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Breast Cancer Patient with Widespread Metastases and en Cuirasse Presentation Refractory to Multiple Lines of Chemotherapy alone or with Anti-HER-2-neu Agents and Radiation Cleared Rapidly and Durably of all Skin Metastases by Intravenous Trastuzumab-Deruxtecan

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Abstract

62-year-old lady with Her-2-neu overexpressing ER/PR negative infiltrating ductal carcinoma with brain, bone, lung and skin metastases who failed multiple lines of treatment and electron beam radiation was finally able to clear painful, bleeding en cuirasse metastases with intravenous trastuzumab-deruxtecan.

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Introduction

In 4/2014 she was diagnosed with a T4a N3a M0 HER-2-neu overexpressing infiltrating ductal carcinoma of the left breast. She received adjuvant AC followed by TH and external beam radiation treatment.

Going forward lymphedema only notable adverse event. Recurrent disease detected 7/2016 in right breast with 6.3 cm mass. She received 4 cycles of TAC in Mexico. She did not complete recommended treatments and returned to the USA for ongoing care. Follow up MRI of right breast in 3/2017 confirmed refractory disease and she was started on THP. Right mastectomy done revealing T4b N1a M0 HER-2.neu overexpressing infiltrating ductal carcinoma. Treatment response in breast was a PR (6.3 cm to 3 cm). Follow up response to treatment imaging on January 25th, 2019 revealed one brain metastasis, lung metastases and metastasis to right kidney. Metastatic disease confirmed by lung biopsy. Skin biopsy January 30th, 2019 confirmed metastatic breast in diffuse skin presentation. Over the preceding 2 years multiple skin biopsies were non-diagnostic. Patient then started on Capecitabine and Herceptin. She frequently only took Capecitabine. Progressively worsening diffuse skin metastases noted December 31st, 2019. Skin metastases were not better in terms of size, number or symptoms of pain and bleeding, so carboplatin, gemcitabine and Herceptin was ordered 5/2020. Response in visceral sites was marginal but skin metastases progressed unabated. Topical 5-fluorouracil ointment was applied to skin lesions under an occlusive dressing but only a PR noted in terms or size and only a modest reduction in serosanguinous secretions. Electron beam radiation ordered in view of treatment failures. Skin metastases extended onto scalp, around entire neck, all of torso, left arm and forearm and below the inguinal folds on the right. Radiation controlled some of the torso-based lesions well but left arm and forearm metastases were not controlled.

Materials and Methods

Progression of skin metastases despite radiation treatment and progression of lung metastases were the primary reasons for staring trastuzumab-deruxtecan, 5.4 mg/kg IV over 90 min day 1 every 21 days. Marked improvement noted for all skin lesions after 2 cycles of trastuzumab-deruxtecan. Complete resolution of skin metastases and very good partial remission of visceral metastases were observed.

Inspection as a means of assessing patient response was quite fascicle since the lesions were raised, palpable, red and oozing serosanguinous fluids. Of note despite an almost 4-month hiatus from trastuzumab-deruxtecan caused by change in insurance the skin metastases did not recur.

Unfortunately, brain and lung metastases progressed off trastuzumab-deruxtecan. Resumption

of trastuzumab-deruxtecan maintained remission of skin metastases and caused ongoing partial regression of brain and lung metastases.

Results and Discussion

This is the first report of the successful use of trastuzumab-deruxtecan in breast cancer with the en cuirasse presentation [1,2]. The recent approval of this agent for HER-2-neu low expression breast cancer makes this agent more widely applicable for this difficult clinical scenario [3]. Intravenous drug was used but perhaps the subcutaneous version will prove superior. Inflammatory breast cancer would likely benefit from the upfront use of this agent. Future research should address these issues. It is not yet known why this drug was so effective when other anti HER-2 agents failed. Perhaps the efficacy rests in the unique structure of a chemotherapeutic agent linked to the anti-HER-2 antibody.

Additional observations of note include the concomitant occurrence of herpes zoster outbreak in the left T-10 dermatomal distribution. This occurred prior to use of trastuzumab-deruxtecan and electron beam radiation. The skin lesion of these co-occurrences of breast cancer skin metastases and shingles formed a trench like area of severe tissue atrophy in the left T-10 dermatome. Oral antibiotics were used when cellulitis was suspected based on marked increase in a single lesion's pain associated with erythema going beyond the visible nodularity or mucosa I disruption caused by the skin metastases.

About 65% of her body surface area was involved by breast cancer metastases with almost all lesions draining serosanguinous fluid. She experienced problems with feeling cold, volume depletion and the inability to cover this large area of open wounds so as to prevent soilage of her clothes and bedding. Her clothing would stick to her skin causing severe pain and bleeding when she changed clothes. Due to the COVID pandemic in home care was greatly limited. Her wounds were cleaned in clinic with sterile saline and then covered with a generous layer of triple antibiotic ointment. Sterile 4×4 gauzes were unfolded to maximum dimensions and applied over the layer of triple antibiotic. Saran wrap was applied over the sterile gauze layer thereby covering all areas involved. Tape was applied only to the wrap. For additional warmth disposable paper gowns were applied over the plastic wrap. Dressings were changed every 3 to 4 days. This provided her good symptom relief and excellent hygienic results. The cost of Vaseline gauze prohibited its use.

The patient was given topical potent steroid ointments by dermatology consultants prior to diagnosis of breast cancer skin metastases. She was being seen by these consultants due to her complaints of rash. Multiple skin biopsies during this time failed to demonstrate breast cancer skin metastases. While perhaps some decrease in pruritis occurred the use of high potency fluorinated topical steroids caused severe hyperglycemia with glucoses well over 400 mg/di. The use of these agents may have delayed clinical recognition of skin metastases as well (vide supra). While the patient voiced understanding and was agreeable to stopping their use in clinic she persisted in the use of these potent topical steroids at home. Her family confiscated all prescriptions of same resulting in a marked improvement in her glucose control. During this time period of severe hyperglycemia along with uncontrolled cutaneous metastases she developed Candida line sepsis. Again, these point out the need to avoid potent topical steroids for cutaneous metastases from breast cancer.

Last but not least, her left upper extremity lymphedema varied directly with the degree of skin metastases control. Therefore, controlling her cutaneous metastases profoundly improved her symptom burden from lymphedema.

Conclusion

En cuirasse presentations are very uncommon and difficult to control. A very new agent, trastuzumab-deruxtecan, provides a very welcome weapon in the control of difficult to treat presentation of breast cancer.

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