CLINICAL VIGNETTE

A Rare Side Effect of Aromatase Inhibitors

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Background

Breast cancer is the leading new cancer diagnosis, with approximately 245,000 cases in the United States in 2016.[1] Estrogen and its metabolites are associated in the pathogenesis of hormone receptor positive breast cancer, and hormone therapy plays a vital role.[2,3] Aromatase inhibitors are the treatment of choice in post-menopausal women with localized hormone sensitive breast cancer, and are generally well tolerated. Common adverse effects include menopausal symptoms including vaginal dryness, and hot flashes, muscle cramping, arthralgias, and an increased risk of osteoporosis and osteopenia.[4] Autoimmune hepatitis is a very rare adverse effect of anastrozole.[5-7] We report a case of autoimmune hepatitis related to anastrozole.

Case Report

A 59-year-old woman with no significant past medical history presented with a self-palpated right axillary breast lump. She underwent right diagnostic mammography and ultrasound which showed an irregular hypoechoic mass at 8 o'clock measuring 11 x 7 x 10 mm with 2 abnormal appearing axillary lymph nodes. Biopsy of the breast mass and one axillary lymph noded demonstrated invasive ductal carcinoma, Nottingham grade 3, ER 25%, PR1%, and HER2 IHC 3+, Ki67 70%. Staging PET/CT was negative for metastatic disease. Further evaluation with breast MRI confirmed a 20 x 12 x 16 mm right breast mass at 7 o'clock and confluent right axillary lymphadenopathy.

She received neoadjuvant chemotherapy with taxotere, carboplatin, trastuzumab, and pertuzumab for 6 cycles followed by lumpectomy and sentinel lymph node biopsy demonstrating a pathological complete response. Treatment course was complicated by port-associated deep venous thrombosis, which was treated with 3 months of therapeutic anticoagulation with rivaroxaban. She received adjuvant trastuzumab and pertuzumab and was started on anastrozole following her surgery. She also received adjuvant radiation to the right breast which was performed concurrently with adjuvant systemic therapy. Three months after starting anastrozole routine labs noted elevation of her AST and ALT from baseline normal to 357 and 311. Bilirubin and alkaline phosphatase remained normal. Anastrozole was held, abdominal ultrasound was normal, hepatitis serologies were negative, but ANA antibody returned positive at greater than 1:1280 in the centromere pattern. The remainder of the autoimmune testing was normal including dsDNA, nDNA, histone antibody, smooth muscle antibody, RNP, SSA, SSB, RF, Scl-70, and anti-CCP. Patient did not have rash, Raynauds, cardiopulmonary symptoms, GI symptoms, or sclerodactyly suggest concurrent or underlying autoimmune process. One week after discontinuation of anastrozole, the AST and ALT normalized. Repeat ANA antibody obtained 6 weeks after the initial ANA above remained positive with titer 1:1280. Her transaminases have remained normal off anastrozole, which was not re-started due to patient preference.

Conclusion

Aromatase inhibitors are widely used for post-menopausal women with localized hormone receptor positive breast cancer. Although usually well tolerated, rare side effects including autoimmune hepatitis have been reported. Previous cases report, onset of autoimmune hepatitis from 3 months to 9 months after initiation of therapy. They are associated with a high titer of antinuclear antibody, and resolves upon discontinuation of anastrozole. It is important for practitioners to be aware of this rare and potentially organ threatening side effect, and to have a low threshold to hold aromatase inhibitors while evaluating liver enzyme elevation.

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