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CLINICAL CASE

Long-standing complete remission following mitomycin-C/vinblastine chemotherapy for cutaneous and lymph node metastases from breast cancer resistant to multiple chemotherapy and hormonal lines and extensive radiotherapy: an unusual case

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Summary

Widespread cutaneous and lymph nodes recurrence in breast cancer is regarded as therapy-resistant disease. We describe a 50-year-old patient who presented with treatment-refractory disease following multiple lines of chemo- and hormonotherapy, photodynamic therapy and radiotherapy, including re-irradiation to extended volumes of her chest, upper abdomen, back and regional lymph nodes. Following treatment with mitomycin-C (MMC)/vinblastine (VLB) alone, she entered sustained complete remission of 1-year duration without any side effects. A brief review of the current literature is also presented.

The MMC/VLB combination might achieve reasonable response and improvement of quality life even in patients with advanced breast cancer.

Key words: advanced breast cancer, complete remission, mitomycin-C, skin involvement, therapy resistant, vinblastine

Introduction

The role of treatment of advanced breast cancer following failure of multiple lines of chemo-, hormono- and radiotherapy is still palliative [1]. Visceral and widespread involvement of the skin and underlying soft tissues is regarded as end-stage disease and is largely therapy-resistant [2]. MMC is active in many solid tumors and has a cumulative response rate of 5-35% in refractory breast cancer, depending on patient characteristics, type of previous therapy and the dose schedule used [1,3]. Its major toxic side effect is delayed and cumulative myelotoxicity. VLB is a vinca alkaloid with a nearly 20% response rate in refractory breast cancer as single agent [1,3,4]. Several reports in the literature support the use of MMC and VLB in therapy-resistant advanced breast cancer. However, long-standing complete remission has not been reported so far.

We present a patient with therapy-resistant advanced breast cancer with massive cutaneous and lymph node involvement who achieved complete remission of her disease of 1-year duration following treatment with MMC/VLB combination chemotherapy.

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Case presentation

In 1991 a 38-year-old Caucasian female was diagnosed in Russia with right-sided breast cancer

(clinical stage unknown, probably T3 N2-3 M0). She was treated with preoperative radiation therapy to the breast (daily fraction and number of fractions: unknown; total dose: 4,400 cGy; Table 1), and lymphatic drainage, radical mastectomy, and 6 cycles of chemotherapy. Details concerning the chemotherapy schedule remain unclear.

The patient remained well until 1994 when a biopsy-proven scar recurrence was diagnosed. Metastatic work-up was negative; estrogen and progesterone receptors were positive and Her2/neu receptor was negative. She was treated with 6 cycles of CNF (cyclophosphamide, mitoxantrone, 5-fluorouracil; Table 2) and radiation therapy (Table 1), achieving complete remission which lasted until 1997 when massive cutaneous lesions in the right chest wall and nodal disease in both supraclavicular fossae appeared. These were treated with all available chemotherapeutic lines (Table 2), re-irradiation (Table 1) and various hormonal treatments (tamoxifen, megace, arimidex, aromasin). Various degrees of remission were achieved but never a complete response, and the patient absconded often due to bouts of depression, re-appearing only when her disease became symptomatic. As a last option, she was treated with photodynamic therapy (topical application of a photosensitizing agent to the skin lesions, followed by exposure to a specific wavelength of light that produces tumor-cell killing by reactive oxygen species) which resulted in near-complete disappearance of her skin lesions, albeit of brief duration.

When she represented a year ago, she was severely symptomatic, suffering from severe pain over her chest wall, itching, and recurrent cellulitis at multiple sites. On physical examination, she demonstrated massive skin nodules and diffuse extension of the underlying skin layers involving the right chest wall, upper abdomen bilaterally and right back, with hard lymphadenopathy on both sides of her neck and supraclavicular fossae. Metastatic work-up, including whole-body CT scan, bone scan, biochemical and hematological profile, and tumor markers, was negative.

She was started on VLB 6 mg every 3 weeks and MMC 12 mg every 6 weeks, both given bolus i.v. Marked regression of the disease was seen after 3 cycles of chemotherapy, with complete regression of all skin nodules and involved lymph nodes after 6 months of treatment. The patient is still on treatment, feeling well and showing no side effects.

Table 2. Details of chemotherapy

Date	*Regime*	*No. of cycles*
1991	Unknown[1]	6
1994	CNF[2]	6
1997	PE[3]	6
1998	Docetaxel[4]	6
2000	Oral VP-16 (etoposide)[5]	4
2001	5-FU/LCV/vinorelbine[6]	6
2001	Capecitabine[7]	8
2002	Doxorubicin[8]	5

[1]Adjuvant treatment following preoperative radiotherapy and right-sided radical mastectomy; [2]cyclophosphamide 500 mg/m^2 i.v.; mitoxantrone 12 mg/m^2 i.v.; 5-fluorouracil 500 mg/m^2 i.v. - every 3 weeks; [3]cisplatin 80 mg/m^2 i.v., day 1; etoposide (VP-16) 100 mg/m^2 i.v., days 1-3 - every 3 weeks; [4]100 mg/m^2 i.v. - every 3 weeks; [5]50/100 mg alternating daily for 3 weeks, one week break; [6]5-fluorouracil 500 mg/m^2 i.v.; leucovorin 200 mg/m^2 i.v., vinorelbine 25 mg/m^2 i.v. - days 1 and 8 (80% of total dose) - every 3 weeks; [7]1,250 mg/m^2 orally for 2 weeks, one week break, repeat; [8]60 mg/m^2 i.v. - every 3 weeks (75% of total dose due to heavy pre-treatment, cumulative dose of 225 mg/m^2)

Table 1. Details of radiation therapy

No.	*Date*	*Site of disease*	*Irradiated volume*	*Treatment facility*	*Total dose (cGy)*	*Daily fraction (cGy)*	*Number of fractions*
1.	05.1991	Right breast	Right breast + lymphatic drainage[1]	Unknown (most probably cobalt-60)	4,000	Unknown	Unknown
2.	1994	Scar recurrence	Right chest wall	9 MeV electrons	3,000	300	10
			Scar "boost"	6 MeV electrons	1,000	200	5
3.	1997	Right chest wall	Right chest wall	6 MeV electrons	3,960	180	22
		Right s/c[2]	Both s/c[2]	6 MV photons	3,960	180	22
		Left s/c[2]	Left s/c[2] ["boost"]	6 MV photons	1,080	180	6
4.	2002	Left neck, both s/c[2], upper abdomen, right-side back	Left neck + both s/c[2,3]	9 MeV electrons	2,600	200	13
			Abdomen bilaterally[3]	9 MeV electrons	2,000	200	10
			Right-side back	9 MeV electrons	2,600	200	10
				9 MeV electrons	2,600	200	13

[1]Treatment was given in Russia preoperatively. No other details are known; [2]s/c = supraclavicular fossa; [3]With 1.0 cm bolus

Discussion

MMC has been combined frequently with vinca alkaloids in metastatic breast cancer, based on *in vitro* studies suggesting synergy between these drugs, due to different mechanisms of action [1,2,5]. A wide range of response rates has been reported with the combination MMC/VBL as salvage therapy for metastatic breast cancer, which appears to be better than the response reported for the individual drugs used alone. A median time to progression of 6 months, including anthracycline- and taxane-resistant metastatic breast cancer and in soft-tissue metastases, has been reported [5-7]. However, to the best of our knowledge, this is the first documented case of a long-standing complete remission following failure to every known mode of hormono-, chemo- and radiotherapy.

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