Aromatase inhibitors induce ‘male pattern hair loss’ in women?

Female androgenetic alopecia (FAGA) is a common and distressing cause of hair loss, caused by androgens in genetically susceptible women [1, 2], in which dihydrotestosterone (DHT) binds to androgen receptors leading to miniaturization of scalp hair follicles [3]. FAGA, characterized by a specific diffuse loss of hair of the parietal or frontovertical regions (‘in the crown’), where 5α-reductase is expressed, maintains the frontal hairline, where aromatase is localized, with a uniform miniaturization of hair from centroparietal regions causing diffuse alopecia of oval form that is surrounded by a circular band of hair, with normal density [4, 5].

We studied 15 menopausal women aged from 50 to 60 years, with hormone receptor-positive breast cancer, between the ages 50 and 65 years, receiving aromatase inhibitors (AIs), anastrazole or letrozole, according to the American Society of Clinical Oncology guidelines. After 1 year of therapy, they had hair loss and were not subjected to any other therapies and currently they are still subjected to AIs therapy. We observed hair findings by Global photo and videodermoscopic assessment, after 12(T0) and 24 months (T24) of anastrazole therapy. Evaluation of alopecia was carried out for each patient, with a score (from −3 to +3), derived by a comparison of the global photos taken at the beginning (T0) and at T24 (20–70× Trichoscan Dermoscope FotoFinder®). Recession of the frontal and parietal hairlines and diffuse hair loss (Figure 1a and b) were observed. Miniaturization of follicles in the fronto-temporal area (Figure 1c) was revealed. Behind the scalp area sensible to aromatase, in the frontal region, the diameter of hair was normal without any alterations, with normal hair density (Figure 1d).

Aromatase (P450arom) is an enzyme located in outer root sheath, converting androstenedione to estrone and testosterone to estradiol, decreasing testosterone and DHT levels [2]. Levels of p-450arom in frontal and occipital follicles of women are...
higher than in frontal and occipital follicles of men [1]. Estrogens operate as potent hair growth modulators and as hair protective factors, so p-450arom has important protective function on frontal hair lines.

AIs, blocking the synthesis of estrogens, induce a relative enhancement in the activity of 5α-reductase. This enhancement leads to a relative increase in amount of testosterone available for conversion to DHT, causing a male pattern hair loss, mimicking a FAGA, which could be called ‘pseudo male pattern androgenetic alopecia’. In fact our patients presented recession of frontal and parietal hairlines, mimicking a typically FAGA with male patterns, which should not to be considered a real FAGA, but should be considered an alopecia induced by the drug.

We cannot label the clinical condition as a real FAGA, but we believe that it is a pseudo androgenetic alopecia with male pattern, because the clinical aspect is drug-induced, in fact patients observed, showed, bitemporal gulf recession without clinical signs of FAGA in central area.

We observed not many subjects but we corroborate data available in the literature about increased activity and clinical signs of FAGA in central area. Patients observed, showed, bitemporal gulf recession without alopecia induced by the drug.

Locoregional recurrence of early-stage surgically resected non-small-cell lung cancer: the importance of close follow-up and consistent definitions

Our group was greatly interested in reading the retrospective study by Lopez Guerra et al. which was recently published in the Annals of Oncology [1]. The authors’ discussion included one of our publications [2]. They stated that our rates of locoregional recurrence were higher than theirs or those previously reported in the literature (In fact, our 5-year rate of locoregional recurrence for patients with resected N1 disease was very similar to the rate reported by Higgins et al. (40%) [3]). However, there are several methodologic reasons why Lopez Guerra et al. may have found a much lower rate of recurrence than in our series.

First, the authors excluded patients who were alive, but who had less than 12 months of follow-up. Some of these patients may have had a locoregional recurrence before 12 months and then been lost to follow-up. The actuarial locoregional failure rate was about 20% in our population by one year, compared with 46% at 5 years (see our Figure 4).

Second, the authors defined local failure only as one occurring at the surgical resection margin. They excluded recurrences in the ipsilateral lung (whether within the same lobe for sub-lobar resection or remaining ipsilateral lung for lobectomy). Many lung tumors do not occur in the middle of a lobe, but near the fissures, chest wall and ipsilateral hilum. Tumors can easily spread by lymphatic vascular pathways or direct extension from these areas to other portions of the ipsilateral lung. Hence, we view such recurrences as resulting from a failure to adequately treat the primary site, which has implications for the extent of surgery as well as the use of postoperative radiotherapy. (It should be noted that Radiation Therapy Oncology Group also defines local recurrences to include any occurring within the ipsilateral lung.)

Finally, we feel that the authors should have assessed the impact of other factors on recurrence, such as patient co-morbidities (e.g., diabetes, the Charlson co-morbidity index) and more details of treatment (e.g., the type of chemotherapy, the extent of nodal dissection) [4], in addition to the usual histopathologic parameters. Their omission may have resulted in the relatively low predictive power of their ROC models for local (AUC 0.70) and regional recurrence (AUC 0.60).

In summary, there is still substantial uncertainty about the ultimate risk of locoregional relapse following potentially curative resection of non-small-cell lung cancers and the role of adjuvant therapy [4]. We encourage the use of standardized definitions of local recurrence [5], which may lead to a better