

CLINICAL VIGNETTE

Tamoxifen and a Facial Rash

Maurice Berkowitz, M.D., and Karo Arzoo, M.D.

Case Presentation

The patient is a 56-year-old, premenopausal female with a past medical history significant for stage IIa (pT2N0) estrogen receptor positive, progesterone receptor positive, HER-2/neu not overexpressed breast cancer. The breast mass was initially noted on routine screening mammography and post confirmation of invasive ductal carcinoma, she underwent a lumpectomy with sentinel lymph node biopsy. She then underwent external beam radiation therapy to the breast. An OncotypeDx assay revealed a score of 17, in the low-risk range. She subsequently started on Tamoxifen 20mg daily.

Approximately six weeks after starting the tamoxifen, she developed a rash limited to her face (Figure 1). The lesions were described as erythematous tender nodules and not associated with fever, malaise, or other systemic symptoms. No pustules were noted. The tamoxifen was temporarily suspended and she was started on Keflex 500mg four times daily. One week later, the exanthem had resolved and the patient resumed the tamoxifen. Two weeks later the patient reported recurrent facial lesions (Figure 2). She was seen by dermatology and the skin findings were attributed to a drug allergy, but no biopsy was done. The tamoxifen was stopped permanently; the lesions resolved and never returned.

Discussion

Tamoxifen is an oral selective estrogen receptor modulator. Since 1977, it has continued to play a significant role in the management of estrogen or progesterone receptor positive ductal carcinoma in situ, early stage invasive cancer, locally advanced and metastatic breast cancers. It is also indicated for breast cancer prevention in certain populations.¹

Many side effects have been attributed to Tamoxifen. The most commonly reported side effects are hot flashes, fatigue, alopecia, and leg cramps with incidence greater than 10%. Current literature reports skin rash less than one percent of the time.¹ The rash described is variable and usually is a pruritic erythematous macular exanthem extends over the trunk and extremities.

In contrast, this patient's lesions are nodular and localized to both sides of her face. They clinically resemble Erythema nodosum (EN). Classically EN presents as an acute eruption characterized by erythematous tender circular nodules, usually 1-6 cm in diameter. The duration of the symptoms is usually

measured in weeks and the lesions resolve spontaneously without residual dermal consequences.

EN is the most common clinical form of panniculitis (inflammation of subcutaneous fat tissue) and is thought to be a hypersensitivity reaction that is associated with several systemic diseases or drug exposures. EN is usually limited to the extensor aspects of the lower legs, although other areas of involvement have been reported.² To date, there has been no direct association made between Tamoxifen and EN, although associations have been established between EN and estrogens, oral contraceptives and aromatase inhibitors.³ Tamoxifen has been shown to cause elevations in the levels of IFN- γ , and IL-2 and to decrease levels of IL-10, IL-1 and TNF- α . These cytokine changes are key inflammatory responses associated with the formation of EN.⁴

This patient likely had a limited form of EM and the lesions resolved upon discontinuation of the offending agent. No intervention was required and no lasting sequela were noted.

Figures

Figure 1.



Figure 2.



REFERENCES

1. Nolvadex (Tamoxifen Citrate) label. 9-27-2005. Wilmington, Delaware, AstraZeneca Pharmaceuticals LP
2. **Bock VL, Friedlander M, Waring D, Kossard S, Wood GK.** Cutaneous adverse effects of hormonal adjuvant therapy for breast cancer: a case of localized urticarial vasculitis following anastrozole therapy and a review of the literature. *Australas J Dermatol.* 2014 Nov;55(4):282-5. doi: 10.1111/ajd.12110. Epub 2013 Dec 2. Review. PubMed PMID: 24575835.
3. **Jhaveri K, Halperin P, Shin SJ, Vahdat L.** Erythema nodosum secondary to aromatase inhibitor use in breast cancer patients: case reports and review of the literature. *Breast Cancer Res Treat.* 2007 Dec;106(3):315-8. Epub 2007 Feb 15. PubMed PMID: 17972174.
4. **Chowaniec M, Starba A, Wiland P.** Erythema nodosum - review of the literature. *Reumatologia.* 2016;54(2):79-82. doi: 10.5114/reum.2016.60217. Epub 2016 Jun 3. Review. PubMed PMID: 27407284; PubMed Central PMCID: PMC4918048.

Submitted May 15, 2017