



Diffuse Vasculitis Marking the Recurrence of Breast Cancer: Case Report and Literature Review

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Abstract

Diffuse vasculitis involving all surface areas excluding the palms and soles started less than one year after the patient completed 5 years of adjuvant Arimidex for localized breast cancer. Extensive work ups by her Primary Care Physician and Dermatologist were nondiagnostic. She did not respond to oral or topical steroids and antihistamines. Dapsone was also ineffective. Biopsy of affected skin revealed a lymphocyte rich infiltrate with numerous neutrophils in and around blood vessels. Concern arose for a possible paraneoplastic process and a CT/PET was obtained. Adenopathy in the left axilla and right external iliac chain were observed. A biopsy of the left axillary node revealed metastatic breast cancer. Initiation of chemotherapy resulted in resolution of the vasculitis rash, but her cancer progressed in one left cervical node, left tonsil and was stable in the iliac node. The disconnect between response to treatment for breast cancer and the rash high lights the need for heightened level of surveillance for cancer response regardless of clearance of the paraneoplastic vasculitis.

Introduction

Paraneoplastic syndromes may occur before, simultaneously or after recognition of the cancer afflicting the patient. Vasculitis as a paraneoplastic syndrome is rare but most commonly occurs with hematologic malignancies. In one series only 16 patients out of 766 with cutaneous vasculitis were found to have an underlying cancer. Only 7 had solid tumors and only one breast cancer patient was found in this group [1]. Treatment of cancer even when successful does not ensure success in treatment of the paraneoplastic syndrome. The patient presented required PET scanning to detect recurrence of breast cancer. Skin metastases from breast cancer have been reported to be FDG avid [2]. Her vasculitis did not cloud the PET images with a diffuse background FDG uptake. The patient's breast cancer metastases were HER-2-neu overexpressing lesions whereas the original cancer did not overexpress HER-2-neu. The connection between her breast cancer recurrence and the vasculitis is not known.

Materials and Methods

The patient was 57 when she presented with a mammographically detected left infiltrating ductal carcinoma. She was compliant with regular mammograms since she had three first degree relatives with breast cancer. The cancer was a T2NOMO 7/9 strongly ER and PR cancer that did not overexpress HER-2 neu. The initial site of disease was in the nipple areola complex. A left mastectomy and sentinel lymph node biopsy were done. She had no complications. She received four cycles of TC followed by 5 years of adjuvant Arimidex. She had hot flashes and small joint arthralgias with the Arimidex. Her aromatase inhibitor side effects resolved rapidly after stopping the Arimidex. She then successfully underwent left breast reconstruction with a silicone-based implant. She had no complications. She was BRCA1 and 2 negative. However, she did undergo a prophylactic right simple mastectomy with silicone-implant reconstruction.

Less than one year after stopping her Arimidex she saw her primary care physician because of a diffuse red pruritic skin rash sparing her palms and soles (Figures 1-6). Its cause was refractory to extensive laboratory evaluation by her Primary Care Physician and her Dermatologist. Labs included CBC with differential, pathologist review of peripheral blood smear, CMP, ESR, CRP, LDH, RPR, Hepatitis serologies, SPEP, ANCA, C1 esterase inhibitor, anti-double stranded DNA, CEA, CA 15-3 and CA 27-29. An ANA was positive at 1:40. A biopsy of a lesion on her right leg revealed a lymphocyte predominant infiltration with numerous neutrophils in and around blood vessels. This was read as consistent with an urticarial rash.

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After a trial of avoiding detergents, deodorants and perfumes failed, she received a series of treatments. The rash did not improve with topical or oral steroids and dapsone was also not effective. The use of antihistamine, loratadine, alone or with these other treatments was also not effective.

CT scans were unrevealing. In view of the severity of the rash a CT/PET was obtained. Adenopathy was noted. An excisional biopsy of the left axillary node revealed recurrent breast cancer in the node with focal extracapsular spread. Biomarker testing revealed the node harbored infiltrating breast cancer identical to her primary except now the cancer was overexpressing HER-2-neu by FISH. The original tumor and the metastatic lesion were both 2+ by IHC.

Results and Discussion

At the time of initiation of her chemoimmunotherapy, trastuzumab, pertuzumab and paclitaxel, she was off all other treatments for her rash. After 2 cycles her rash completely resolved. After 6 cycles of chemoimmunotherapy she continued just combined anti-HER-2-neu immunotherapy. Repeat CT/PET revealed progression of disease with new metastases to the left tonsil, a left cervical node as well as persistence of her right iliac node met. Her rash has still not returned. The connection between her breast cancer and the vasculitis is not known. Perhaps soluble HER-2-neu released by her metastases caused a bystander effect when detected by her immune system setting off her vasculitis [3-10].

Conclusion

Paraneoplastic syndromes may run a clinical course completely different than the underlying malignancy. The underlying malignancy



Figure 1: Right upper extremity.



Figure 2: Face and lips.



Figure 3: Left knee.



Figure 4: Right arm on separate flare episode.



Figure 5: Right arm on separate flare episode.



Figure 6: Close up of Figure 5.

may be quite occult as in this case requiring repeated testing in order to identify its presence. In this case the vigorous vasculitis rash did not obscure PET scan identification of metastases. The role

of acquisition of HER-2-neu in the development of her vasculitis is not known but release of soluble HER-2-neu could have acted as an antigenic stimulus. It is not known if the vasculitis or very high level of soluble HER-2 reduced the efficacy of the treatment. Heightened vigilance is prudent when patients with a known cancer or a high risk of cancer present with vasculitis syndromes.

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