosis carcinoma is the most common gynecological cancer in the USA and in most of the industrialized world; its relationship with hyperestrogenism is well established although the carcinogenic mechanism is not yet clarified. Many reports of individual cases of high grade endometrial cancer including very aggressive carcinosarcomas have also been reported in Tam treated patients. Endometrial cancers were seen more often in older patients, and in those treated for a longer duration. Despite these unfavorable side effects Tam is still used for its beneficial effect in preventing and treating breast cancer. Recently however it was established that Aromatase Inhibitors (A.I.) stop the production of estrogen in post-menopausal women by blocking the enzyme Aromatase which turns androgens to estrogens, resulting in a decrease of the available Estrogen to stimulate ER positive breast cancer cells. The use of A.I. is therefore less associated with estrogen-agonist side effects; it may however have other side effects such as cardiac anomalies and osteoporosis. Tam and A.I. are still both considered effective and may be used in the prevention and adjuvant therapy of Breast Cancer.

Biography

Liane DELIGDISCH was trained in Obstetrics-Gynecology and Pathology after her graduation from Medical School in Bucharest Romania, Trained at the Ichilov Hospital Tel Aviv Medical School, Magee Women's Hospital, Pitsdburgh, Pa, BostonFree Hospital for Women, Harvard Medical School. Founded the Division of Gynecologic Pathology and the course of Gynecologic Pathology at Mount Sinai Medical School where she is Professor of Pathology and Obstetrics-Gynecology since 1986. Editor and Author of 8 textbooks related to Gynecologic Pathology, Author of 152 articles in peer-reviewed medical journals. Elected Member of the French National Academy of Medicine since 2007.

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