The Breast Journal

LETTER TO THE EDITOR

Comprehensive Cryotherapy for Recurrent Breast Cancer with Distant Metastases after Failure of Radical Surgery

To the Editor:

Recurrent breast cancer with distant metastases is tradtionally considered a severe and incurable disease (1–3). In contrast, curative treatment is generally attempted for local recurrence (4). The 5-year overall survival (OS) after an isolated chest wall recurrence is 68% and that after an intra-breast recurrence is 81% (5). Conventional therapies can easily be implemented synchronously with cryoablation with fewer side effects when used in the treatment of malignant breast tumors, primarily, early-stage tumors (6). For the effective prevention of local recurrence and metastases of breast cancer, many immunologic methods have been studied (7). These methods can improve physical and immune function in patients, without causing any obvious side effects and are sustainable in the long term.

Between September 2005 and October 2012, 64 patients who were treated in Guangzhou Fuda Cancer Hospital met the restrict inclusion criteria and were enrolled in this study (8,9). All the study patients had received various therapies in different medical centers before the local tumor recurrence and metastases were found at the same time, and our treatment program determined the OS of these patients. Skillful cryosurgery and strict patient selection can effectively prevent the occurrence of severe complications (e.g., liver rupture and failure, respiratory failure and pathological fracture) and reduce the probability of side effects (e.g., hemorrhage at the cryoablation site, thrombocytopenia, nerve damage, hemoptysis, ecchymosis and hematoma, and pain and tenderness at the ablation site). Since most side effects resolved within 2 weeks, either spontaneously or after symptomatic treatment, our comprehensive cryotherapy protocol was considered to be safe during the follow-up period.

We retrospectively assessed the effects of cryotherapy protocols for this cancer. We divided 64 patients who had undergone radical surgery into the comprehensive cryotherapy (35 patients, cryoablation for both recurrence and metastases), recurrence cryotherapy (11 patients), and chemotherapy (18 patients) groups. In the comprehensive cryotherapy group, 17 patients received multiple treatments, while 18 patients were treated only once. In addition, 25 of these patients received comprehensive cryotherapy immediately and 10 patients first received chemotherapy in other centers and underwent cryoablation in our hospital 3 months later. Median OS was significantly longer in the comprehensive cryotherapy group (59 months) than in the recurrence cryotherapy group (22 months, $p < 0.01$) or the chemotherapy group (27.5 months, $p < 0.001$). In the comprehensive cryotherapy group, longer median OS was associated with multiple (58 months) rather than single (34.5 months) treatments ($p = 0.0001$) and timely (55 months) rather than delayed (31 months) treatments ($p = 0.0079$). The median OS was significantly longer after cryo-immunotherapy (58 months) than after chemo-cryotherapy (31.5 months; $p < 0.001$), cryotherapy alone (39.5 months; $p < 0.01$) and chemotherapy (27.5 months; $p < 0.001$).

With advances in breast cancer research, systemic therapy combined with local treatment has gradually become widely used. As circulating tumor cells are present in the blood in 95% of patients with operable breast cancer (10,11), it appears that conventional radical surgery is merely a cytoreductive treatment, curative treatment is possible if surgical resection is combined with augmentation of natural immunologic defenses (12) and/or chemotherapy (13). Therefore, the effect of local therapy on survival must be considered in the context of systemic therapy. Regular physical examination and timely reduction of the tumor

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load are crucial, which can control the whole body tumor burden in a smaller scale. After cryoablation, numerous breast cancer-associated antigens are gradually released into the blood over a period of a few months, and these antigens act as *in vivo* targets that activate DCs (14). In our study, the survival time after chemo-cryotherapy was lower than that after cryo-immunotherapy. Two major explanations may exist for this observation: first, all cancer cells eventually become resistant to chemotherapeutic agents, resulting in decreased overall sensitivity to chemotherapy over time, and second, a rare subpopulation of cells with tumorigenic potential is resistant to therapy right from the beginning of treatment (15). In summary, we have retrospectively analyzed the therapeutic effects of percutaneous comprehensive cryotherapy for local recurrence and metastases after the failure of radical surgery and obtained significantly better results than chemotherapy in terms of OS. We recommend timely and multiple sessions of cryo-immunotherapy for these patients.

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